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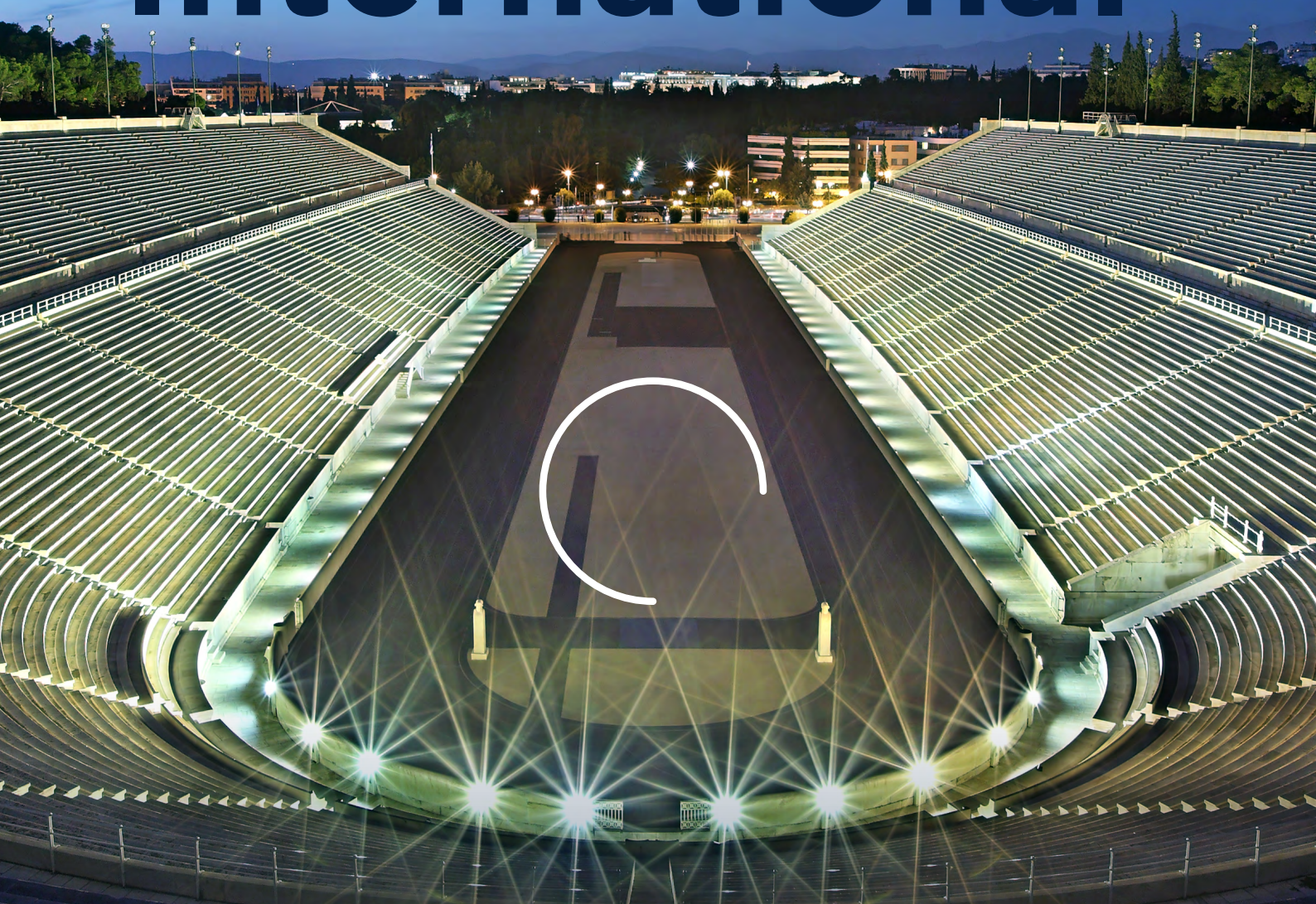

21st Congress of the European Society for Organ Transplantation

17 September - 20 September 2023. Athens, Greece

esotcongress.org

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About the European Society for Organ Transplantation

The European Society for Organ Transplantation (ESOT) was founded nearly 40 years ago and has been dedicated to pursuing excellence in organ transplantation ever since.

Facilitating a wealth of international clinical trials and research collaborations over the years, ESOT remains committed to its primary aim of improving patient outcomes in transplantation.

With a community of transplant professionals from around the world, ESOT is an influential international organisation and the facilitator of the biennial ESOT Congress. ESOT attracts the foremost transplantation experts to work in its committees and sections. It has an impressive track record in supporting research, extensive education and promoting changes in European policy.

Our Mission

To improve outcomes for patients with terminal organ disease through transplantation, organ regeneration and substitution.

Our Vision

To promote sustainable scientific advancement through multidisciplinary communities of healthcare professionals

To deliver first-class education, training and career advancement opportunities to all healthcare professionals, with specific training programmes for low-income countries

To work with partner organisations, professional bodies and competent authorities to improve public and institutional awareness of the latest research in the field

To develop and promote policies for equitable access to transplantation and related therapeutic strategies

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ESOT LEONARDO DA VINCI TRANSPLANT RESEARCH INNOVATION AWARD

LDV1 BCL-6 INHIBITORS POTENTLY INHIBIT ALLOGENEIC T CELL ACTIVATION - A NOVEL MECHANISM OF IMMUNOSUPPRESSION?

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Background: Bcl6 is a key transcription factor regulating T cell fate. We explored the potential of novel Bcl6 inhibitors (Bcl6i) as immunosuppressants in transplantation.
Methods: First, we determined Bcl6 expression in T cells in KTx biopsies (10 TCMR, 10 non-rejection) using multiplex immunofluorescence ISH. To test the effects and mechanism of Bcl6i on T cell activation, we performed mixed lymphocyte reactions (MLR) using healthy donor PBMC. Briefly, CFSE-labeled responder PBMC, or sorted CD4+ naïve (Tn), central (Tcm) or effector (Tem) memory T cells were cocultured with irradiated third party stimulator PBMC in the presence of different Bcl6i (79.6 or FX1), the Bcl6 degrader BI-3802, and the vehicle control. After 5 days, CD4 and CD8 T cell proliferation and expression of cytokines, granzyme B and perforin were measured. In addition, we tested Bcl6i action in PBMC from KTx patients with (n=9) and without rejection (n=7).
Results: Indeed, we found pronounced Bcl6 expression in T cells during TCMR. Next, we studied the immunosuppressive effects of Bcl6i, which potently inhibited proliferation and function (IFN-γ, GrB, Perf) of CD4 and CD8 T cells compared to vehicle (max. 90% inhibition) without affecting viability. This appeared to be a class effect, since FX1, 79.6 and BI-3802 showed similar effects. Bcl6i interfered with early (d0-3) rather than late (d4-6) activation and Tn, Tcm and Tem were equally inhibited by Bcl6i. Q-PCR gene expression analysis indicated that Bcl6i affected T cell fate, since canonical Th subset markers were differentially regulated (up: GATA3, IL-4; down: IFN-γ, IL-17, IL-21), while the T cell factor Tcf-1 and inhibitory receptor TIGIT were upregulated. To test whether alloreactive T cells from KTx patients would also respond to Bcl6i and be more responsive during rejection, KTx patients' PBMC were stimulated with donor cells. T cells from rejecting patients showed increased proliferation, Tcm and Tem subsets and cytokine (IFN-γ, IL-2) expression than those from non-rejecting patients, but these parameters were significantly reduced by Bcl6i
Conclusions: We found that Bcl6i potently inhibit the proliferation and function of T cells, especially during rejection. Since Bcl6 is markedly expressed by T cells during rejection, Bcl6i may have potential as novel immunosuppressants.

LDV2 ENGINEERED T CELLS OVERCOMING REJECTION BY ANTIBODIES (CORA-T CELLS): SELECTIVE TARGETING OF ALLOREACTIVE B CELLS IN SOLID ORGAN TRANSPLANTATION

Anna Christina Dragon*[1], Agnes Bonifacius[1], Stefan Lienenklaus[2], Murielle Verboom[1], Richard Taubert[3], Fabio Ius[4], Michael Hudecek[5], Constanca Ferreira de Figueiredo[1], Rainer Blasczyk[1], Britta Eiz-Vesper[1]

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Background: One major complication after solid organ transplantation (SOT) is antibody-mediated rejection (AMR) by anti-donor HLA antibodies as the B-cell alloimmune response is only indirectly affected by modern immunosuppression. Unselective B-cell depletion protocols are inefficient in preventing AMR and associated with an increased infection risk, emphasizing the need for a more precise targeting of alloreactive B cells.
Methods: B cells with anti-donor HLA specificity are uniquely characterized by expressing the corresponding B-cell receptors (BCRs). Using BCRs against a distinct HLA molecule as target, we redirected T cells towards alloreactive B cells by introducing a novel chimeric receptor comprising the respective HLA molecule fused to intracellular 4-1BB/CD3ξ signalling domains to generate T cells overcoming rejection by antibodies (CORA-T cells). CORA-T cells harbouring a receptor with an extracellular truncated HLA-A*02 molecule were further modified to abrogate CD8 binding and confer resistance to immunosuppression. Their ability to recognize and selectively eliminate anti-HLA-A*02 B cells to limit antibody release was tested *in vitro* as well as *in vivo*.
Results: Upon co-cultivation with B-cell lines expressing and releasing anti-HLA-A*02 antibodies, CORA-T cells were specifically activated (expression of CD25, CD69, CD137), released pro-inflammatory cytokines (e.g. IFN-γ, granzyme B), and exhibited strong cytotoxicity resulting in an effective reduction of the anti-HLA-A*02 antibody release. In a xenograft mouse model, CORA-T cells significantly reduced growth of anti-HLA-A*02 B cells. Modification of the HLA-A*02 α3-domain abrogated T-cell sensitization against the CORA receptor. Additionally, CRISPR/Cas9-mediated knockouts of selected binding proteins endowed CORA-T cells with the ability to resist immunosuppressive treatment.
Conclusions: Our results demonstrate that CORA-T cells are able to specifically recognize and eliminate alloreactive B cells, having the potential to selectively prevent the formation of anti-HLA antibodies even under immunosuppressive conditions. This suggests CORA-T cells as a potent novel approach to specifically combat AMR and to improve long-term graft survival in SOT patients while preserving their overall B-cell immunity.

LDV3 COMBINATION OF TCR-DEFICIENT CAR-TREGS AND ANTI-CD3 MONOCLONAL ANTIBODIES TO PROMOTE TRANSPLANT TOLERANCE

Tifanie Blein[1], Akshay Joshi[2], Soeli Charbonnier[1], Nicolas Ayas[3], Lucas Rabaux[2], Baptiste Lamarthée[2], Julien Zuber*[3]

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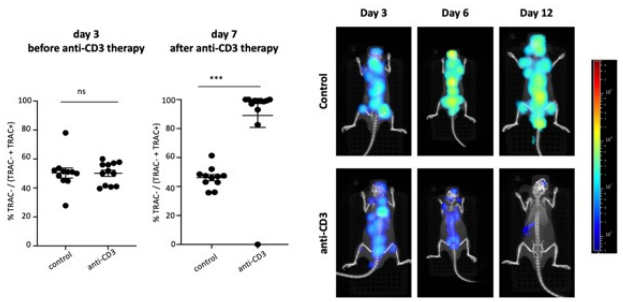
Background: Solid organ transplantation remains the best therapeutic option for life-threatening organ failure, yet is associated with severe complications inherent to life-long immunosuppressive regimen. In this respect, CAR-Treg therapy is a very promising strategy to get rid of immunosuppressive drugs through the induction and maintenance of transplant tolerance. We are developing a powerful tolerogenic strategy, meant to debulk alloreactive T cells, while tipping the balance toward donor-specific CAR-Tregs. We hypothesize that *T Cell Receptor Alpha Constant* (*TRAC*)-deleted CAR-Tregs would act synergistically with anti-CD3 therapy.
Methods: *TRAC*-deficient HLA-A2-targeted CAR Tregs were manufactured through subsequent lentiviral transduction and Crispr-Cas 9 gene editing over 7 days of culture. For the *in vivo* model, NSG mice were intravenously injected with HLA-A2+ peripheral blood cells at day 0 and then with a mix of two populations of HLA A2-targeted CAR-T, either mCherry+ Luciferase+ TRAC+ or GFP+ TRAC-, cotransferred at a 1:1 ratio, the following day.
Results: We first confirmed that *TRAC*-deficient T cells lost surface CD3 expression. We next established the ability to stimulate CAR-Tregs, as assessed by CD25, 4-1BB and HLA-DR expression, in a HLA A2-specific manner, irrespective of the presence of TCR. Notably, hallmark Treg markers, including FOXP3 and HELIOS, were maintained regardless the disruption or not of the *TRAC* gene. In order to evaluate the selective *in vivo* deletion of *TRAC*-sufficient CAR-T cells, we administered a mix of TRAC-sufficient and TRAC-deficient HLA A2-targeted CAR-T cells, along with HLA A2+ PBMCs into NSG mice. Strikingly, TRAC+ cells, unlike their TRAC- counterparts, were wiped out from the blood upon anti-CD3. Moreover, bioluminescent cell tracking showed a dramatic reduction of TRAC+ cells in the lymphoid organs of animals treated with anti-CD3 vs saline solution (Figure). We are currently exploring the tolerogenic potential of this Combo strategy in skin and islet transplantation models in humanized mice.
Conclusions: Together, our data show that anti-CD3 therapy can provide an *in vivo* life-advantage to TRAC-deficient CAR-Treg cells, over resident TRAC-sufficient T cells. This combo strategy will reduce the number of CAR-Tregs needed to produce a cell product.



ESOT LEONARDO DA VINCI TRANSPLANT RESEARCH INNOVATION AWARD

LDV4 RECIPIENT FCγR3A POLYMORPHISM INFLUENCES THE PROGNOSIS OF AMR AND THE RESPONSE TO IVIG IN RENAL TRANSPLANTATION

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Background: Antibody-mediated rejection (AMR) is the first cause of kidney graft failure but its heterogeneous prognosis makes difficult to assess the risk of graft loss and to choose a therapeutic strategy at the time of diagnosis.
The binding of anti-donor antibodies (DSA) to the surface of graft endothelial cells induces the recruitment of innate immune effectors via their Fcγ receptors (depending on the cell type: FcγR2A, FcγR2B, FcγR2C, FcγR3A and FcγR3B), for which many SNPs modulating their affinity for IgG Fc have been described. The aim of this ranslational study was to determine which polymorphism(s) in recipient FcγRs were associated with poor prognosis at the diagnosis of AMR and the possible therapeutic consequences.
Methods and Results: Among 1682 kidney transplant recipients at Lyon University Hospital who underwent graft biopsy between 2004 and 2017, 135 (8%) were diagnosed with AMR. Of the 5 functional FcγR polymorphisms described in the literature, only Fcγ RIIIa*559A>C (rs396991; p=0.005) was statistically associated with graft survival. Global and single-cell transcriptomic analyses of AMR biopsies demonstrated that non-classical monocytes and NKs are the only innate effectors expressing FcγR3A. In vitro cocultures between these human purified innate effectors and allogeneic endothelial cells covered with DSA confirmed that effector cells with high-affinity FcγR3A i) activated more strongly and caused more damage to target, but ii) that these same effectors were also more effectively controlled by the addition of IVIg in the culture medium. The latter in vitro therapeutic results were confirmed in a second independent clinical cohort of kidney transplant patients treated with IVIg.
Conclusions: Our work demonstrates that a single functional polymorphism of FcγR3A influences the severity of AMR and suggests that patients at high risk are also those who respond the best to IVIg treatment.

LDV5 CLINICAL VALIDATION OF AUTOMATED URINARY CHEMOKINE ASSAYS FOR NON-INVASIVE DETECTION OF KIDNEY TRANSPLANT REJECTION: A PROSPECTIVE COHORT STUDY

Elisabet Van Loon*[1], Claire Tinel[2;3], Xavier Bossuyt[1], Jasper Callemeyn[1], Maarten Coemans[1], Priyanka Koshy[1], Dirk Kuypers[1], Amaryllis Van Craenenbroeck[1], Dany Anglicheau[4], Maarten Naesens[1]

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Background: Non-invasive diagnostic markers for kidney transplant rejection can provide useful information, but often do not reach the stage of clinical implementation. Previous studies have demonstrated the diagnostic potential of the urinary chemokines CXCL9 and CXCL10 for rejection. However, before clinical application can begin, the relationship with rejection subtypes and clinical confounders, the context of use, and the added benefit of these markers must be demonstrated.
Methods: In this single-center prospective cohort study, we analyzed 1559 biopsy-paired urinary samples from 622 kidney transplants performed between April 2013 and July 2019. We quantified urinary CXCL9 and CXCL10 using an automated immuno-assay platform and normalized the values to urinary creatinine.
Results: Here we show that urinary chemokines, integrated in a multivariable model with routine clinical markers (eGFR, donor-specific antibodies and polyoma viremia) had high diagnostic value for detection of acute rejection (N=150) (ROCAUC 81.3%, 95% CI 77.6-85.0). With the integrated score, 59 protocol biopsies per 100 patients could be safely avoided when the risk of rejection was predicted to be lower than 10%. The diagnostic performance of urinary chemokines further improved when molecular rejection was taken into account compared to Banff histological rejection. Performance of the integrated model was validated externally (independent validation cohort, N=986 samples).
Conclusions: Our results demonstrate that an integrated score of urine chemokines and clinical markers allows for non-invasive monitoring of rejection and can significantly reduce the number of unnecessary biopsies from kidney transplantation. We expect this study to pave the way for the eventual implementation of urine chemokines as a noninvasive diagnostic tool for rejection in routine clinical follow-up after kidney transplantation.

LDV6 RACE-FREE EGFR EQUATION IN KIDNEY RECIPIENTS: A DEVELOPMENT AND VALIDATION STUDY

Marc Raynaud*[1], Solaf Alawadhi[1], Ivana Juric[1], Gillian Divard[1], Yannis Lombardi[1], Nikolina Basic-Jukic[1], Olivier Aubert[1], Laurence Dubourg[1], Ingrid Masson[1], Christophe Mariat[1], Dominique Prié[1], Vincent Pernin[1], Timothy Larson[1], Mark Stegall[1], Boris Bikbov[1], Piero Ruggenenti[1], Laurent Mesnard[1], Arthur Matas[1], Brian Nankivell[1], Stephan Bakker[1], Christophe Legendre[1], Nassim Kamar[1], Flavio Vincenti[1], Giuseppe Remuzzi[1], Andrew Bentall[1;2], Carmen Lefaucheur[1], Alexandre Loupy[1]

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Background: We aimed to assess the performances of the current eGFR equations, including the race-free CKD-EPI-2021 equation, in the kidney transplant population, and compare these performances to those of a race-free kidney-recipient-specific (KRS) GFR equation.
Methods: We included adult kidney recipients transplanted between 01/01/2000 and 01/01/2021 in 17 academic cohorts in Europe, the USA and Australia comprising 14 transplant centres and three clinical trials (NCT05229939). Measured GFRs (mGFR) were assessed using ^{51}Cr-EDTA, ^{99}Tc-DTPA, inulin, iothalamate or iohexol clearance, according to the local practice. A KRS GFR equation was developed using additive and multiplicative stepwise linear regressions and its performance was compared to those of the current GFR equations. The performances were assessed with the P_{30} and the correct classification of chronic kidney disease (CKD) stage metrics.
Results: The study included 15 489 patients, having 50 464 GFR values both measured and estimated by creatinine-based equations. Among the current GFR equations, race-free CKD-EPI-2021 equation showed the lowest performance compared with MDRD and CKD-EPI-2009 equations. We then built a race-free KRS GFR equation based on an additive model including creatinine, age, and sex. We showed that using race did not increase the performance of the equation. We found that the race-free KRS GFR equation showed significantly improved performance compared with the race-free CKD-EPI-2021 equation and performed well in the external validation cohorts (P_{30} ranging from 73.0% to 91.3%). Finally, we showed that the race-free KRS GFR equation performed well in a series of kidney transplant recipient subpopulations stratified by race, sex, age, body mass index, donor type, therapeutics, creatinine and GFR measurement methods and timing. Based on these results we developed an online application that estimates GFR based on recipient's age, sex and creatinine : https://transplant-prediction-system.shinyapps.io/eGFR_equation_KTX/
Conclusions: Using multiple, international cohorts of kidney recipients, we developed and validated a new race-free KRS GFR equation that demonstrated high accuracy and outperformed the race-free CKD-EPI-2021 equation developed in individuals with native kidneys.

LDV7 DONOR-DERIVED CELL FREE DNA AS A SURVEILLANCE TOOL FOR ACUTE CELLULAR REJECTION IN HEART TRANSPLANTATION: RESULTS FROM THE FREE-DNA CAR STUDY

Marta Jimenez-Blanco*[1], María Generosa Crespo-Leiro[2], Dolores García Cosío[3], Raquel López-Vilella[4], Carlos Ortiz Bautista[5], Marta Farrero[6], Alba Maestro[7], Beatriz Diaz Molina[8], Carles Diez Lopez[9], Diego Rangel Sousa[10], Nahikari Salterain Gonzalez[11], Iris Garrido[12], Sara Lozano Jimenez[1], Javier Segovia Cubero[1]

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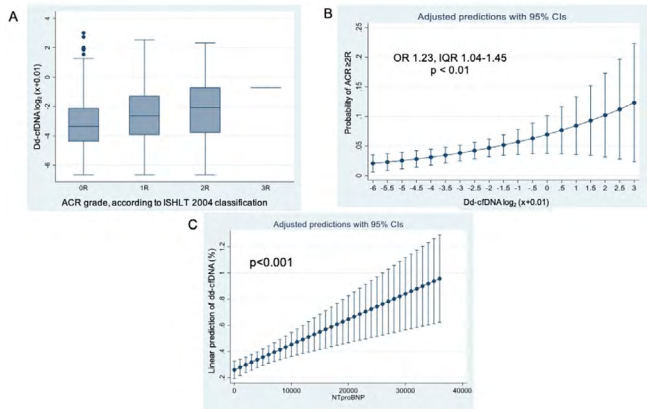
Background: There is growing interest in the potential utility of donor-derived cell-free DNA (dd-cfDNA) as a non-invasive biomarker for surveillance of acute cellular rejection (ACR) in heart transplant (HT) recipients, thus allowing avoidance of repeated endomyocardial biopsies (EMB).
Methods: Prospective, multicenter study performed between 2019 and 2022 (NCT 04973943). All patients underwent surveillance EMB at 0.5, 1, 2, 3, 4, 6 and 12 months post-HT. Dd-cfDNA levels were determined prior to each EMB, using Next Generation Sequencing technology (Allonext® assay, Eurofins Genome). The primary end-point was the association between dd-cfDNA levels and the presence of ACR (defined as grade ≥2R) in EMB. The correlation between dd-cfDNA and NTproBNP levels was also studied.
Results: A total of 206 patients from 12 HT centers were included (mean age 54 ± 11 years, 73% male). We analyze here the first 848 pairs of EMB and dd-cfDNA determinations. ACR was present in 35 EMB (4.1%) and AMR ≥1 in

14 EMB (1.7%). Median (IQR) dd-cfDNA values for each ACR group were: 0R 0.088% (0.038-0.22), 1R 0.15% (0.056-0.4), 2R 0.23% (0.06-0.6) and 3R 0.6% (Figure 1A, with %dd-cfDNA logtransformed as log2(x+0.01) in order to reduce the skewness). AMR0 and AMR ≥1 median values were 0.1% (0.04-0.24) and 0.2% (0.075-0.7), respectively. Using GEE (generalized estimating equation) models, a significant association between %dd-cfDNA and ACR ≥2R was found (OR 1.23, IQR 1.04-1.45, p <0.01) (Figure 1B). A 0.15% dd-cfDNA threshold showed a negative predictive value of 97%.Median (IQR) NTproBNP values for each ACR group were: 0R 1100 pg/ml (450-2580), 1R 1367 pg/ml (588-3298), 2R 2401 pg/ml (1115-6680) and 3R 4740 pg/ml. A statistically significant correlation between both biomarkers was found (GEE model shown in Figure 1C), with a coefficient of 0.002 ± 0.0006, meaning that for every increase of 100 units of NTproBNP, %dd-cfDNA increased in 0.002 (p <0.001).

Conclusions: Dd-cfDNA appears to be an excellent biomarker to rule out ACR, and shows a good correlation with NTproBNP levels. Further studies are needed in order to determine if the combination of both biomarkers could improve individual performance and increase the number of EMB that may be safely avoided.



LDV8 LONG-TERM OUTCOMES AFTER HYPOTHERMIC OXYGENATED MACHINE PERFUSION (HOPE) AND TRANSPLANTATION OF 1291 DONOR LIVERS USING REAL-WORLD DATA

Janina Eden[*1], **Isabel M.A. Brüggenwirth[2], Gabriela A. Berlakovich[3], Bettina Buchholz[4], Florin Botea[5], Stefania Camagni[6], Matteo Cescon[7], Umberto Cillo[8], Luciano De Carlis[9], Riccardo De Carlis[9], Fabio Colli[10], Fabrizio Di Benedetto[11], Jule Dingfelder[3], Dulce Diogo[12], Daniele Dondossola[13], Jiri Fronek[14], Giuliana Germinario[7], Enrico Gringeri[8], Georg Gyoeri[3], Matej Kocik[14], Efrayim Küçükerbil[15], Hwai-Ding Lam[16], Georg Lurje[17], Paolo Magistri[11], Diethard Monbaliu[18], Damiano Patrono[10], Wojciech Polak[15], Michel Rayar[19], Matteo Ravaioli[7], Renato Romagnoli[10], Gustaf Sörensen[20], Deniz Uluk[17], Andrea Schlegel[1], Robert J. Porte[15], Philipp Dutkowski[1], Vincent E. de Meijer[2]**

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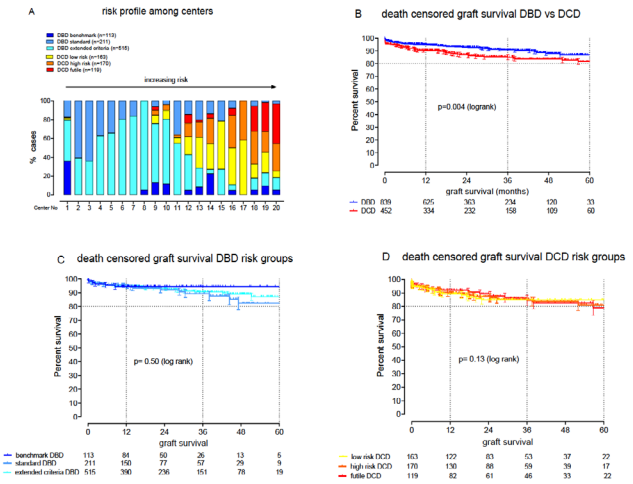
Background: Benefits of hypothermic oxygenated perfusion (HOPE) over cold storage of donor livers on short-term outcomes after transplantation have been confirmed by several randomized controlled trials. According to the IDEAL-D (Idea, Development, Exploration, Assessment, Long-term study-Framework for Devices), scientific evidence for HOPE has currently reached stage 3. We aimed to assess outcomes after transplantation of donor livers preserved by HOPE based on real-world data (IDEAL-D stage 4).

Methods: In this international, multicenter, observational cohort study, we included adult recipients of a HOPE-preserved liver transplanted between January 2012 and December 2021. Analyses were stratified for donation after brain death (DBD) and circulatory death (DCD) liver grafts. DBD grafts were classified as benchmark (primary transplant, lab MELD<20, BAR-score<9), standard, or extended criteria (ECD, according to EASL). DCD livers were classified according to the UK-DCD-risk score as low-risk (0-5 points), high-risk (6-10 points), or futile (>10 points). The primary study outcome was death-censored graft survival. Secondary outcomes included the incidence of primary non-function (PNF) and ischemic cholangiopathy (IC).

Results: We included 1291 transplantations (65% DBD) performed at 20 centers, with a median follow-up of 23 (IQR:13-42) months. For DBD, a total of 113 benchmark (13%), 211 standard (25%), and 515 ECD (61%) cases were recorded. For DCD, 163 transplants were classified as low-risk (36%), 170 as high-risk (38%), and 119 as futile (26%), with significant risk profile variations among centers (**Fig. 1A**). Actuarial 1-, 3-, and 5 year graft survival for DBD and DCD was 95%, 91% and 87% vs. 90%, 85% and 80%, respectively (Logrank p=0.004; **Fig. 1B**). Within DBD and DCD strata, graft survival was similar among risk groups (Logrank p=0.50; **Fig. 1C**, p=0.13; **Fig. 1D**). Graft loss due to PNF or IC was 3% and 0.7% (DBD), and 5.1% and 5.8% (DCD).

Conclusions: This study shows excellent 5 year graft survival after transplantation of HOPE-treated DBD and DCD livers with low rates of graft loss due to PNF or IC, despite considerably high rates of ECD DBD and high-risk/futile DCD grafts. HOPE-treatment has now reached IDEAL-D stage 4, which further supports implementation of HOPE in routine clinical practice.



FULL ORALS

Translational immunology of rejection

OS1_1 TOWARDS DECIPHERING HLA IMMUNOGENICITY - ONE STEP FORWARD

Chelsea Maguire[1], **Pietro Crivello[2], Sebastiaan Heidt[3], Vasilis Kosmoliaptsis[4], Anat Tambur*[1]**

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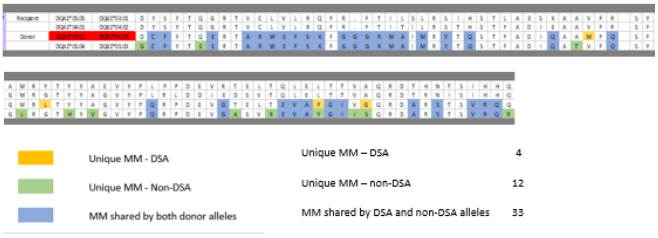
Background: Development of de-novo HLA-donor-specific-antibody (dnDSA) posttransplant is associated with increased risk for rejection and poor allograft outcome. Molecular Mismatch Load (MML) analysis was proposed as means to predict risk to develop dnDSA, yet some patients develop dnDSA despite low MML, whereas others, with high MML, do not develop dnDSA for many years. We used alternative approaches to gain insight into HLA immunogenicity.
Methods: 239 kidney transplant recipients from our center and 460 patients from the International Histocompatibility Epitope Working-Group, with high resolution HLA typing and HLA antibody testing data, were enrolled. CRISPR/Cas9 site directed mutagenesis and human HLA-DQ monoclonal antibodies were used for adsorption/elution (ad/elu) studies. Electrostatic Mismatch Score 3D (EMS3D) evaluation and Molecular Evolutionary Genetic Analysis (MEGA) were performed.
Results: About 25% of the two cohorts consisted of patients who received donor organs with 2 HLA-DQ mismatches but with dnDSA development only against one of the mismatches (2MM1DSA). Analysis of this unique patient group demonstrated almost complete segregation of the HLA-DQ heterodimers into high/low immunogenicity groups; validated also in the larger cohorts. Evaluation of molecular mismatches in the 2MM1DSA cohort further demonstrated that not all molecular mismatches contribute equally to formation of dnDSA (Fig1). CRISPR/Cas9 mutated cells and ad/elu studies using human HLA-DQ monoclonal antibodies and sera from sensitized patients demonstrated that eplet ("functional epitope") assignment does not necessarily correlate with antibody/epitope reactivity. EMS analysis emphasized contribution of the HLA-DQα to the overall DQ-heterodimer. Finally, MEGA substantiated the evolutionary difference between the higher and lower immunogenicity barriers between different HLA-DQ alleles.
Conclusions: Increased immunogenicity is not a consequence of increased MML, and eplets should not be considered "functional epitopes". Increased immunogenicity is likely a consequence of increased evolutionary divergence. Functional studies understanding the immunobiology of allorecognition are required to decipher immunogenicity to improve transplant outcome.



Total mismatched with DSA allele – 37, but only 4 mismatches are unique to the DSA

OS1_2 SOLVENT-ACCESSIBLE AMINO ACID MISMATCHES ON DONOR HLA ARE ASSOCIATED WITH KIDNEY GRAFT OUTCOMES; A STEP TOWARDS PERSONALIZING POST-TRANSPLANT CARE?

Soufian Meziyerh[*1;2], **Suzanne Bezstarosti[1;3], Jesper Kers[4], Teun van Gelder[5], Danny van der Helm[2], Paul van der Boog[1;2], Johan de Fijter[1;2], Dirk Jan Moes[5], Dave Roelen[3], Geert Haasnoot[3], Aiko De Vries[1;2], Sebastiaan Heidt[3]**

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Background: Current guidelines advise the use of HLA antigenic mismatches to assess the risk of alloimmunity in kidney transplant recipients (KTR). This approach is however too crude to allow personalization of post-transplant care. Recently, the HLA epitope mismatch algorithm (HLA-EMMA) was developed to quantify solvent-accessible amino acid (saAA) mismatches that could interact with B cell receptors responsible for the humoral allo-immune response. Until date, HLA-EMMA has only been associated with graft outcomes in relatively small cohorts with a limited number of events. This observational study aimed to examine the relationship between HLA-EMMA and transplant outcomes in a large and deeply phenotyped cohort of 1580 KTR by cox regression analyses.
Methods: Outcomes of interest were patient death, death-censored graft failure (DCGF), biopsy-proven acute rejection (BPAR), overall de novo donor-specific antibody (dnDSA) development, and dnDSA development per HLA locus (A, B, C, DQ, and DR). Hazard ratios (HR) and confidence intervals (CI) were adjusted for type of transplantation, recipient and donor age/gender, number of prior transplantations, and pre-transplant DSA's.
Results: During a median follow-up of 5.5 years (IQR: 2.8-9.0), 270 (17%) patients died, 185 (12%) suffered from graft failure, 302 (19%) suffered from BPAR, and 272 (17%) developed dnDSA. dnDSA against HLA-DQ were most common (n=164). Multivariable analysis showed that HLA-EMMA (total, class I, and class II saAA) mismatch scores were independently and significantly associated with patient death, DCGF, BPAR, overall dnDSA occurrence as well as HLA-specific dnDSA formation as shown in Figure 1. For locus-specific dnDSA, HRs per 10 saAA mismatches were 2.68 (95% CI: 1.93-3.71,p<.001), 2.34 (95% CI:1.34-4.09,p<.001), 3.78 (95% CI: 1.91-7.47,p<.001), 2.13 (95% CI: 1.77-2.55,p<.001), and 2.06 (95% CI: 1.68-2.53,p<.001) for HLA-A, -B, -C, -DQ, and -DR, respectively.
Conclusions: This is the first study to investigate the association between saAA mismatches and kidney transplant outcomes calculated by HLA-EMMA in a large and deeply phenotyped cohort of KTR. These findings suggest that HLA-EMMA may be a useful tool to stratify immunological risk to potentiate personalized surveillance and immunosuppression after transplantation.

HLA-Epitope Mismatch Algorithm (HLA-EMMA)

Biopsy-proven Acute Rejection

Per 10 SA AA MM	Multivariable* HR (95% CI)	p-value
Total saAA	1.15 (1.09-1.21)	<.001
Total Class I saAA	1.02 (1.01-1.03)	<.001
HLA-A saAA	1.13 (0.98-1.30)	.090
HLA-B saAA	1.63 (1.30-2.05)	<.001
HLA-C saAA	1.33 (1.05-1.68)	.016
Total Class II saAA	1.19 (1.10-1.28)	<.001
HLA-DQ saAA	1.37 (1.19-1.57)	<.001
HLA-DR saAA	1.19 (1.06-1.34)	.003

Death-censored Graft Failure

Total saAA	1.15 (1.08-1.23)	<.001
Total Class I saAA	1.23 (1.10-1.37)	<.001
HLA-A saAA	1.17 (0.98-1.39)	0.087
HLA-B saAA	1.44 (1.06-1.95)	.018
HLA-C saAA	1.80 (1.37-2.40)	<.001
Total Class II saAA	1.16 (1.05-1.28)	.003
HLA-DQ saAA	1.34 (1.12-1.60)	.001
HLA-DR saAA	1.14 (0.98-1.32)	.082

Patient death

Total saAA	1.08 (1.02-1.13)	.006
Total Class I saAA	1.08 (0.99-1.18)	.074
HLA-A saAA	1.09 (0.95-1.24)	.213
HLA-B saAA	1.22 (0.97-1.53)	.087
HLA-C saAA	1.09 (0.87-1.37)	.432
Total Class II saAA	1.09 (1.01-1.18)	.019
HLA-DQ saAA	1.19 (1.04-1.36)	.009
HLA-DR saAA	1.08 (0.97-1.20)	.179

Overall dnDSA development

Per 10 saAA MM	Multivariable* HR (95% CI)	p-value
Total saAA	1.22 (1.15-1.29)	<.001
Total Class I saAA	1.19 (1.09-1.31)	<.001
HLA-A saAA	1.24 (1.07-1.44)	.004
HLA-B saAA	1.30 (1.02-1.66)	.035
HLA-C saAA	1.49 (1.17-1.90)	.001
Total Class II saAA	1.34 (1.23-1.45)	<.001
HLA-DQ saAA	1.62 (1.40-1.87)	<.001
HLA-DR saAA	1.36 (1.21-1.54)	<.001

HLA-A-DSA Development

Total Class I saAA	1.77 (1.44-2.18)	<.001
HLA-A saAA	2.68 (1.93-3.71)	<.001

HLA-B-DSA Development

Total Class I	1.19 (96-1.48)	.116
HLA-B saAA	2.34 (1.34-4.09)	.003

HLA-C-DSA Development

Total Class I	1.47 (1.12-1.95)	.006
HLA-C saAA	3.78 (1.91-7.47)	<.001

HLA-DQ-DSA Development

Total Class II saAA	1.51 (1.36-1.67)	<.001
HLA-DQ saAA	2.13 (1.77-2.55)	<.001

HLA-DR-DSA Development

Total Class II saAA	1.63 (1.42-1.87)	<.001
HLA-DR saAA	2.06 (1.68-2.53)	<.001

*: adjusted for type of transplantation, recipient and donor age/gender, number of prior transplantations, and pre-transplant DSA's

OS1_3 DIRECT PROFILING OF CLINICALLY RELEVANT HUMORAL IMMUNITY IN TRANSPLANTATION AND BEYOND

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Background: Antibody (Ab) characterisation is fundamental in transplantation and infectious diseases, but current immunoassays cannot determine two fundamental Ab properties, affinity (K_D) and concentration ([Ab]). We aimed to overcome these limitations to allow in-depth profiling of Abs directly in sera.
Methods: Using a microfluidic diffusional sizing-based strategy, we developed microfluidic antibody affinity profiling (MAAP), a novel in-solution immunoassay that simultaneously determines antibody K_D and [Ab] directly in serum. MAAP was developed and validated using the HLA-alloantibody system and applied in HLA Ab-incompatible (HLAi) transplantation and in anti-SARS-CoV-2 immunity.
Results: MAAP enabled quantification (K_D and [Ab]) of alloantibody-HLA interactions in purified and Ab-spiked sera. We showed single-antigen-bead (SAB), and cellular (FC, CDC) HLA immunoassays were avidity and [Ab]-dependent, but antibody-mediated cytotoxicity is proportional to Ab-HLA K_D. Micromolar antibody-HLA interactions were functionally insignificant despite high SAB signal. In HLAi transplants, MAAP was able to differentiate clinically significant donor-specific-alloantibodies that lead to rejection from those that were tolerated, despite similar SAB output, and provided insights into memory re-activation and immune-monitoring post-transplantation. In SARS-CoV-2, MAAP showed wide variation in anti-RBD Ab K_D, which showed good correlation with neutralisation capacity ($p<0.001$). In convalescent sera (n=32), evidence of affinity maturation was seen 3-months post-infection, despite a reduction in [Ab]. In post-vaccine sera from healthy (n=15) and immunocompromised (n=15) patients, anti-RBD Ab K_D was significantly weaker against Omicron than wild-type ($p<0.001$), where the anti-RBD response in the immunocompromised cohort was significantly reduced.
Conclusions: This work outlines a path towards in-depth antibody profiling and demonstrates the importance of antibody abundance and affinity in clinically relevant humoral immunity.

OS1_4 ADOPTIVE CELLULAR IMMUNOTHERAPY FOR THE CONTROL OF HLA CLASS II ANTIBODY- MEDIATED REJECTION IN TRANSPLANTATION

Carolt Arana*[1;2], Sergi Betriu[3], Jordi Rovira[2], Ainhoa Garcia[2], Marina Matilla[2], Maria Jose Ramirez-Bajo[2], Elisenda Banon-Maneus[2], Marta Lazo[2], Ariadna Bartoló[3], Manel Juan[3], Beatriu Bayés[1], Josep M Campistol[1;2], Eduard Palou[3], Fritz Diekmann[1;2]

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Background: Antibody-mediated rejection (ABMR) is a major complication after transplantation that is associated with poor graft prognosis. The presence of donor-specific anti-HLA antibodies (DSA) class I and II, especially class II, increases the risk of developing ABMR. Current therapies are aimed at controlling the immune response, but there is no specific therapy to selectively reduce the generation of DSA. The objective was to establish a new therapeutic tool to specifically eliminate anti-HLA-DQ*03:01 antibody-producing B cells by generating cytotoxic lymphocytes transduced with chimeric HLA-DQ*03:01 antibody receptors (DQB1*03-CHAR).
Methods: This is a pre-clinical trial, using human cells, specifically cytotoxic T lymphocytes obtained from healthy volunteers who do not have HLA-DQ*03:01. The design, generation and production of DQ*03:01-CHAR will be carried out, with subsequent evaluation of their cytotoxic action and cytokine production, through an in-vitro model.
Results: We have identified and cloned the genetic sequence corresponding to HLA class II, specifically HLA DQ*03:01 (both the α DQA1*05:01 domain and the β DQB1*03:01 domain). The DQ*03:01-CHAR construct has been generated from domain binding; leader peptide (PL), extracellular domain (HLA-DQ*03:01) and intracellular domains (from A2-CHAR, generated in our laboratory). We produced lentiviral particles with the construct in HEK-293T cells. After isolation of CD3+ cells from a voluntary donor, transduction and production of DQ*03:01-CHAR-Tc is performed.
Conclusions: We are developing a new selective and specific therapy against B lymphocytes producing anti-HLA class II antibodies. With the development of this therapy, we will have a new tool for the desensitization of hypersensitized patients as well as for the control of ABMR, improving the results of graft survival, without increasing the infectious complications associated with conventional immunosuppressive therapy.

OS1_5 TCL1A PROTEIN INVOLVEMENT IN B CELLS AND TOLERANCE IN KYDNEY TRANSPLANTATION

François Brinas*[1], Nicolas Sailliet[1], Gaelle Tilly[1], Laurence Delbos[1], Clarisse Kerleau[1], Nicolas Degauque[1], Magali Giral[1], Sophie Brouard[1], Richard Danger[1]

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Background: Operational tolerance is defined as allograft acceptance without immunosuppression. We reported that tolerant patients (TOL) have a higher frequency of total B cells in blood associated with a higher susceptibility to apoptosis and a defect of differentiation. The gene *TCL1A*, notably shown to prevent apoptosis in B cells and associated with early differentiation transcription factors expression, is also overexpressed in the blood of TOL. The goals of our study are to define whether this increased expression of *TCL1A* in TOL is associated with particular blood B cells and how it confers their pro-apoptotic character and contributes to the fine control of B cell homeostasis in these patients.
Methods: We performed a phenotype analysis of peripheral blood cells by spectral cytometry (34 markers) of a cohort composed of TOL (n=8) and patients under immunosuppression with stable function transplanted for one year (STA, n=8) or for more than 5 years (long-term transplanted: LTT, n=6) and healthy volunteers (HV, n=10).
Results: Supervised analysis shows an increase of total B cells and $GZMB^+$ B cells frequencies in TOL, in accordance with previous reports. Regarding TCL1A expression, unsupervised analysis highlighted that naïve B cells are divided in two populations, with an increase frequency of the $TCL1A^{low}$ subset in TOL (median= 37,50%) compared to non TOL (STA, p= 0,0016 and LTT, p= 0,0079).
Conclusions: The emergence of such a naive $TCL1A^{low}$ B cell population in patients who developed tolerance is consistent with previous studies showing a pro-apoptotic behavior and a differentiation defect of TOL B cells, contributing to maintain a fine control of blood B cell homeostasis. Ongoing deeper characterization of this population, associated with the study of TCL1A expression effect during *in vitro* differentiation assays of TOL B cells will provide important insight on TCL1A role in immune tolerance.

OS1_6 CHARACTERIZATION OF EXTRACELLULAR VESICLES PRODUCED BY REGULATORY B CELLS IN KIDNEY TRANSPLANTATION

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[1]Nantes Université, INSERM, Centre de Recherche en Transplantation et Immunologie Translationnelle, UMR 1064, Nantes, France, [2]MSC-med, INSERM U7057, Université de Paris, Paris, France

Background: Kidney transplantation remains the treatment of choice for patients with end-stage renal diseases. However, it requires lifelong immunosuppressive therapy. Some patients present an operational tolerance following the discontinuation of these treatments. We have demonstrated the increased frequency of regulatory B cells (Breg) in the blood of these patients that can inhibit the proliferation of CD4+ T cells through a partially dependent Granzyme B mechanism (GZMB). Whereas regulatory T cells have been shown to secrete Extracellular Vesicles (EVs) with immunosuppressive properties, we want to determine whether Breg secrete EVs that could mediate their regulatory effect.
Methods: GzmB+ Breg were expanded during 3 days and subjected or not to mechanical stimulation. The EVs produced spontaneously or by stimulation were isolated from the supernatant by differential centrifugation. We characterized their type by cryo-electron microscopy and western blot, and their content by mass spectrometry and RNA-microarray compared with EVs from unstimulated B cells. The EVs were then put in culture for 72h with CD4+ T cells activated by anti-CD3/CD28 beads.
Results: We showed that Breg produce EVs expressing the markers CD9, CD63, CD81 and Tsg101 with a selective expression of Galectin-3 compared to EVs from unstimulated B cells. We also showed that EVs from Breg inhibit the proliferation of CD4+ T cells in vitro. Finally, we showed that mechanical stimulation increases the EVs production by 3 without altering their suppressive properties.
Conclusions: Breg's EVs, due to their inhibitory potential but also the possibility to increase their secretion, open new approaches in kidney transplantation, as therapeutic targets and biomarkers.

FULL ORALS

Translational immunology of rejection

OS1_7 CHARACTERISTICS AND FUNCTION OF DONOR AND RECIPIENT TISSUE RESIDENT LYMPHOCYTES IN KIDNEY TRANSPLANTS

Daphne Hullegie-Peelen*[1;2], Hector Tejeda Mora[1;2], Dennis Hesselink[1;2], Eric Bindels[3], Thierry van den Bosch[4], Marian Clahsen-van Groningen[1;4], Marjolein Dieterich[1;2], Sebastiaan Heidt[5], Robert Minnee[1;6], Georges Verjans[7], Martin Hoogduijn[1;2], Carla Baan[1;2]

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Background: Tissue resident lymphocytes (TRL) are key players in local immune surveillance. In immunosuppressed transplant recipients, however, the function and characteristics of TRL are less well defined. The current study aims 1) to investigate which TRL populations are present in kidney transplants, 2) to examine the frequencies and characteristics of donor and recipient TRL populations and 3) to unravel the function of TRL.
Methods: Renal lymphocytes were obtained by enzymatic digestion of kidney transplantectomy specimens (n=24) and were subsequently examined by flow cytometry to identify TRL populations and their origin (donor or recipient). The molecules CD69, CD103 and CD49a were used to define tissue residency and HLA-discrepancies between donor and recipient to define the origin of TRL. In-depth analysis of donor and recipient TRL functionality was performed using single-cell transcriptome sequencing, single-cell T cell receptor (TCR) sequencing and virus dextramer staining.
Results: CD4 tissue resident memory (TRM), CD8 TRM, NK resident, NKT resident and helper innate lymphoid cells were all present in kidney transplants (median: 13%, 67%, 7%, 4%, 2% of total TRL, respectively). TRL chimerism was present in 43% of kidney transplants with the highest proportion of donor cells observed among NKT resident cells (median: 32%). The proportion of donor TRL was negatively correlated with the time between transplantation and explantation (r=-0.74, p=0.046). Single-cell sequencing showed that recipient but not donor TRM cells have an activated phenotype and hyper-expanded TCR clonotypes, suggestive of alloreactivity. Tissue resident regulatory T cells of recipient origin were also detected, indicating that recipient TRL may not be solely harmful. Virus dextramer staining revealed that CD8 TRM of both donor and recipient origin showed antigen specificity against EBV, BKV, CMV and Influenza.
Conclusions: This study detected innate and adaptive TRL populations of both donor and recipient origin in kidney transplantectomy specimens. Infiltrating recipient TRL have alloreactive and regulatory properties. CD8 TRM of donor and recipient origin are responsive to several viral pathogens supporting the notion that these cells play a role in local immune surveillance.

OS1_8 TARGETING INTRAGRAFT CELL-CELL COMMUNICATIONS DURING KIDNEY TRANSPLANT REJECTION

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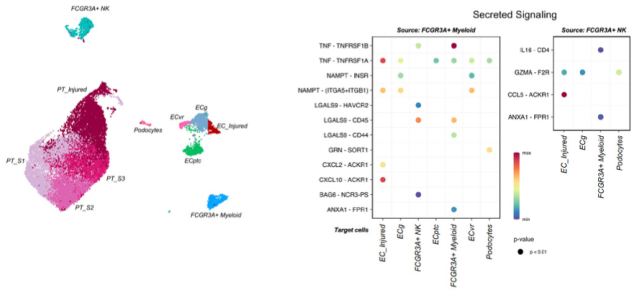
Background: How the immune system participates in kidney transplant rejection has not been fully elucidated. We previously reported that *FCGR3A*⁺ NK cells and *FCGR3A*⁺ monocytes as key players during kidney transplant rejection using single-cell (sc) transcriptomics. Here, we examined cell-cell interactions at single-cell (sc) resolution between these two cell types and kidney structural cells.
Methods: We studied sc-suspensions (N= 35,152 individual cells) from 16 different kidney transplant biopsies, with a representative mix of clinicopathological phenotypes (3 antibody-mediated rejection (ABMR), 1 T-cell mediated rejection (TCMR), 8 borderline changes, and 4 stable cases). Using ligand-receptor analysis (CellChat package), we assessed the interactions of innate immune cells such as NK or monocytes and kidney structural cells in human transplanted kidneys.
Results: Unsupervised clustering analysis was performed on the 16 cases, and we identified 18 distinct cell types, including all major immune cell types and most kidney cell types. After reintegration of *FCGR3A*⁺ cells and structural kidney cells, we observed a very limited cell-cell interactions with proximal tubules cells or podocytes. In contrast, *FCGR3A*⁺ cells mainly interact with endothelial cells through TNF-TNFRSF1A, CXCL10-ACKR1 and CCL5-ACKR1 signaling pathways. The increase of TNF, CXLC10 and CCL5 secretion was confirmed at protein level using an antibody-dependent cell cytotoxicity model recapitulating NK/monocytes interactions with kidney endothelium. Ultimately, inhibition of the Syk pathway, induced by antibody recognition and leading to cytokine secretion by *FCGR3A*⁺ cells, completely abrogated CXCL10, TNF and CCL5 release.
Conclusions: Our study provides new insights in the role of the different innate immune cell populations and their interactions with the kidney structural cells and unravels inflammatory cytokine signaling between *FCGR3A*⁺ cells and endothelial cells. Inhibition of the Syk pathway completely dampens such signaling, suggesting its potential interest as therapeutic target for kidney transplant rejection.



Basic science immunology

OS2_1 A NOVEL BI-SPECIFIC FUSION PROTEIN WITH CTLA4IG/PDL2 AS A NOVEL IMMUNOSUPPRESSANT MOLECULE MODULATING ALLOIMMUNE RESPONSES

Delphine Kervella*[1], Alba Torija[1], Elena Crespo[1], Jordi Guiteras[1], Laura Donadeu[1], Nuria Bolaños Peruga[1], Joan Torras[2], Josep M Grinyó[3], Oriol Bestard[1;4]

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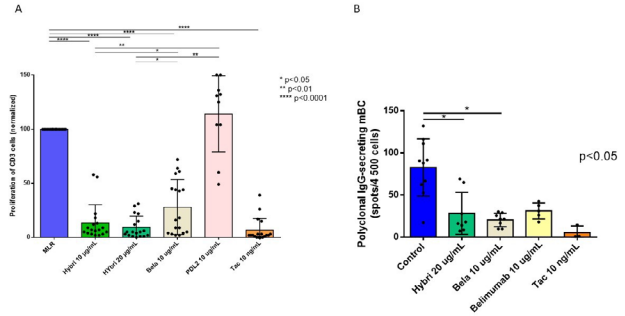
Background: The CD28-CD80/86 costimulatory and PD-1-PD-L1/L2 coinhibitory pathways are key regulators of adaptive alloimmune responses, driving effector T-cell activation and T-follicular helper and B-cell survival.
Methods: We have developed a hybrid recombinant bi-specific fusion protein (Hybri) that concomitantly stimulates the inhibitory CD80/86 pathway with a human CTLA4-Ig extracellular domain on APC and the inhibitory PD-1 signal on T cells with a human PD-L2 extracellular domain (EP19382017.2). Its capacity to inhibit T and B-cell proliferation *in vitro* was assessed in allogeneic mixed lymphocyte reactions (MLR) with Flow Cytometry in peripheral blood mononuclear cell samples from highly sensitized kidney transplant candidates and healthy volunteers (n=18 combinations) and was compared to the calcineurin inhibitor Tacrolimus (TAC 10 ng/ml), Belatacept (Bela 10 ug/mL) and a PD-L2 fusion protein (10 ug/mL). Also, its capacity to hinder memory B-cell (mBc) differentiation to IgG-secreting plasmablasts was assessed using a FLuorSpot assay evaluating both polyclonal and antigen-specific IgG-producing memory B-cell responses against Flu (H1N1) and HLA allo antigens (n=9).
Results: Compared to untreated allogeneic MLR, all treatments but PD-L2 alone significantly reduced CD3+ cell proliferation (p<0.0001, **figure A**). Hybri exerted a mean reduction of proliferation of 87 ± 17% at 10 ug/mL, 91 ± 10% at 20 ug/mL, Bela a reduction of 72 ± 25%, and TAC a reduction of 93±11% compared to untreated MLR. Proliferation of CD3+CD4+PD-1+ cells was significantly more reduced by Hybri than with other therapies (**figure B**, Hybri showed a reduction of proliferation of 74±18% at 10 ug/mL, 78±19% at 20 ug/mL vs only 53±30 % with Bela and 88±19% with TAC). The relative reduction of polyclonal IgG-producing mBc frequencies compared to the untreated control was of 64±33% and 68±17% when adding Hybri and Bela during polyclonal mBc proliferation, respectively (p<0.05 vs control). Antigen-specific mBc responses were also significantly reduced by Hybri (mean number of spots/450.000 cells of 11 for Hybri and 37 for the control condition).
Conclusions: This novel bispecific co-stimulation Hybri molecule (CTLA4Ig/PDL2) shows high potential to effectively abrogate T and B cell alloimmune responses.



OS2_2 VISUALIZING THE EFFECT OF BCL6 INHIBITION ON B AND T LYMPHOCYTES BY THE SMALL MOLECULE COMPOUND 79-6 BY MEANS OF IMAGING FLOW CYTOMETRY

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Background: BCL6 is a transcription factor involved in T and B cell activation during germinal center formation and maintenance, which is essential for antibody formation. Therefore, targeting BCL6-expressing T and B cells might prevent humoral alloreactivity. Using imaging flow cytometry, which combines conventional flow cytometry with single cell fluorescence images, we were able to study the effect of a small molecule BCL6 inhibitor (79-6) on immunological T-B cell synapse formation and activation, and the expression of BCL6 on T and B cells before and after polyclonal stimulation.
Methods: To study 79-6's effect on T-B cell synapse formation, stimulated T cells of healthy controls (HC) (1-day PHA, 6-days IL-2) and Raji cells were co-incubated with a superantigen (staphylococcal enterotoxin B), either with/without 100 µg/ml of 79-6 to induce synapse formation and activation. To test the effect of 79-6 on BCL6 expression, naïve T helper cells and B cells from HC's were both polyclonally stimulated (α-CD3/α-CD28/IL-12/IL-21 and α-IgM/α-CD40L/IL-21, respectively) in the presence/absence of 100 µg /ml of 79-6, and studied using imaging flow cytometry.
Results: After co-incubation, immunological synapses were successfully formed and polarization of LFA-1 indicated synapse activation, as shown in figure 1. The presence 79-6 had no significant effect on synapse formation and activation. In naïve T helper cells, before polyclonal stimulation, BCL6 expression could not be detected, as compared to its isotype control (IC). 5 days of stimulation, led to upregulation of BCL6, (MFI 90%> IC), while in the presence of 100 µg/ml of 79-6 this was partly inhibited (MFI 39%> IC). In B cells, BCL6 expression was detected before stimulation (MFI 67%> IC). After stimulation, BCL6 expression was markedly increased (MFI 159%> IC), while in the presence of 79-6, this was decreased to MFI 15%> IC.
Conclusions: Using imagestream technology, we were able to show that direct activation of immunological synapses between T and B cells was not affected by BCL6 inhibitor 79-6. Nevertheless, this compound was able to lower BCL6 expression of both B and T cells after polyclonal stimulation, implying inhibition of humoral responses.

OS2_3 PROTECTIVE EFFECT OF RECOMBINANT THROMBOMODULIN ALPHA AGAINST LONG COLD ISCHEMIA REPERFUSION INJURY IN A RAT KIDNEY TRANSPLANT MODEL

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Background: Thrombomodulin (TM) extensively expresses on the endothelial cells in the steady state and is known to prevent hypercoagulation via combining with thrombin and inactivating its procoagulant activity. In inflammatory situation, it is known that the expression of TM decreases. We investigated whether perfusate solution saturated with recombinant TM alpha (rTM) can protect the kidney grafts from long cold ischemia reperfusion injury.
Methods: We employed a rat syngeneic kidney transplant model using Lewis strain. Donor kidney grafts were preserved in a cold UW perfusate solution saturated with rTM (Group A, n=7), or not (Group B, n=8) for 24 hours. Then kidney transplantation was performed. Blood and urine samples were sequentially collected to measure creatinine clearance. Neutrophil gelatinase-associated lipocalin (NGAL), an acute kidney injury marker, was also measured by ELISA. Kidney graft samples in an acute phase (2 hours after operation) were collected to investigate the grade of tubular damage. TUNEL assay and immunohistochemistry (IHC) for TM was also performed.
Results: IHC revealed that the expression of TM on kidney grafts after 24-hour cold ischemia was extensively reduced compared with those after 0-hour ischemia. Creatinine clearance (ml/min/kg) in Group A was significantly ameliorated compared with that in Group B: mean (SD) of Group A vs Group B; 0.68 (0.33) vs 0.23 (0.13) on POD 1; 1.22 (0.40) vs 0.59 (0.30) on POD 2; and 2.63 (1.41) vs 1.17 (0.69) on POD 7; p=0.02. Furthermore, serum levels of NGAL (µg/ml) in Group A were significantly lower than those in Group B: mean (SD) of Group A vs Group B; 6.5 (1.7) vs 9.1 (1.1) on POD 1; and 4.3 (2.7) vs 8.9 (1.8) on POD 2; p=0.021.Fewer damaged tubular cells and apoptosis positive cells at a very acute phase were observed in Group A, compared with in Group B.
Conclusions: Perfusion with rTM significantly attenuates long cold ischemia reperfusion injury by abrogating apoptosis in tubular cells.

OS2_4 NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE INHIBITION AS A NOVEL TREATMENT TARGET IN ALLOGRAFT REJECTION

Bernhard Texler[*1], **Anh-Vu Nguyen**[1], **Giulio Ciucci**[2], **Fabian Egger**[1], **Katharina Lackner**[1], **Stefan Schneeberger**[1], **Jakob Troppmair**[1], **Serena Zacchigna**[2], **Manuel Maglione**[1]

[1]*Medical University Innsbruck, Daniel Swarovski Research Laboratory, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck, Austria,* [2]*International Centre for Genetic Engineering and Biotechnology (ICGEB), Cardiovascular Biology Laboratory, Trieste, Italy*

Background: T cell metabolism has been established to be highly relevant for T cell differentiation and effector function. Targeted suppression of activated non-regulatory T-cells by starving them of nicotinamide adenine dinucleotide (NAD) through inhibition of Nicotinamide phosphoribosyltransferase (NAMPT) has been shown to reduce the burden of inflammatory diseases.
Methods: We performed a heterotopic heart transplantation (HTx) model in mice using either an allogenic (C3H/J donors and C57BL/6 recipients) or a syngenic (C57BL/6 donors and recipients) setting. At day 6, we analyzed graft tissue samples for mRNA expression of inflammatory cytokines, performed histopathology to assess the severity of the rejection and quantified serum NAMPT levels via ELISA. Furthermore, we isolated $CD4^+$ and $CD8^+$ T cells from human peripheral blood, to perform a viability assay and measure cytokine expression in T-cell receptor stimulated and unstimulated cells with or without NAMPT inhibition. Additionally, we isolated primary rat cardiomyocytes and treated them with the NAMPT inhibitor to exclude cardiotoxic effects.
Results: We confirmed that our HTx model is well suited to investigate acute allograft rejection, as we observed a significantly higher number of infiltrating cells and upregulation of pro-inflammatory cytokines in the allogenic group. We unveiled an increased NAMPT expression in the serum of allogenic transplanted mice, indicating NAMPTs involvement during allograft rejection. We analysed the effect of NAMPT inhibition on different T cells and could observe a cytotoxic effect and a reduction in the mRNA and protein expression of Interferon-γ after application of the inhibitor, which was more prominent in $CD8^+$ T cells than $CD4^+$ cells and had little effect on regulatory T cells. We characterized the effect of our NAMPT inhibitor on primary rat cardiomyocytes, and observed no effects on proliferation, cell size and cell number after up to 72 hours of treatment.
Conclusions: We could show that NAMPT is upregulated during allograft rejection and that perturbing NAMPT is effective in suppressing activation of alloreactive T cells without affecting regulatory T cells. These data suggest NAMPT as a promising treatment target in acute allograft rejection.

OS2_5 NK-MEDIATED INNATE ALLORECOGNITION CONTROLS THE EARLY PRODUCTION OF DONOR SPECIFIC ANTIBODIES BY THE INVERTED DIRECT PATHWAY

Xavier Charmetant[*1], **Chien-Chia Chen**[2], **Carole Saison**[3], **Virginie Mathias**[3], **Alice Koenig**[1], **Jerôme Le Pavec**[4], **Olivier Brugière**[5], **Pierre Mordant**[6], **Jean-Luc Taupin**[7], **Valérie Dubois**[3], **Emmanuel Morelon**[1], **Olivier Thaunat**[1]

[1]*Lyon University Hospital-INSERM U1111, Lyon, France,* [2]*National Taiwan University Hospital, Taipei, Taiwan,* [3]*Etablissement Français du Sang, Décines, France,* [4]*Marie Lannelongue Hospital, Le Plessis Robinson, France,* [5]*Hôpital Foch, Suresnes, France,* [6]*APHP Hôpital Bichat, Paris, France,* [7]*Hôpital Saint-Louis, Paris, France*

Background: Two pathways of allorecognition lead to the production of donor specific antibodies (DSA) after transplantation: the indirect pathway (involving recipient $CD4^+$ T and B cells), and the recently described inverted direct pathway (involving donor $CD4^+$ T cells originating from the graft and recipient B cells). The inverted direct pathway results in an early and transient wave of DSA, which can be observed in some patients transplanted with a T cell-rich graft (such as lung and intestine). This inter-individual heterogeneity led us to investigate the mechanisms involved in controlling the inverted direct pathway of DSA generation.
Methods and results: Reproducing the clinical inter-individual heterogeneity, a cardiac graft from CBA ($H\text{-}2^k$) mice induces an early DSA response in a CD3εKO C57BL/6 ($H\text{-}2^b$) recipient mouse by the inverted direct pathway, whereas a Balb/c ($H\text{-}2^d$) heart graft does not. Using adoptive transfer of T cells, we observed that $CD4^+$ T cells from Balb/c donor survive much shorter than their CBA counterparts in recipient mice. This difference was explained by the fact that, in contrast with CBA T cells, T cells from Balb/c are promptly eliminated by recipient's NK cells, thus preventing their interaction with recipient's B cells. Depletion of NK cells in CD3εKO C57BL/6 recipient mice prolonged the survival of transferred allogeneic Balb/c $CD4^+$ T cells, thereby restoring DSA production through the inverted direct pathway. The clinical validity of these original experimental findings is currently being investigated in a large cohort of lung transplant patients.
Conclusions: In the context of transplantation, NK cell-mediated allorecognition is a double-edged sword that protects against the microvascular lesions resulting from the generation of DSA through the inverted direct pathway, while it is now known that these same alloreactive NK can be the cause of missing self-induced chronic vascular rejection.

OS2_6 ALLOREACTIVE T CELL REPERTOIRES DISPLAY BIASED VARIABLE SEGMENT USAGE AND FINE-TUNING OF PEPTIDE SPECIFICITY BY COMPLEMENTARITY-DETERMINING REGION 3B

Moumita Paul-Heng[1], Martina Denkova[1], Eric Taeyoung Son[1], Johanna Tuomisto[2], Claerwen Jones[2], Pirooz Zareie[2], Mario Leong[1], Anthony Purcell[2], Nicole Lagruta[2], Nicole Mifsud[2], Alexandra Sharland[*1]

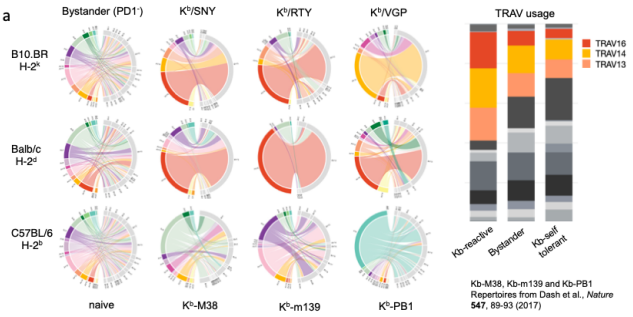
[1]The University of Sydney, Faculty of Medicine and Health, Sydney, Australia, [2]Monash University Biomedicine Discovery Institute, Biochemistry and Molecular Biology, Melbourne, Australia

Background: Directly alloreactive CD8 T cells recognise epitopes formed by an allogeneic MHC I molecule loaded with an endogenous peptide. We have identified over 40 immunogenic peptides presented by H-2K^b. We are now profiling the T cell receptor (TCR) repertoire of CD8 T cells responding to a subset of these epitopes to deepen our understanding of the molecular basis of alloreactivity.
Methods: An enriched population of alloreactive CD8 T cells was isolated from B10.BR (H-2^k) or Balb/c (H-2^d) mouse liver following a prime-boost against H-2K^b. B10.BR samples were stained with a panel of 12 oligonucleotide-barcoded K^b-peptide dextramers, single cells were captured for parallel analysis of paired TCR sequences, specificity and gene expression (BD Rhapsody). Results were integrated with TCR repertoires obtained from sorted populations positive for single pMHC dextramers.
Results: TCR alpha variable (TRAV) segments 13, 14 and 16 were over-represented among alloreactive T cells recognising three prominent epitopes (Kb-SNYLFTKL, Kb-RTYTYEKL and Kb-VGPRYTNL) from both recipient strains, and within the global alloreactive population (Figure 1a). This differs markedly from the segment usage for self-restricted CD8 T cells recognising K^b with viral epitopes, suggesting preferential binding of these TRAV to the H-2K^b framework. A family of closely-related clonotypes (metaclonotype) recognising the abundant epitope K^b-SNYLFTKL has been detected in 12/12 B10.BR mice examined (Figure 1b). Within this public metaclonotype, the sequence of the beta chain complementarity-determining region 3 (CDR3b) confers fine specificity in peptide recognition; TCRs with threonine in the 5th position of CDR3b bind SVYVYKVL>SNYLFTKL, whereas TCRs with an acidic residue at this position bind SNYLFTKL exclusively (Table 1, Figure 1c-d).
Conclusions: Recognition of H-2K^b by alloreactive TCR is linked to the expression of particular TRAV segments, while fine specificity for the peptide is conferred by the CDR3b sequence.

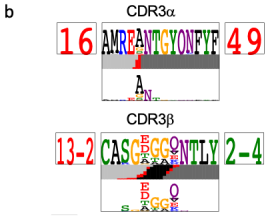
Table 1.

TRAV/TRAJ	CDR3a	TRBV/TRBJ	CDR3b	Peptide binding
16D/DV11/49	CAMREANTGYQNFYF	13-2*01/2-4	CASGDGAQNTLYF	SNYLFTKL only
16D/DV11/49	CAMREGNTGYQNFYF	13-2*01/2-4	CASGDGAQNTLYF	SNYLFTKL only
16D/DV11/49	CAMREANTGYQNFYF	13-2*01/2-4	CASGTGGQNTLYF	SVYVYKVL > SNYLFTKL
16D/DV11/49	CAMRESNTGYQNFYF	13-2*01/2-4	CASGTGGQNTLYF	SVYVYKVL > SNYLFTKL

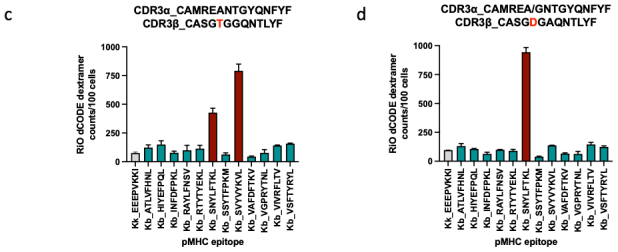
Figure 1.



a: CIRCOS plots of paired TCR α–β segment usage showing strong bias towards TRAV13/14/16 among pMHC-restricted alloreactive TCRs. This bias is also evident in the global Kb-reactive population. For each group n = 3 mice.



b. TCR motif for a public metaclonotype corresponding to recognition of Kb-SNYLFTKL. c-d. Within this metaclonotype, TCRs with T at position 5 of CDR3β bind SVYVYKVL in addition to SNYLFTKL, while TCRs with an acidic residue at this position bind only SNYLFTKL. c. n=3 expanded clones (50-89 cells each) isolated from three individual mice. d. n=2 clones (49-75 cells each) isolated from two different mice.



OS2_7 MAPPING THE CELLULAR AND MOLECULAR LANDSCAPE OF ADAPTIVE IMMUNE RESPONSES IN KIDNEY ALLOGRAFT REJECTION

Kevin Louis[*1], Camila Macedo[2], Elodie Bailly[1], Parmjeet Randhawa[2], Adriana Zeevi[2], Carmen Lefaucheur[1], Diana Metes[2]

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Background: Although the clinical and histological differences between antibody-mediated rejection (ABMR) and T-cell mediated rejection (TCMR) are well established, in-depth analyses of cellular and molecular determinants that contribute to such alloimmune responses are sparse.
Methods: In a cohort of 76 kidney transplant recipients (stable, N=41; ABMR, N=23; TCMR, N=12) and 16 healthy controls (HC), we used high dimensional flow cytometry and single-cell RNA seq to deeply profile blood CD4 T cells and B cells. Additionally, we assessed 55 plasma cytokines.
Results: Compared to HC and stable subjects, ABMR patients displayed significantly expanded cell populations of activated ICOS$^+$ IL-21R$^+$ T follicular helper cells (Tfh) and effector CD11c$^+$ IL-21R$^+$ B cells. TCMR patients showed specific expansion of Th1/Th17 CD28$^+$ CD4 T cells and naïve B cells. Plasma from ABMR patients displayed elevated IL-21, IL-8 and ICAM-1, while those from TCMR patients were enriched for IFN-g, TNF-a and IL-17a. At the single-cell transcriptional level, ABMR was characterized by elevated transcripts related to antigen receptor activation and IL2RG-STAT3 pathways in both Tfh and B cells, while TCMR was associated with enrichment in cell-mediated cytotoxicity, type-1 interferon and FcγR signaling pathways in effector memory CD4 T cells.
Conclusions: We identified predominant IL-21-driven Tfh and B cell effector differentiation and activation during ABMR, while TCMR was characterized by type-1 inflammatory and cytotoxic CD4 T cell changes. Thus, our study highlights novel cellular pathomechanisms associated with ABMR and TCMR, and therefore identifies novel therapeutic targetable pathways to tackle kidney allograft rejection.

FULL ORALS

Basic science immunology

OS2_8 SINGLE CELL TRANSCRIPTOME OF ALLOREACTIVE CD8 T CELLS SUPPORTS ROLES FOR BOTH DELETION AND EXHAUSTION IN TOLERANCE INDUCTION

Moumita Paul-Heng[1], Martina Denkova[1], Eric Taeyoung Son[1], Mario Leong[1], Thomas Ashhurst[2], Chuanmin Wang[1], David Bowen[1], Patrick Bertolino[3], Anthony Purcell[4], Nicole Lagruta[4], Nicole Mifsud[4], Alexandra Sharland[*1]

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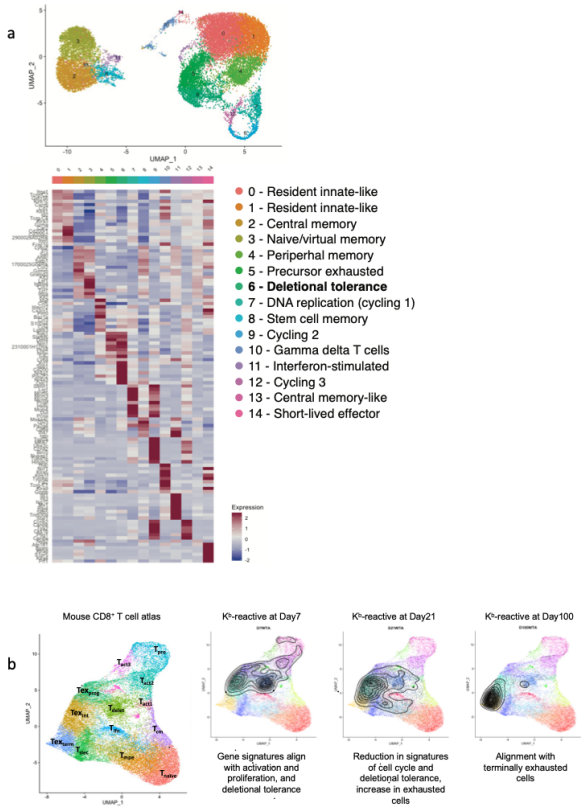
Background: Expression of allogeneic donor MHC class I in recipient hepatocytes using adeno-associated viral (AAV) vectors induces tolerance to subsequent skin grafts bearing the same mismatched MHC, even in the presence of pre-existing immune memory against the donor strain. The mechanisms underpinning tolerance induction are incompletely understood.
Methods: B10.BR (H-2^k) mice were primed with an H-2K^b-bearing skin graft. 30 days after rejection of the primary graft, they were inoculated with AAV-K^b, followed by secondary skin grafting. Liver leucocytes were isolated at intervals between d5 and d100 following vector administration – paired TCR sequence, specificity and gene expression were determined for single alloreactive and bystander CD8 T cells (BD Rhapsody).
Results: Alloreactive T cells exposed to their cognate antigens in the liver segregate into several clusters based on gene expression. One major cluster recapitulates a published signature of deletional tolerance, while the other expresses liver-residency markers and receptors typically associated with gamma-delta, NK, and innate lymphoid cells (Figure 1a). Projection of timecourse data onto a mouse CD8 T cell atlas suggests that early during tolerance induction, cells align with the transcriptomic profiles of activation, proliferation and deletional tolerance, while later during this process, the signature of terminal exhaustion predominates (Figure 1b). The proportion and absolute number of cells bearing the public K^b-reactive TCR clonotype TRAV16D/AJ49 TRBV13-2/BJ2-4 decline rapidly between d7 and d21 post-AAV inoculation, consistent with deletion. Ingenuity pathway analysis points to upregulation of metabolic pathways that may contribute to cell death in the deletional tolerance cluster – these include polyamine catabolism, lipid peroxidation and ferroptosis. These cells express high levels of CD200, whereas the resident innate-like cluster is marked by expression of inhibitory CD200 receptors suggesting that interactions between this receptor-ligand pair could also influence cell fate and transplant outcome.
Conclusions: Taken together, these data support roles for both deletion and immune exhaustion in tolerance mediated by liver-specific expression of donor MHC I in skin graft recipients.

Figure 1.



Transplant Plus: Regenerative therapies and Xenotransplantation

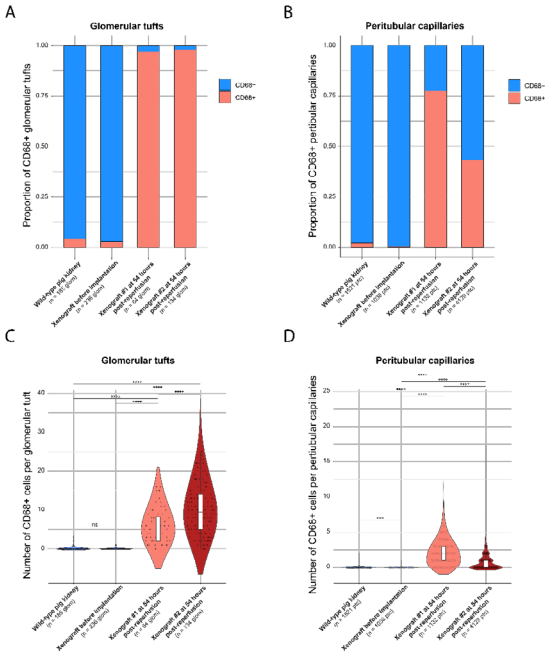
OS3_1 AUTOMATED DETECTION AND QUANTIFICATION OF IMMUNE CELL INFILTRATES IN THE TWO FIRST SUCCESSFUL PIG-TO-HUMAN KIDNEY XENOTRANSPLANTS

Erwan Morgand[*1], Valentin Goutaudier[1], Alessia Giarraputo[1], Fariza Mezine[1], Blaise Robin[1], Anais Certain[1], Harvey Pass[2], Aurélie Sannier[1], Ming Wu[2], Adam Griesemer[2], David Ayares[3], Vasishta Tatapudi[2], Jeffrey Stern[2], Massimo Mangiola[2], Patrick Bruneval[1], Robert Montgomery[2], Alexandre Loupy[1]

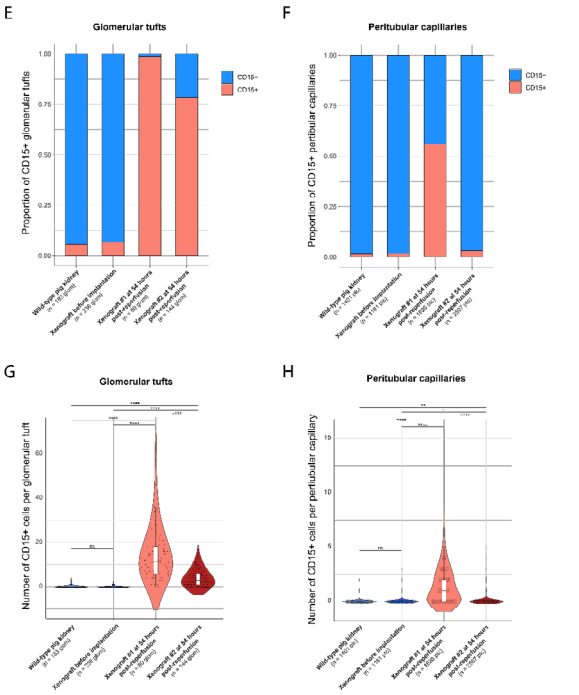
[1]Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, [2]NYU Langone Transplant Institute, NYU Langone Health, New York, United States, [3]Revivicor Inc, Blacksburg, United States

Background: The two first successful pig-to-human xenotransplants displayed indolent intravascular immune cell infiltrates. In this study, we aimed to use digital pathology to precisely quantify xenograft immune infiltration and better understand underlying injury mechanisms.
Methods: Tissue sections of the two first xenografts and two controls (xenograft before implantation and wild-type pig kidney) were stained by immunohistochemistry with anti-CD68 and anti-CD15 antibodies to detect the predominant immune cell infiltrates (i.e., macrophages and neutrophils) and then digitized. Using 1432 annotations performed by 3 expert nephropathologists, we trained convolution neural networks to automatically detect and quantify CD68 and CD15 positive cells in the microcirculation (glomerular and peritubular capillaries) on whole slide images.
Results: The proportions of CD68+ glomerular tufts were 96.9% in xenograft 1, 97.8% in xenograft 2, 3.0% in xenograft before implantation, and 4.3% in wild-type pig kidney (p<0.0001, A). The proportions of CD68+ peritubular capillaries were 77.4% in xenograft 1, 43.3% in xenograft 2, 0.4% in xenograft before implantation and 2.0% in wild-type pig kidney (p<0.0001, B). For xenograft 1 and 2, respectively, median densities of CD68+ cells were 5.5 [IQR, 2–8.2] and 9.5 [IQR, 5–14] per glomerular tuft (C), and 2 [IQR, 1–3] and 0 [IQR, 0–1] per peritubular capillary (D). Control densities were below the limit of quantification. The proportions of CD15+ glomerular tufts were 98.7% in xenograft 1, 78.4% in xenograft 2, 6.8% in xenograft before implantation, and 5.5% in wild-type pig kidney (p<0.0001, E). The proportions of CD15+ peritubular capillaries were 56.1% in xenograft 1, 3.0% in xenograft 2, 1.7% in xenograft before implantation, and 1.6% in wild-type pig kidney (p<0.0001, F). For xenograft 1 and 2, respectively, median densities of CD15+ cells were 11.5 [IQR, 6–18.2] and 3 [IQR, 1–6] per glomerular tuft (G), and 1 [IQR, 0–2] and 0 [IQR, 0–0] per peritubular capillary (H). Control densities were below the limit of quantification.
Conclusions: We automatically detected and quantified an extensive infiltration of the microcirculation of the first two pig-to-human kidney xenografts by macrophages and neutrophils, suggesting an ongoing active antibody-mediated rejection.

Automated quantification of intravascular CD68+ and CD15+ cells in xenograft kidneys



Automated quantification of intravascular CD68+ and CD15+ cells in xenograft kidneys



OS3_2 MULTIMODAL DEEP PHENOTYPING OF GENETICALLY MODIFIED PIG KIDNEY XENOGRAFTS TRANSPLANTED TO HUMAN RECIPIENTS REVEALS ANTIBODY-MEDIATED REJECTION

Valentin Goutaudier*[1], Alessia Giarraputo[1], Erwan Morgand[2], Fariza Mezine[1], Blaise Robin[1], Sapna Mehta[3], Brendan Keating[4], Anais Certain[1], Pierre-Louis Tharaux[5], Navneet Narula[3], Harvey Pass[3], Aurélie Sannier[1], Ming Wu[3], Adam Griesemer[3], David Ayares[6], Vasishta Tatapudi[3], Jeffrey Stern[3], Carmen Lefaucheur[1], Patrick Bruneval[3], Massimo Mangiola[3], Robert Montgomery[3], Alexandre Loupy[1]

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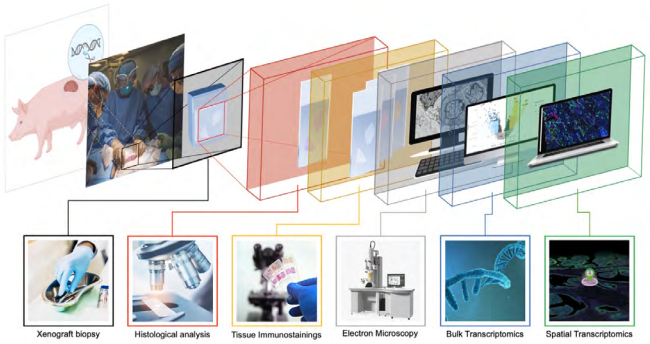
Background: Genetic modifications have revolutionized xenotransplantation by recently allowing pig-to-human kidney transplantation. There is an unmet need and unprecedented opportunity for a precise characterization of the immune response of xenografts transplanted to humans.
Methods: We performed a complete phenotyping of the two-world premiere successful kidney xenografts transplanted to decedent humans. We used a multimodal strategy combining i) morphological evaluation, ii) multiplex immunophenotyping, iii) ultrastructural assessment, iv) gene expression profiling, v) whole-transcriptome digital spatial profiling and cell deconvolution (**Figure 1**). Xenografts before implantation as well as wild-type pig kidneys were used as controls.
Results: Xenografts revealed early signs of antibody-mediated rejection, circulating IgM and IgG xenoantibodies, and microvascular inflammation with linear capillary deposits of IgM and IgG. Capillary inflammation was mainly composed of intravascular CD68+ and CD15+ innate immune cells, as well as NKp46+ cells. Both xenografts displayed intense von Willebrand factor staining in capillary endothelial cells. Ultrastructural findings revealed swollen endothelial cells with abnormal cytoplasmic expansions in glomerular and peritubular capillaries, confirming their activation. Both xenografts showed increased expression of transcripts biologically related to a humoral response, including monocyte/macrophage activation, NK cell burden, endothelial activation, complement activation, and T-cell development. Whole transcriptome digital spatial profiling revealed that antibody-mediated injury was mainly located in the glomeruli of xenografts, with significant enrichment of transcripts associated with monocytes, macrophages, neutrophils, and NK cells.
Conclusions: This study shows for the first time the evidence for ongoing antibody-mediated rejection in pig kidney xenografts transplanted to humans. These results open avenues for further refinement of pig constructs and pathways to optimize the control of the humoral harm of rejection, for improving xenotransplant outcomes and next-generation clinical trials.

Figure 1. Multimodal deep phenotyping of pig kidney xenografts.



OS3_3 HYDROGEL-BASED, PREVASCULARIZED, RETRIEVABLE ENDOCRINE CONSTRUCT TO TREAT TYPE 1 DIABETES

Fanny Lebreton*[1;2;3], Kevin Bellofatto[1;2;3], Reine Hanna[1;2;3], Laura Mar Fonseca[1;2;3], Juliette Bignard[1;2;3], Andrea Peloso[4], Philippe Compagnon[2;4], Vanguard Consortium[1], Ekaterine Berishvili[1;2;3;5]

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Background: The aim of our study was to generate a functional, preveascularized endocrine construct utilizing amniotic membrane derived hydrogel, islets and blood outgrowth endothelial cells (BOECs) to be transplanted in diabetic hosts.
Methods: Human amniotic membranes were decellularized, lyophilized, and solubilized to obtain hydrogels. To study the impact of generated gels on islet function in vitro, both rodent and human derived islets and human BOECs were admixed in hydrogels and cultured in vasculogenic media to enhance endothelial cell assembly into tubular, vascular-like structures. To test in vivo function, the vascularized constructs containing either 500 rat islet equivalents (IEQ) or 2000 human IEQ and 2× 105 BOECs were implanted under the skin of the diabetic NSG mice. Control mice has been transplanted with constructs containing islets only. Graft function was accessed by measuring of non-fasting blood glucose levels and intraperitoneal glucose tolerance tests (IPGTT). Graft morphology and vascularization were evaluated by immunohistochemistry.
Results: Engineered vascularized constructs supported islet function, and development of an abundant vascular network well integrated with islets. Blood glucose levels of the mice transplanted with vascularized constructs normalized within 7 days and normoglycemia was maintained long-term. In contrast most of the mice transplanted with islets admixed in hydrogels remained diabetics. Histological analysis of the explanted grafts revealed healthy islet morphology and perfect revascularization. The experiments replicated utilizing human islets had similar outcomes, we observed rapid reversal of diabetes and increase of human C-peptide after transplantation. Explanted grafts displayed excellent islet morphology, hormone expression and most importantly intense vascularization. Presence of red blood cells within the capillaries in the graft area and positive alpha SMA staining indicated that that vessels inside the graft were functional and fully matured.
Conclusions: Our findings show that amnion derived hydrogel seeded with endocrine pancreatic tissue and endothelial cells could be used for functional, preveascularized endocrine construct bioengineering.

FULL ORALS

Transplant Plus: Regenerative therapies and Xenotransplantation

OS3_4 BIOENGINEERING OF VASCULARIZED INSULIN-SECRETING ORGANOIDS FOR TYPE 1 DIABETES CELL THERAPY

Laura Mar Fonseca*[1;2;3], Fanny Lebreton[1;2;3], Kevin Bellofatto[1;2;3], Reine Hanna[1;2;3], Juliette Bignard[1;2;3], Víctor Galván Chacón[1;2;3], Charles-Henri Wassmer[2;4], David Cottet Dumoulin[2;3], Lisa Perez[1;2;3], Domenico Bosco[2;3], Philippe Compagnon[2;4], Thierry Berney[2;4;5], Vanguard Consortium[6], Ekaterine Berishvili[1;2;3;4;5]

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Background: Lack of donor organs, inflammation and poor vascularization hamper long term outcomes of intraportal islet transplantation. Based on our previous experience with generating islet organoids, we propose an improved strategy to engineer pre-vascularized islet organoids (PVO) composed of dissociated insulin-secreting cells, human amniotic epithelial cells (hAECs) and blood outgrowth endothelial cells (BOECs). BOECs are easily obtained from recipients' peripheral blood, making them an ideal source of autologous endothelial cells.
Methods: PVOs were generated on microwell platforms by combining different ratios of insulin-secreting cells (EndoC-βH1 or rat islet cells), hAECs and BOECs (1000 cells/organoid). Cell integration, viability and function were assessed *in vitro*. To evaluate *in vivo* function, a marginal mass of 300 native islet equivalents (NI), islet cell spheroids (IC) and the best performing PVOs (50% rat islet cells, 25% hAECs, 25% BOECs) containing an equivalent islet cell mass, were transplanted in the epidydimal fat pad of diabetic NSG mice. Graft function was assessed by measuring non-fasting blood glucose levels and by intraperitoneal glucose tolerance tests (IPGTT). Graft morphology and vascularization were evaluated by immunohistochemistry.
Results: Generated PVOs displayed good viability and function, indicating that supporting cells did not impair insulin secretion. 6 out of 7 mice transplanted with the marginal mass of PVOs reversed diabetes and the median time to reach normoglycemia was 7 days. PVO group stayed within normoglycemic range for 3 months and IPGTT at 1- and 3-months post-transplant were similar to non-diabetic controls. In contrast, transplantation of the same mass of ICs or NIs did not reverse diabetes. Removal of the PVO grafts led to recurrence of hyperglycemia within 24h. PVO retrieved grafts presented a bigger β-cell mass and vascularization compared to controls.
Conclusions: Here we demonstrate that adding hAECs and BOECs in the islet organoids significantly improved engraftment, leading to prompt reversal of diabetes, indicating that our strategy has the potential to solve the problem of scarcity of donor supply and poor islet engraftment. Furthermore, our approach could be a primordial step toward the engineering of a bioartificial pancreas.

OS3_5 EXTRAHEPATIC BILE DUCT ORGANOIDS AS A MODEL TO STUDY ISCHEMIA/REPERFUSION INJURY DURING LIVER TRANSPLANTATION

Elke Eggenhofer[1], Philipp Kreiner[1], Hans Schlitt[1], Edward Geissler[1], Stefan Brunner[1], Henrik Junger*[1]

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Background: Biliary complications are still a major cause for morbidity and mortality after liver transplantation. Ischemia/reperfusions injury (IRI) leads to disruption of the biliary epithelium. Yet little is known about the underlying molecular mechanism. We introduce a novel model to study the effect of IRI on human cholangiocytes using extrahepatic cholangiocyte organoids (ECOs)
Methods: Extrahepatic bile duct tissue was collected during liver transplantation (n=15), and control sections after cholecystectomy (n=5) and stained using in-situ-hybridization. ECOs were cultured and expanded from extrahepatic biliary tissue. Multiplex immunofluorescence, in-situ hybridization and qRT-PCR were performed to identify verify cells being of cholangiocytic phenotype in cultured organoids. IRI was induced by introducing cells to a hypoxic chamber for 48h, followed by reoxygenation. In-situ-hybridization and qRT-PCR were performed to study markers of programmed cell death induced by IRI.
Results: ECOs formed circular structures recreating a tubular structure similar to that found in the extrahepatic bile duct. Analysis revealed a cholangiocyte phenotype with high expression of EpCAM, Sox9, LGR5 & CK19 and low expression of albumin & AHH. After hypoxia and even more pronounced after re-oxygenation, ECOs showed increased expression of ACSL4, HIF1-α and VEGF-α. Expression patterns were similar to those found in the bile duct biopsies.
Conclusions: ECOs are in-vitro cellular systems that self-organize through mechanisms like those found in-vivo. They recapitulate the structure and exhibit similar patterns of ACSL4, VEGF-α and HIF1-α expression as extrahepatic bile duct during liver transplantation and thus provide a suitable model to study IRI in choanocytes after liver transplantation.

OS3_6 GENERATION OF 'UNIVERSAL' LOW-IMMUNOGENIC HUMAN PRIMARY CHOLANGIOCYTE ORGANOIDS FOR TREATMENT OF BILE DUCT DISORDERS

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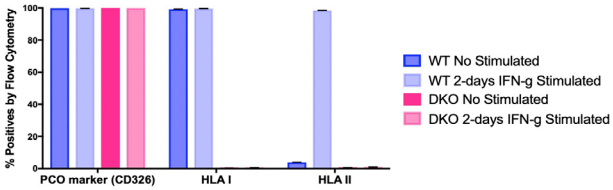
Background: Other than complex surgery or transplantation, there are no current curative therapies for bile duct diseases/cholangiopathies affecting the intra- or extrahepatic biliary tree. We have previously shown that human bile duct epithelial cells can be cultured as 3D organoids to generate mature primary cholangiocyte organoids (PCOs) for the treatment of cholangiopathies. Since the generation of autologous PCOs is likely to remain logistically and economically prohibitive for the foreseeable future, immune rejection of allogeneic PCOs remains a key outstanding barrier to their clinical translation. We thus aimed to develop 'universal' low-immunogenic cholangiocyte organoids for regenerative medicine applications.
Methods: After systemic testing of numerous conditions, human leukocyte antigen (HLA) I and II double knock out (DKO)-edited PCOs (ePCOs) were generated using CRISPR-Cas9 by dissociating PCOs into single cells, electroporation with the guide-Cas9 complex and sorting for the specific double negative cells. Assessment comparing to parental wild-type (WT) cells was carried out by flow cytometry, functional readouts, co-culture with human peripheral blood mononuclear cells (PBMC) *in vitro*, and by engraftment under kidney capsule of immunodeficient mice. Mutational load and CRISPR-driven off-target genetic mutations of parental vs ePCOs was quantified using whole genome sequencing and Nanoseq techniques.
Results: The HLA I and II DKO ePCOs generated maintain a mature PCO phenotype demonstrated by flow cytometry and functional analyses. Immune characterization *in vitro* by co-culture with PBMC experiments show that ePCOs have a reduced immunogenicity compared to WT cells. Additionally, off-target analysis and mutation burden of parental vs ePCOs do not show CRISPR-driven off-target sites nor excess mutation in ePCOs. Additional experiments are ongoing to assess the immune response *in vivo* using humanised mouse models.
Conclusions: Human PCOs lacking HLA I and HLA II can be successfully generated using a CRISPR-Cas9 approach. ePCOs retain the phenotypic characteristics of mature PCOs and show reduced immunogenicity when co-cultured with PBMC compared to parental cells. Genomic data show no CRISPR-driven off-target mutational burden in ePCOs.



OS3_7 MODELING KIDNEY FIBROSIS AND EXPLORING THE ANTI-FIBROTIC ACTIVITY OF MEMBRANE PARTICLES GENERATED FROM MESENCHYMAL STROMAL CELLS IN KIDNEY ORGANOIDS

Shengbing Li*[1], Zhaoyu Du[2], Sander Korevaar[2], Amanda Bas-Cristóbal Menéndez[2], Hui Lin[2], Quincy Nlandu[2], Thierry van den Bosch[3], Carla Baan[2], Marlies Reinders[2], Martin Hoogduijn[2]

[1]transplant institute, Rotterdam, Netherlands, [1]transplant institute, Rotterdam, Netherlands, [3]Department of Pathology, Rotterdam, Netherlands

Background: Ischemia, inflammation and aging drive kidney fibrosis, which leads to loss of function. Human induced pluripotent stem cell (iPSC) derived kidney organoids may represent a tool for studying fibrosis and the development of antifibrotic medicines. Mesenchymal stromal cells (MSC) have anti-fibrotic properties, but use of these cells has some challenges such as poor biodistribution and short life-span after administration. Nanosize membrane particles (MP) generated from the membranes of MSC could be an alternative. Hence, the aim of this study was to set up a kidney organoid fibrosis model and explore the anti-fibrotic activity of MSC-derived MP.
Methods: Kidney organoids were exposed to 1% O2 for 48h and 100ng/ml IL-1β for 96h at day 12 of differentiation. Subsequently, organoids were cultured under standard conditions for 14 days. MP generated from 0.5×106 MSC were added to the medium concurrently with fibrosis-inducing stimulations for 4 days or added until the end of the experiments for 14 days.

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Results: Immunohistochemistry confirmed that kidney organoids developed PODXL+ glomeruli, Villin-1+ proximal and ECAD+ distal tubular structures. After fibrosis-inducing stimulations, collagen type 1A1+(COL1A1) and transforming growth factor beta (TGF-β) mRNA were upregulated, and kidney structures were partly replaced by COL1A1+ and α-smooth muscle actin+ (α-SMA) fibrosis-driving cells. Early treatment with MP inhibited fibrosis processes through inhibition of TGF-β expression. Treatment at later phases was not effective.
Conclusions: We developed an in vitro human kidney organoid fibrosis model that recapitulates the key features of kidney fibrosis. MP demonstrated an anti-fibrotic effect at the early phase of the fibrosis process.

OS3_8 HLA-DQ EPLET MISMATCH LOAD MAY IDENTIFY KIDNEY TRANSPLANT PATIENTS ELIGIBLE FOR TACROLIMUS WITHDRAWAL WITHOUT DSA FORMATION AFTER MSC THERAPY

Suzanne Bezstarosti*[1,2], Soufian Meziyerh[2], Marlies Reinders[2], Kim Bakker[1], Koen Groeneweg[2], Dave Roelen[1], Jesper Kers[3], Johan de Fijter[2], Sebastiaan Heidt[1]

[1]Leiden University Medical Center (LUMC), Department of Immunology, Leiden, Netherlands, [2]Leiden University Medical Center (LUMC), Department of Internal Medicine (Nephrology), Leiden, Netherlands, [3]Leiden University Medical Center (LUMC), Department of Pathology, Leiden, Netherlands

Background: Recently, the randomized Triton study demonstrated that mesenchymal stromal cell (MSC) therapy could facilitate early tacrolimus withdrawal in living donor kidney transplant (KTx) recipients. Here, we analyzed *de novo* donor-specific HLA antibody (dnDSA) formation in context of the degree of HLA eplet mismatches (MM).
Methods: All patients underwent a first, living-donor KTx and received alemtuzumab induction, steroids, tacrolimus and everolimus. Patients in the MSC group received 2 infusions of autologous MSC at week 6 and 7 post-KTx. Subsequently, tacrolimus was tapered and completely withdrawn at week 8. HLA-specific antibodies were measured by single antigen bead (SAB) assay; positivity was defined as MFI > 1000. Patients and donors were HLA typed on 11 loci by NGS. Eplet MM were calculated using HLAMatchmaker 2.0.
Results: At 6 months, 7/29 patients (24%) in the MSC group and 1/27 patient (3.7%) in the control group had developed dnDSA. In the MSC group, all dnDSA were anti-HLA-DQ; two patients had anti-DQ alone and five patients combined with anti-class I, HLA-DR or -DP. Despite excess dnDSA formation in the MSC-arm of the study, the evolution of eGFR (CKD-EPI) and proteinuria were comparable 2 years post-Tx. All dnDSA were complement-binding and three patients had antibody-medicated rejection in the protocol biopsy, but overall rejection episodes were not increased. Everolimus had to be discontinued in nine patients due to toxicity, and tacrolimus was reintroduced in six patients because of dnDSA formation. Tacrolimus withdrawal after MSC therapy and HLA eplet mismatches were independently associated with dnDSA (Table 1). A threshold of ≥11 HLA-DQ eplet mismatches predicted subsequent dnDSA in all 11 patients in the MSC group, but specificity was low (44%).
Conclusions: Tacrolimus withdrawal after MSC therapy is associated with an increased rate of dnDSA formation in KTx. Patients with a high HLA class II eplet MM load were less likely to tolerate tacrolimus withdrawal without developing dnDSA, which is in line with previous findings showing that HLA eplet MM load modulates tacrolimus through levels required to prevent dnDSA formation. Further research is warranted to explore HLA molecular mismatch load as a biomarker to guide personalized maintenance immunosuppression in kidney transplantation.

Table 1 Multivariable HRs for dnDSA occurrence

	HR (95% CI)	*P* Value
Model 1		
MSC treatment/Tac withdrawal	4.46 (1.21-16.37)	0.024
HLA Class II eplets (range 8-84)	1.04 (1.01-1.07)	0.004
Model 2		
MSC treatment/Tac withdrawal	4.38 (1.17-16.40)	0.028
HLA-DR eplets (range 0-45)	1.04 (0.97-1.10)	0.282
HLA-DQ eplets (range 0-38)	1.07 (1.02-1.13)	0.008

Risk of transmission of infectious disease and prevention

OS4_1 SHORT-TERM OUTCOME OF TRANSPLANT RECIPIENTS FROM SARS-COV-2-POSITIVE ORGAN DONORS IN GERMANY

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Background: The SARS-CoV-2 pandemic had a major impact on solid organ transplantation in many countries. A significant decline of performed transplantations was described e.g. in Spain and Italy.Until March 2022, SARS-CoV-2-positive organ donors were excluded from organ donation in Germany because of the uncertainty regarding the transmission of the virus from the donor to the recipients. First results from other countries indicated that organs from carefully selected SARS-CoV-2-positive donors could be transplanted with acceptable risk for the recipients.
Methods: From February 25th to December 31th 2022 all SARS -CoV-2 positive donors from whom at least one organ was successfully transplanted to a recipient were identified. An organ donor was identified as SARS- CoV-2 positive, if at least one PCR test from the lower or upper airways was positive in the 14 days prior to organ removal.The follow-up was done within the framework of the vigilance and surveillance system of the German procurement organization (Deutsche Stiftung Organtransplantation/DSO).
Results: During the study period, 163 organs (22 hearts, 3 lungs, 44 livers and 94 kidneys) were transplanted from 57 SARS-CoV-2-PCR-positive donors to 162 recipients. In none of the cases a transmission of the virus from the donor to any of the recipients was detected in a follow up period of 14 days. One patient developed an acute pulmonary failure after heart transplantation and died, four recipients of a liver graft suffered a primary non-function of the liver, three of them died, one was re-transplanted. 21 recipients of kidney grafts (22 %) showed delayed graft function, three more showed primary non-function. In all other recipients immediate organ function was good, there was no indication that organ function was negatively impacted by the SARS-CoV-2 infection of the donor.
Conclusions: These findings support the early experience from other countries that such organs do not pose a major immediate risk for the transplant recipients. Nevertheless, a close follow-up is needed and experiences especially regarding lung transplantation with SARS-CoV-2 positive grafts are still lacking.

OS4_2 KIDNEY TRANSPLANT RECIPIENTS BECOME LESS ADHERENT TO PREVENTIVE MEASURES AFTER SARS-COV-2 VACCINATION AND AFTER AWARENESS OF ANTIBODY RESPONSE

Sophie Frölke*[1], Pim Bouwmans[2], A. Lianne Messchendorp[3], Hanneke Vervoort[3], Pythia Nieuwkerk[1], Marc Hemmelder[2], Ron Gansevoort[3], Luuk Hilbrands[4], Marlies Reinders[5], Jan-Stephan Sanders[3], Frederike Bemelman[1], Suzanne Geerlings[1]

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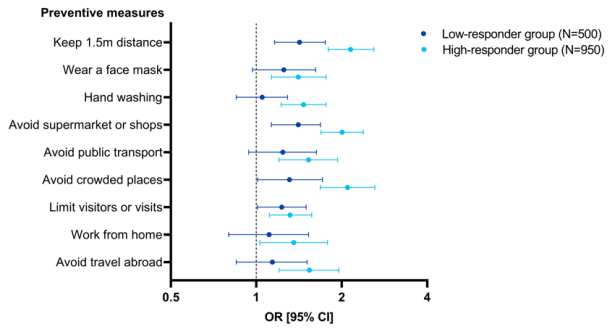
Background: Kidney transplant recipients (KTRs) were advised to tightly adhere to government recommendations to curb the spread of SARS-CoV-2 because of a high risk of morbidity and mortality and decreased immunogenicity after vaccination. The aim of this study was to analyze the change in adherence to preventive measures after vaccination and awareness of antibody response, and to evaluate its effectiveness.
Methods: Questionnaires were sent to 3531 KTRs enrolled in the Dutch RECOVAC studies, retrospectively asking for adherence to nine preventive measures on a 5-point Likert scale before and after SARS-CoV-2 vaccination and after awareness of antibody response. Blood samples were collected 28 days after the second vaccination. Antibody response was categorized as non-responder (≤50 BAU/mL), low-responder (>50 ≤300 BAU/mL) or high-responder (>300 BAU/mL), and shared with participants as a correlate of protection. Adherence before and after vaccination were compared by the Wilcoxon signed rank sum test. Logistic regression analysis was performed to estimate the association between antibody response and adherence, and adherence on acquiring SARS-CoV-2 infection.
Results: In 2939 KTRs (83%) who completed the first questionnaire on adherence to preventive measures, adherence was higher before than after SARS-CoV-2 vaccination (4.56, IQR 4.11-4.78 and 4.22, IQR 3.67-4.67, p<.001). Adherence after awareness of antibody response was analyzed in 2399 KTRs (82%) of whom also blood samples were available, containing 949 non-responders, 500 low-responders and 950 high-responders. Compared to non-responders, low- and high-responders reported lower adherence (Figure 1). Higher adherence was associated with lower infection rates before and after vaccination (OR 0.67 [0.51-0.91], p=0.008 and OR 0.48 [0.28-0.86], p=0.010).
Conclusions: To the best of our knowledge, we are the first to show that adherence decreased after SARS-CoV-2 vaccination and in KTRs who were aware of a subsequent antibody response compared to those without. Moreover, preventive measures in this vulnerable group are effective, regardless of vaccination status.

Figure 1. Forest plot for non-adherence to preventive measures after awareness of antibody response by group, taking the non-responder group as reference (N=949)



OS4_3 VIROLOGICAL & CLINICAL OUTCOMES IN ORGAN RECIPIENTS FROM SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) POSITIVE DECEASED ORGAN DONORS

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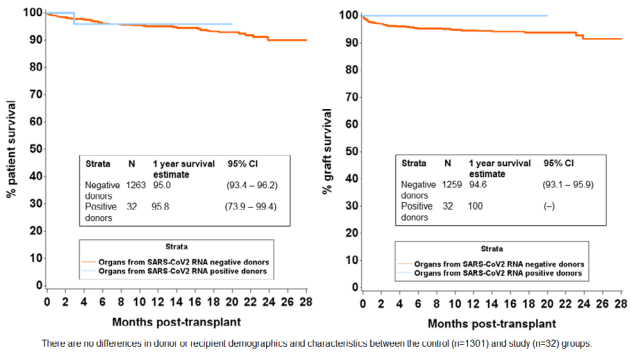
Background/Methods: Nucleic acid testing (NAT) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in upper and lower respiratory tract samples is a prerequisite for deceased organ donation in our country. NAT positive donors are assessed for suitability for organ donation whilst Coronavirus disease 2019 (COVID-19) as a contributory cause of death remains a contraindication for donation. Laboratory proven SARS-CoV-2 infection in deceased donors and solid organ transplant recipients can be captured by national registry linkage. Recipient outcome reports are also received by the national organ donation and transplant organisation at regular intervals. Patients who received organs from donors who tested positive for SARS-CoV2 were compared to a control group whose donors had tested negative at screening, during the same period.
Results: Between March 2020 and December 2022, 5100 potential deceased donors were assessed; 130 tested NAT positive during donor characterisation, with 73 becoming actual donors. 198 organs from these donors were transplanted into 187 recipients (111 kidney-only, 12 simultaneous pancreas-kidney, 42 whole liver, 6 split liver, 1 pancreas, 8 heart, 3 bilateral lungs). Recipients were screened for SARS-CoV-2 infection as per routine local protocols, with no demonstrable cases of donor-derived transmission. Recipient outcome data are being collated and here we present a subset of liver recipients. Analysis of 32 adult liver recipients with a median follow up time of 127 days (interquartile range 87.5–203.5 days), showed no evidence in outcome differences as regards to graft function and patient survival, when compared to the control group. (Figure 1)
Conclusions: Our national experience to date indicates that organs other than lungs can be considered for transplantation from appropriately assessed SARS-CoV-2 NAT-positive deceased donors. There is no evidence of graft-related transmission of infection. A complete data set for recipients of all organ types, with follow-up to or beyond 2 years is being collated; available data does not indicate there is a cause for concern in terms of graft and recipient outcome. It is hoped that such data will help consolidate guidance and increase organ utilization as we transition to the recovery phase of the COVID-19 pandemic.

Figure 1 **Patient and graft survival after a first adult elective liver only transplant from a SARS-CoV2 RNA positive donor, 1 June 2020, 31 August 2022**



There are no differences in donor or recipient demographics and characteristics between the control (n=1301) and study (n=32) groups.

OS4_4 TWO-YEAR FOLLOW-UP OF LIVER GRAFTS FROM COVID-19 DONORS

Margherita Saracco[1], **Donatella Cocchis[2], Francesco Tandoi[2], Federica Rigo[2], Renato Romagnoli[2], Silvia Martini*[1]**

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Background: SARS-CoV-2 infections complicated by thrombosis and secondary sclerosing cholangitis were reported; however, solid non-lungs transplantation from COVID-19 donors showed excellent early results, but medium/long-term data are lacking. We aimed to describe the outcome of our LT patients (pts) who received a graft from COVID-19 donors.
Methods: We consecutively enrolled all pts transplanted in our Center from 11/2020 to 03/2022 who received a liver graft from COVID-19 donors. Pts underwent protocolar liver biopsy and magnetic resonance cholangiopancreatography (MRCP) after at least 1 year from LT. Follow up was closed in January 2023.
Results: In the study period, among 213 adult LTs, 12 (5.6%) received a COVID-19 donor (11 active and 1 resolved COVID-19)[1]. Recipients' and donors' characteristics are reported in table 1. None of the pts developed COVID-19 after LT. Two recipients tested SARS-CoV-2 RNA positive in nasopharyngeal swab immediately before LT and one was treated with sotrovimab on day-1 after LT. Eleven pts underwent end-to-end biliary anastomosis and 1 biliodigestive anastomosis. One pt underwent successful hepatic artery thrombectomy at day-1. Eleven pts underwent protocolar MRCP (median time from LT 573 days, IQR 290-648), which showed: no visible abnormalities in 8, 1 donor-recipient's bile duct size discrepancy, and 2 caliber changes <50% at anastomotic level (without cholestasis and which were not treated). Ten pts underwent liver biopsy (median time from LT 557 days, 391-682) which showed 1 acute rejection (RAI 4/9) successfully treated with steroids and no signs of rejection, biliopathy or fibrosis in the other 9. After a median time from LT of 669 days (344-737) 11 pts are alive and 1 died after 320 days for hepatocellular carcinoma recurrence.
Conclusion: After a median time from LT of 1.8 years, 11/12 pts who received a liver graft from COVID-19 donors are alive, without evidence of SARS-CoV-2 RNA transmission. Protocolar MRCP and liver biopsy did not show signs of biliopathy or fibrosis supporting the safe utilization of COVID-19 donors to expand the donor pool and reduce the waiting list mortality.
[1]Peghin M, Grossi PA. J Hepatol. 2022

Table:

	Recipients n = 12	Donors n = 12
Age, years	61 [56-65]	59 [52- 63]
Sex, male	9 (75%)	8 (67%)
Body mass index, kg/m^2	27 [24-28]	25 [24-27]
Hepatocellular carcinoma	9 (75%)	NA
Model for end stage liver disease at LT	10 (8- 14)	NA
SARS-CoV-2 vaccination before LT	4 (33%)	1 (8%)
SARS-CoV-2 IgG positive before LT	12 (100%)	1 (8%)
SARS-CoV-2 RNA swab positive at LT	2 (17%)	2/3 (67%)
SARS-CoV-2 RNA BAL positive at LT	NA	9/9 (100%)
Donor risk index	2 (1.6-2.2)	
SARS-CoV-2 RNA PCR negative on liver biopsy	11/11, 100%^	
Hypothermic machine perfusion	3 (25%)	
Normothermic machine perfusion	1 (8%)	

Table 1. Pts' and donors' characteristics at liver transplant. ^The COVID-19 resolved donor was not tested.

FULL ORALS

Risk of transmission of infectious disease and prevention

OS4_5 CELLULAR HUMORAL MEMORY PROTECTS TRANSPLANT RECIPIENTS FROM EMERGING SARS-COV-2 VARIANTS OF CONCERN THAT RESIST CIRCULATING NEUTRALIZING ANTIBODIES

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Background: The protection of vaccinated KTRs against COVID-19 depended upon the generation of neutralizing antibodies (Nabs). However, the decrease of antibody titers with time as well as the emergence of variants of concern (VOC) create a situation in which even KTRs that responded to vaccine are left without serological protection after a few months.
Methods & Results: The severity of 211 infections with the Omicron BA.1 VOC, diagnosed in a cohort of vaccinated KTRs, was stratified according to i) the peak of Nabs, and ii) the Nabs status immediately prior the omicron infection. As expected, responders to the vaccination who maintained high titers of NAbs at the time of BA.1 infection never (0/22) developed severe disease, while patients who did not respond to vaccination (never had detectable Nabs) developed severe infections in 31/110 (28%). Surprisingly, among the 59 patients who initially responded to vaccination but had no longer NAbs at the time of BA.1 infection, only 3/59 (5%) developed a severe COVID-19, suggesting that they benefited from a remanent vaccinal protection independent of Nabs.
In order to identify the mechanisms underlying Nabs-independent late vaccinal protection, the humoral immune effectors specific for Wuhan (vaccinal strain) and BA.1 (VOC that they never seen) were enumerated at the peak and >6 months post-vaccination in an independent cohort of 34 vaccinated KTRs. Viral seroneutralisation assay against Wuhan was used to identify the responders (Nabs at peak) vs non-responders to vaccine. At 6 months, Wuhan-specific memory B Cells (mBC) were detected by ELISPOT in the circulation of 16/19 (84%) of responders versus 2/14 (14%) of non-responders, suggesting that mBCs are generated during the same vaccine-induced germinal center reaction as NAbs. Importantly, while only 2/20 responders had Nabs able to neutralize BA.1 at 6 months, 53% of mBCs at this time point were directed against BA.1.
Conclusion: We concluded that in contrast with the humoral serological memory that goes fading due to a decrease in Nabs titer and a narrowing of the Ig repertoire, a diverse pool of memory B cells persist over time offering an efficient long term protection to KTRs against VOC.

OS4_6 THE HUMORAL RESPONSE TO COVID-19 VACCINATION OF KIDNEY TRANSPLANT RECIPIENTS IS PREDICTIVE OF SURVIVAL AFTER SARS-COV-2 INFECTION

Markus Hovd*[1;2], Karsten Midtvedt[1;2], Fridtjof Lund-Johansen[2;3], Kristian Heldal[1;2], John Torgils Vaage[2;3], Ludvig Munthe[2;3], Anders Asberg[1;2]

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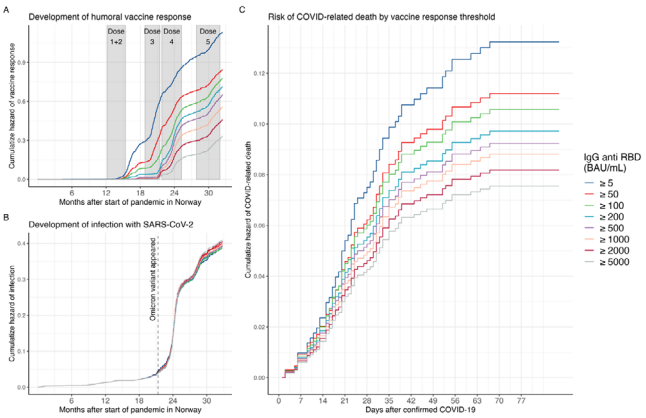
Background: Kidney transplant recipients (KTR) are more susceptible to infections and prior to introduction of SARS-CoV-2 vaccines had a very high mortality from COVID-19. The coronavirus vaccination programme aimed to reduce the spread and severity of COVID-19, especially in high-risk groups. KTR had a reduced humoral vaccine induced response and repeated vaccinations were warranted. In a national cohort, we here evaluate the monitored effect of humoral vaccine response on risk of SARS-CoV-2 infection and COVID-19 related death.
Methods: All KTR in Norway who were alive with a functioning graft at the beginning of the pandemic (February 20th, 2020) were included in the analysis. Event history analysis of vaccination, monitored vaccine response, infection with SARS-CoV-2, COVID-related and -unrelated death was analysed using a multi-state, competing risk model approach combined with Cox proportional hazard regression. Events after November 11th, 2022 were right-censored. Vaccine response was determined towards the receptor binding domain (RBD) of Spike; IgG anti-RBD BAU/mL above threshold was evaluated within the range of 5 to 5000 BAU/mL.
Results: A total of 3607 KTR (64% male, age 58±14 years) were included, of which 38% had received a kidney from a living donor. During the study period, 28% (n = 1018) of vaccinated KTR developed breakthrough infection. In total 7% (n = 74) died due to COVID-19 (63 following vaccination). Cumulative incidence of vaccine response increased with each additional dose (Fig. 1A), but risk of infection was unaffected by vaccine response (Fig. 1B). Increased vaccine response was associated with reduced risk of COVID-related death (Fig. 1C), and poor responders (< 5 BAU/mL) had a relative risk of death of 1.7 compared to good responders (>5000 BAU/mL) 40 days post-infection. Following infection, the 1-year cumulative hazard of non-COVID-19 related death in survivors (0.036 [95% CI: 0.024, 0.054], n = 30) was not different from that in KTR without any history of infection (0.043 [95% CI: 0.036, 0.050], n = 405).
Conclusions: In KTR, humoral vaccine response does not protect against infection with SARS-CoV-2. Yet, increased vaccine response, assessed by IgG anti-RBD BAU/mL level after vaccination, protected against COVID-related death. No excess post-COVID mortality was detected in KTR.



OS4_7 SARS-COV-2-SPECIFIC IMMUNOLOGICAL MEMORY PREDICTS SUCCESSFUL BOOSTER IMMUNIZATION AND SEVERE COVID-19 IN SOLID ORGAN TRANSPLANT PATIENTS

Laura Donadeu*[1], Susana Gomez-Olles[2;3], Elena Crespo[1;4], Manuel López Meseguer[2;3;5], Laura Llado[6], José Gonzalez-Costello[7], Isabel Campos[8;9], Alexandre Favà[10], Marina Muñoz[11], Jesús Quintero[12], Maria Francesca Cortese[13], Alba Torija[1], Maria Meneghini[1;14], Delphine Kervella[1], Francesc Moreso[14], Oriol Bestard[1;14]

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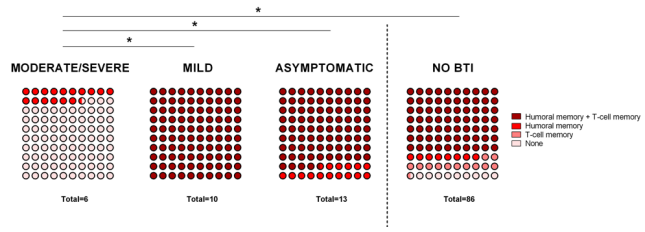
Background: Immune correlates of successful immunization and protection against COVID-19 are highly needed in Solid Organ Transplant (SOT), to establish individualized preventive strategies.
Methods: In a large, prospective, multicentre study, we investigated the kinetics, interconnection, and protective role of main SARS-CoV-2-specific immune memory compartments (antigen-specific neutralizing antibodies (NAb), memory B and Th1/Th2 cells) in peripheral blood from SOT and immunocompetent (IC) individuals undergoing three doses of COVID-19 mRNA vaccine. The study involved 836 samples from 148 SOT and 32 IC assessed at 5 time points.
Results: SOT recipients displayed significant delayed and weaker responses at all memory compartments than IC (45% and 65% SOT, versus 88% and 100% IC, p<0.001, showed complete detectable responses at all memory compartments after a 2nd and 3rd dose, respectively). A strong correlation was observed between all immune responses at each time-point and over time (p<0.001), and were challenged by recipient age, time after transplant and MMF-based therapy, but not by type of SOT or mRNA vaccine. While serological memory tended to diminish between 2nd and 3rd vaccine (p<0.005), memory B and T-cell compartments remained steadily active. IgG-producing memory B cells and Spike-specific IL-2-producing T cells prior to booster vaccination independently predicted successful NAb responses (AUC 0.828). Notably, SOT recipients developing severe breakthrough COVID-19 despite three booster vaccinations were unresponsive at most immune compartments (Fig. 1), especially at the memory B-cell and IL-2-producing T-cell levels (mBc (0 [0-0.0004] vs. 0.238 [0.098-0.482], p<0.001), IL-2 T-cell (1 [0-4.75] vs. 59 [21-104.75], p=0.001 for severe and asymptomatic BTI, respectively; mBc (0 [0-0.0004] vs. 0.096 [0.023-0.292], p=0.004), IL-2 T-cell (1 [0-4.75] vs. 47 [15.75-88.38], p=0.004) for severe and mild BTI, respectively).

Risk of transmission of infectious disease and prevention

Conclusions: Our data has relevant clinical implications for immune-risk stratification against COVID-19 and may guide preventive strategies in SOT. Here we show the particular relevance of measuring mBc and memory T cells producing IL-2 to identify patients more likely to respond to a booster vaccine and those at high risk of developing severe forms of COVID-19.



OS4_8 HEPATITIS E VIRUS (HEV) INFECTION IN DECEASED ORGAN DONORS – OBSERVATIONS FROM THE FIRST 5 YEARS OF UNIVERSAL SCREENING

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Background: Universal HEV RNA screening of deceased organ donors was implemented by our national organ procurement organisation in 2017. Post-transplant donor testing for HEV Ribonucleic Acid (RNA) is done centrally and allows recipient follow up and management, with the aim to avoid chronic HEV infection due to inadvertent graft-related transmission of infection.
Methods: The outcome of donor screening and impact on recipients of organs from donors with detectable viremia is hereby summarised. All transplant centres are notified of positive donor results in real time and advised to commence testing, with hepatology referral if found to be viraemic. The outcome of each recipient is recorded centrally.
Results: 9500 deceased potential organ donors were screened between October 2017 and October 2022, with 9 confirmed viraemic cases identified; this incidence of 0.94 per 1000 is 4 times higher than that seen in our blood donor population. Eight proceeding donors, with plasma viral load (VL) ranging from 100 to 270,000 IU/ml, donated 14 kidneys and 6 livers to 20 recipients. All liver recipients became infected regardless of the donor's plasma VL value. 8 kidney recipients became infected, 4 did not and information is awaited from one. Recipient infection was also documented in the presence of pre-existing HEV antibodies. All infected recipients received ribavirin; time to achieve sustained viral clearance in plasma and stool ranged from less than 3 and up to 24 months. Rapid viral clearance was observed in two liver recipients who were commenced on ribavirin immediately upon detection of viraemia, in contrast to those who were treated after 12 weeks from first positive result.
Conclusions: Immediate post-transplant detection of donor HEV viraemia triggers notification to transplant centres. Transmission through solid organs is very efficient, with 100% observed rate through liver grafts, even in the presence of pre-existing specific antibodies. Donor plasma VL seems to influence transmissibility through infected kidneys, but transmission was documented even with low VL values. Knowledge of donor HEV status allows targeted testing and identification of recipient infection, mitigating the risk of accelerated inflammatory liver changes seen in chronic infection in immunosuppressed individuals.

Managing myself after transplantatin- a fulltime job

OS5_1 SYMPTOM BURDEN IN KIDNEY TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL STUDY

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Background: Kidney transplant recipients (KTR) often report a poor health-related quality of life (HRQoL), which may partly be attributable to symptoms caused by kidney disease or treatment after kidney transplantation. We therefore aimed to assess symptom prevalence, symptom distress, and symptom burden, which is a combination of prevalence and distress, in a large cohort of KTR. Furthermore, we aimed to assess associations of symptom burden with clinical outcomes, such as HRQoL, medication adherence, depression, and societal participation.
Methods: Data of KTR at least 6 months after transplantation, enrolled in the TransplantLines Biobank and Cohort Study between June 2015 and February 2022, were used. Symptoms were assessed using the revised Modified Transplant Symptom Occurrence and Distress Scale (MTSOSD-59R). RIDIT analyses, an effective technique to analyse ordered categorical data, was performed to calculate RIDIT scores of symptom prevalence and symptom distress. Symptom burden was calculated by multiplying symptom prevalence by symptom distress. HRQoL was assessed using the Short-Form 36.
Results: We included 936 KTR (39% female; mean age 56 ± 13 years) at median [IQR] 2 [1 to 9] years after transplantation. Tiredness, bruises, and lack of energy were the most prevalent symptoms (Figure 1). Menstrual problems (female), impotence (male), and joint pain were the most distressful symptoms. Bruises, lack of energy and tiredness were the most burdensome symptoms. In linear regression analyses, higher burden scores were associated with both lower mental and physical HRQoL (β -3.00, 95% CI -3.32 to -2.67, p<0.001; β -2.29, 95% CI -2.56 to -2.03, p<0.001; respectively; Table 1). In regression analyses, higher burden scores were strongly associated with medication non-adherence, depression, and less societal participation. All results remained significant after adjustment for potential confounders.
Conclusions: Symptoms after transplantation are a major clinical problem among KTR, and the burden of symptoms is strongly associated with lower HRQoL, less medication adherence, more depression, and less societal participation. Our findings highlight the need to reduce symptom burden in KTR, for instance by individualizing immunosuppression.

Table 1 | Linear regression analyses of squared root symptom burden with health-related quality of life as dependent variable in 740 kidney transplant recipients

Model	Physical component scale		Mental component scale	
	B (95% CI)	P-value	B (95% CI)	P-value
Crude	-3.00 (-3.32 to -2.67)	<0.001	-2.29 (-2.56 to -2.03)	<0.001
Model 1	-3.03 (-3.36 to -2.71)	<0.001	-2.30 (-2.57 to -2.03)	<0.001
Model 2	-3.00 (-3.33 to -2.68)	<0.001	-2.31 (-2.58 to -2.03)	<0.001
Model 3	-2.94 (-3.27 to -2.61)	<0.001	-2.29 (-2.57 to -2.01)	<0.001
Model 4	-2.93 (-3.26 to -2.60)	<0.001	-2.30 (-2.59 to -2.01)	<0.001
Model 5	-2.91 (-3.25 to -2.58)	<0.001	-2.29 (-2.58 to -2.00)	<0.001

Abbreviations: 95% CI: 95% confidence interval. **Model 1**: adjusted for age and sex; **model 2:** model 1 + time since transplantation; **model 3**: model 2 + polypharmacy, diabetes and anaemia; **model 4:** model 3 + haemoglobin, eGFR, albumin and NT-pro-BNP; **model 5:** model 4 + tacrolimus use, cyclosporine use, prednisone or prednisolone use and proton pump inhibitor use.

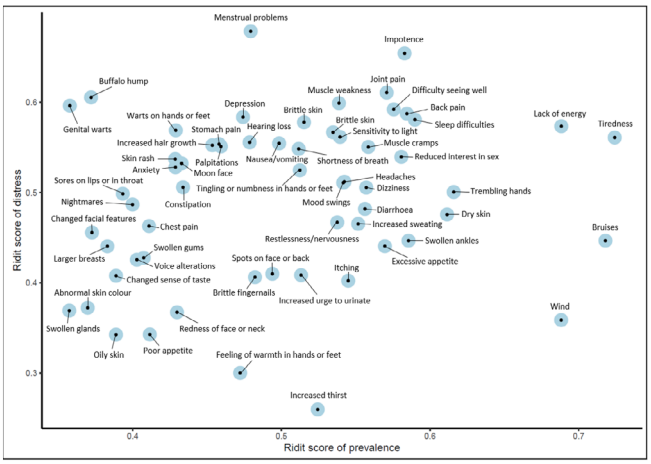

Figure 1 | RIDIT score of symptom prevalence and symptom distress of 60 symptoms of the MTSOSD-59R

OS5_2 THE LONGITUDINAL DEVELOPMENT OF TRANSPLANT SPECIFIC WELL-BEING AND PROMINENT SYMPTOMS FROM PRE-TRANSPLANT TO FIVE YEARS AFTER HEART TRANSPLANTATION

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Background: The Swedish multicentre "Self-management after thoracic transplantation" study (SMATT) has until now produced 23 papers, two doctoral theses and numerous master theses focusing on symptom burden and barriers for self-management among heart and lung recipients. Findings have revealed that the post-transplant adaptation is challenging involving an extensive symptom burden, fatigue, and chronic pain. The designs have either been cross-sectional or qualitative and longitudinal. Now it is time to present the first data from the longitudinal cohorts. Thus, the aim of this study was to analyse and present prospective data on chronic pain, fatigue and transplant specific wellbeing from pre-transplant to five years after heart transplantation (HTX).
Methods: This prospective study involves the first 31 heart recipients, 80 % men and 20 % women, followed for five years from pre-transplant to five years after heart transplantation. The inclusion criteria were being a heart or lung recipient transplanted at either of the two Thoracic transplant centres in Sweden performing thoracic transplantation, Swedish speaking, not hospitalized nor in treatment of on-going acute rejection and mentally lucid. We used non-parametric statistics to analyse the Organ Transplant Symptom and Well-being Instrument, the Pain-O-Meter and the MFI-19 measuring fatigue.
Results: Chronic pain evolves two years after HTX compared to pre-tx (p=.054) and even worse after three years (p=.017) involving severe joint and muscle pain and foot pain. There were no differences in transplant specific well-being after three and four years compared to pre-tx. It takes one year to experience decreased mental fatigue. The level of mental fatigue then remains stable until five years post-transplant when the fatigue is equal to pre-transplant again.
Conclusions: The findings confirm previous results from the SMATT-study showing that chronic pain is a major concern after HTX along with fatigue. It is obvious that the pain problems accelerate two-four years post-transplant. Transplant specific well-being is the same as pre-transplant three to four years after HTX. Chronic pain and fatigue remain the most prominent concerns up to five years after heart transplantation and needs specific attention from the transplant professionals.

OS5_3 QUANTITATIVE FINDINGS FROM THE COMPASSIONATE MINDFUL RESILIENCE PROGRAMME IN ADULT PATIENTS WITH CHRONIC KIDNEY DISEASE (THE COSMIC STUDY)

Anna Wilson*[1], Clare Mckeaveney[1], Claire Carswell[1], Karen Atkinson[2], Stephanie Julie Burton[1], Clare Mcveigh[1], Lisa Graham-Wisener[1], Erika Jaaskelainen[3], William Johnston[4], Daniel O'rourke[5], Joanne Reid[1], Soham Rej[6], Ian Walsh[1;7], Helen Noble[1]

[1]Queen's University Belfast, Belfast, United Kingdom, [2]MindfulnessUK, Taunton, United Kingdom, [3]University of Oulu, Oulu, Finland, [4]Northern Ireland Kidney Patients Association, Belfast, United Kingdom, [5]Northern Ireland Kidney Patients Association, Belfast, United Kingdom, [6]McGill University, Montreal, Canada, [7]Kingsbridge Private Hospital, Belfast, United Kingdom

Quantitative findings from the COmpassionate Mindful ReSilience PrograMme in Adult Patients with Chronic Kidney Disease (The COSMIC Study)

Background: People with advanced kidney disease face multiple challenges associated with the disease and associated treatments including difficult symptoms such as anxiety and dperession1. This study aimed to examine the initial effect of the Compassionate Mindful Resilience (CMR) programme for patients with stage 4 or 5 chronic kidney disease including those who had received a kidney transplant, in collaboration with Kidney Care UK (KCUK).
Methods: A single group, quasi-experimental study was conducted. Participants with stage 4 or 5 kidney disease, or post-transplant, were recruited to take part in the CMR programme via a KCUK email newsletter and their patient support Facebook group. Power analysis was used to estimate an adequate sample size of 75 patients. Participants attended the 4-week, group-based programme online, with trained mindfulness teachers. Eight CMR groups took place between June, July and October of 2022 and the study completed in February 2022. Anxiety, depression, self-compassion, the ability to be mindful, wellbeing, and resilience were measured at baseline, completion of programme and at 3-months post using the GAD-7, PHQ-9, self-compassion scale - short form (SCS-SF), Five Facet Mindfulness Questionnaire (FFMQ), Warwick–Edinburgh Mental Well-Being Scale (WEMWBS) and Mental Toughness Questionnaire (MTQ48).
Results: In total, 66 participants completed the programme. Most were female (66%) and post-transplant (63%). As compared to pretest scores, participants reported a reduction in anxiety and depression and improvement in self-compassion, mindfulness, resilience, and wellbeing.
Conclusions: Our findings suggest that the CMR programme had the potential to improve psychological outcomes among people with advanced kidney disease. Future randomized controlled trials are required to further test its effectiveness.
Hackett, M.L.; Jardine, M.J. We need to talk about Depression and Dialysis: But what questions should we ask, and does anyone know the answers? Clin. J. Am. Soc. Nephrol. 2017, 12, 222–224

OS5_4 MEDITERRANEAN DIET AND METABOLIC SYNDROME: A DIETARY INTERVENTION STUDY TO REDUCE METABOLIC SYNDROME RISK AFTER HEART TRANSPLANTATION

Michela Marinoni*[1], Veronica Ferrara[1], Giulia Valdi[2], Chiara Nalli[1], Concetta Di Nora[1], Sandro Sponga*[1;2], Giovanni Benedetti[1], Ugolino Livi[1;2], Maria Parpinel[2], Igor Vendramin[1]

[1]University Hospital of Udine, Cardiothoracic Department, Udine, Italy, [2]University of Udine, Department of Medicine , Udine, Italy

Background: heart-transplanted (HTx) patients are inclined to develop the Metabolic Syndrome (MetS), mainly due to the side effects of immunosuppressive therapy. The Mediterranean Diet (MD) has proven to be effective preventing MetS in general population. Thus, the aim of the study was to assess the impact of a dietary intervention based on MD principle in HTx patients with high risk of MetS.
Methods: at baseline (T0), after 6 (T1), and 12 months (T2) patients were invited to compile a 4-day dietary record (4dDR) to bring at the scheduled visits. During the meetings, a nutritionist detected dietary habits and provided personalised nutritional advices, monitoring the improvement during the follow-ups. At each timepoint, clinical, anthropometric, and body composition data were assessed. To estimate nutrient intakes from 4-dDR was used The Italian Food Composition Database (BDA). The study was approved by the Regional Ethics Committee.
Results: at T0, 50 patients were enrolled, 30 of them have reached the T1, and 17 the T2. The mean age of the subjects was 57±13 years (males: 87%). During the study period, dietary habits showed: a significant increase of the MD score [T0=4.5 (3.0 – 5.0) vs. T2=6.0 (4.0 – 7.0); p=0.004]; a significant decrease of daily total energy intake and, in particular, of total fats and saturated fatty acids [T0=18.5 (15.6 – 24.8) g/day vs. T1=16.3 (12.6 – 19.5) g/day; p=0.001]; a significant increase of fiber, vitamin E, and DHA intakes between T0 and T2. Together with the improvement of dietary habits, body composition showed already at T1 a significant decrease of fat mass (%) (T0=22.3 ± 7.7 vs. T1=18.3 ± 7.8; p=0.002), and a significant increase of fat free mass (%) (T0=77.5 ± 7.9 vs. T1=81.4±8.2; p=0.002). Furthermore, MetS diagnosis criteria improved at each timepoint and its prevalence showed an important reduction from 50% at T0, to 37% at T1, to 29% at T2.
Conclusions: the dietary intervention providing personalized dietary advices exerted multiple beneficial effects on MD adherence, body composition, and MetS criteria of HTx patients.

OS5_5 THE EFFECT OF SYSTEMCHANGE™ ON MEDICATION ADHERENCE IN KIDNEY TRANSPLANT RECIPIENTS: A RANDOMIZED CLINICAL TRIAL

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[1]Dokuz Eylul University, Nurisng Faculty, Izmir, Turkey, [2]Medicana Hospital, Nephrology Department, İzmir, Turkey, [3]Izmir University of Economics, Faculty of Health Science Department of Nursing, İzmir, Turkey, [4]University of Missouri-Kansas City, School of Nursing and Health Studies , Kansas City, MO, United States

Background: The SystemCHANGE™ intervention harnesses patients' established daily routines/habits, environment, and important others, as possible solutions that are reoccurring and thus reliable systems that could support medication taking to become a dependable routine/habit. The aim of this study was to evaluate the effect of a six -month SystemCHANGE™ intervention compared to a six-month attention-control education intervention on medication adherence and quality of life in kidney transplant recipients. A six-month maintenance phase where the intervention was withdrawn was also evaluated.
Methods: A randomized controlled trial single-blind (participants) study design was used. After screening for 3 months using electronic monitoring, participants with medication adherence (>.85) were excluded from the study while those with medication nonadherence (</= .85) were randomized. the intervention group (n= 42) received the 6-month SystemCHANGE ™ intervention and the attention control group (n= 42) received the 6-month patient education intervention. The maintenance phase continued for six months afterwards. Electronic monitoring was used to measure medication adherence.
Results: At the completion of the six-month intervention phase, there was a statistically significant difference in medication adherence between the SystemCHANGE™ (median 0.97, IQR 0.93 -0.98) and attention control (median 0.81, IQR 0.71-0.87) groups (U= 4.190, p< .001). At the completion of the 6-month maintenance phase, the statistically significant difference was maintained between the SystemCHANGE™ (median 0.94, IQR 0.81-0.96) and attention control (median 0.76.00, IQR 0.69-0.86) groups (U= 2.843, p< .004, Table 1, Figure 1). There was no difference in the quality of life between groups (p> 0.05).

Conclusion: This study, which had a strong research design, showed that the SystemCHANGE™ intervention was effective in improving patients' medication adherence and outcoes.

Table 1. Comparison of in-group and intergroup adherence levels

	SystemCHANGE™			Attention control				
	N	X̄ ± SD	Median (IQR)	N	X̄ ± SD	Median (IQR)	Test value	p[1]
Baseline	21	0.74 ± 0.11	0.77 (0.72-0.83)	21	0.75 ± 0.13	0.79 (0.72-0.84)	-0.787[u]	0.431
6 months	21	0.93 ± 0.09	0.97 (0.93-0.98)	21	0.77 ± 0.14	0.81 (0.71-0.87)	**4.190[u]**	**<0.001***
12 months	21	0.87 ± 0.13	0.94 (0.81-0.96)	21	0.77 ± 0.12	0.76 (0.69-0.86)	**2.843[u]**	**0.004***
Test value	**31.924[f]**			0.105[f]				
p[2]	**<0.001*, 6 month> 12 month > Baseline**			0.949				

p<0.05; p[1]= intergroup comparison; p[2]: in-group comparison; U: Mann Whitney U test; f: Friedman test

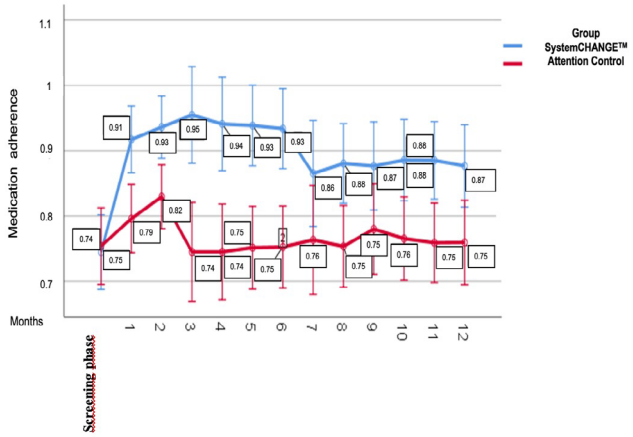

Figure 1. Pattern þf intervention and control group medication adherence levels by months

OS5_6 NURSE-LED SELF-MANAGEMENT SUPPORT AFTER ORGAN TRANSPLANTATION – A MULTICENTER, MULTI-ORGAN STEPPED WEDGE RANDOMIZED CONTROLLED TRIAL

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Background: After organ transplantation effective self-management skills are essential to deal with medical, emotional and role challenges and for optimal clinical outcomes. However, effective interventions to support post-transplant self-management are lacking. The aim of this study was to implement and test effectiveness of a nurse-led intervention to promote self-management skills among heart, kidney, liver and lung transplant recipients in comparison to standard care.
Methods: This multi-centre stepped wedge randomized controlled trial was performed at 6 departments of 5 University Medical Hospitals between September 2020 and November 2022. All departments started in the control group after which the departments were randomly assigned to a start date to commence the experimental group. Before starting the experimental phase the nurse practitioners were trained in delivering the intervention. Patients in the control group received care as usual and completed questionnaires at baseline (T0) and after 6 months (T1). Patients in the experimental group received standard care plus the ZENN intervention and the same questionnaires at T0 and T1. The primary outcome was the Skills and technique acquisition scale of the HeiQ. Secondary outcomes included medication adherence.
Results: The majority of the participants in both control and intervention groups (n=105 vs n=65) were male 68% vs. 55%), had a lower education (40% vs. 43%), had a kidney transplantation (86.7% vs. 83%). The mean age was 53 years old. At baseline (T0) the experimental group scored significantly lower than the control group on self-management skills. Self-management increased between T0 and T1 among the experimental group (p = .03) whereas there was no significant change over time in the control group. There was no significant difference between the control and intervention group at T1 (p = .80). At T1 29.4% of the recipients in the control group did not adhere to their medication, and for the intervention group this was 22.9% (p = .46).
Conclusions: Selection bias appears to have occurred in recruitment of the experimental group. This group benefitted from the intervention self-management skills improved. Preliminary results suggest that among recipients who have difficulties with self-management this intervention may be of added value.

OS5_7 A RANDOMIZED CONTROLLED STUDY OF TELEMONITORING IN KIDNEY TRANSPLANT RECIPIENTS : INTERIM RESULTS OF THE AP'TX TRIAL

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Background: Telemedecine is a matter of growing interest in transplantation. However, its real added value is uncertain. In 2018, we have started to study the medico-economic impact of a less stringent on-site follow-up of our kidney transplant recipients (KTR) using Ap'Telecare®. We present here a preliminary report focusing on 330 KTR with a 2 years follow-up.
Methods: The Ap'Tx study (NCT03750331) is a prospective controlled randomized trial testing the hypothesis that monitoring stable KTR (at least 3 months after transplantation) with Ap'Telecare® is non inferior as compared to a conventional follow-up in terms of the occurrence of graft dysfonction (defined as a decrease in eGFR of 20% or more). On-site consultation scheduling was 2 times less frequent for KTR followed by Ap'Telecare®. Secondary endpoints were the impact of a remote follow-up by Ap'Telecare® on medical workload, economic saving and quality of life.
Results: Six hundred and fifty eight KTR have been randomized so far with 330 of them having a follow-up of 2 years. Among all KTR approached to participate in the study, 37% were not included mainly due to the impossibilty to access internet (44%) or to masterize the app (36%). After randomization, 27% of KTR were considered as non compliant in adequately using Ap'Telecare®. Over the 2 years study duration, graft dysfunction occurred in 16% and 18% of KTR in the Ap'telecare® and conventional arm, respectively (RR of 0.87 (0.56 ; 1.39), non-inferiority confirmed, superiority not significant). Medical time dedicated to handling daily lab results was decreased by a factor 3 for KTR using Ap'Telecare®. Rates of unplanned consultations and hospitalisations were reduced by 26% and 32% for patients using Ap'Telecare®, respectively (p<0.05).
Conclusions: This preliminary report of Ap'Tx suggest that a partial and reasonable remote follow-up of selected KTR is feasible, safe and logistically beneficial. Determining the nature of factors associated with a wider implementation of Ap'Telecare® is underway.

OS5_8 UPTAKE OF HOME-MONITORING AFTER KIDNEY TRANSPLANTATION: A RETROSPECTIVE ANALYSIS

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Background: Innovations in telemedicine, such as teleconsultations and home-monitoring of clinical parameters, are rapidly developing in the field of transplantation, accelerated by the COVID-19 pandemic. In order to facilitate monitoring and treatment at home during the pandemic, we implemented the 'SelfCare after Renal Transplantation' (SeCReT) box and a smartphone application (Luscii®) with a custom made protocol and integration to the electronic patient file (HIX® by Chipsoft). In this study we evaluated uptake and use of this home-monitoring system after kidney transplantation.
Methods: We performed a retrospective analysis of enrollment into the home-monitoring program. The SeCReT-box contained medically certified devices such as a thermometer, pulse-oximeter, weighing scale and blood pressure monitor. All de novo kidney transplant recipients were considered eligible for inclusion, without upfront exclusion criteria. The protocol in Luscii® included measurements (SeCReT-box), questionnaires (on wound healing, pain, stool frequency, smoking, sexual problems, adherence via BAASIS® and satisfaction with the home-monitoring program) as well as info on various topics after kidney transplantation. The frequency of measurements decreased as time after transplantation passed.
Results: A total of 177 patients underwent kidney transplantation of which 167 (94% of all recipients) initiated the home-monitoring program, of which 155 used both the SeCReT-box and Luscii®. 12 patients used only the SeCReT-box, mainly due to digital illiteracy or lack of a smartphone, and wrote their measurements on paper. Of the 167 recipients that initiated home-monitoring, only 4 (2.4%) stopped using the SeCReT-box and/or Luscii® deliberately. Currently there are 142 active users, 8 recipients stopped due to graft failure, 3 recipients died and 10 recipients stopped because they were referred back to their local hospital. In all, 9 of 177 recipients (5.1%) could not start, or stopped home-monitoring deliberately. An in-depth analysis of usage is ongoing.
Conclusions: Uptake and continued use of home-monitoring was very high (95%) among this varied group of kidney transplant recipients. Further analysis is needed on barriers and facilitators of its use, in order to reach a more widely adopted use.

FULL ORALS

Improving outcomes of end-stage heart: instead of MCS to the long-term

OS6_1 5-YEAR OUTCOME AFTER CONTINUOUS FLOW LVAD WITH FULL-MAGNETIC VS HYBRID LEVITATION SYSTEM:RESULTS OF AN ALL-COMERS MULTICENTER REGISTRY

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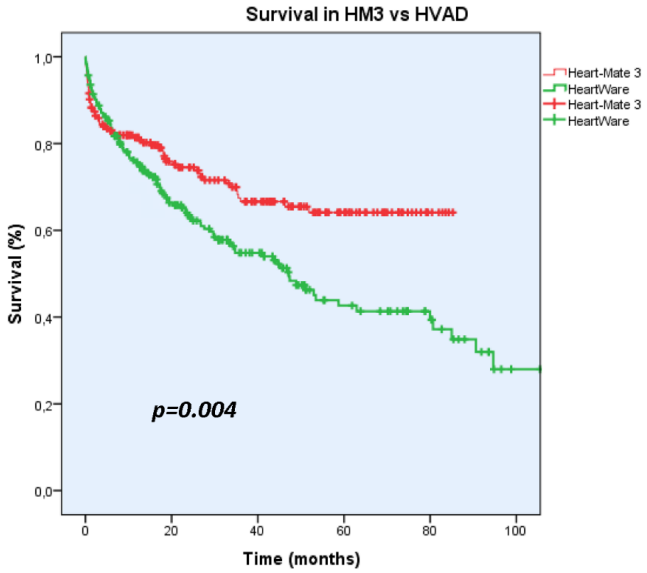
Background: Despite its withdrawal, hundreds of patients are still supported with HeartWare(HW) and a consensus about the long-term management of these patients is still questioned. Published data have focused on short-term outcome. It is the aim of this study to analyse mid-term survival and freedom from major complications in a real-world population supported with HW and HeartMate3 (HM3).
Methods: From 2010 to 2022, the MIRAMACS Italian Registry enrolled all-comer patients requiring third generation LVAD support (HM3 or HW) at seven Cardiac Surgery Centres. Adverse events were defined according to INTERMACS definitions. A Cox-regression analysis adjusted for preoperative confounders was performed to compare survival and freedom from major adverse events at 5 years of follow-up.
Results: A total of 447 patients were implanted with LVAD because of end-stage heart failure: 214 HM3 and 233 HW. The two populations differed in age, heart failure etiology, body surface area, renal and hepatic dysfunctions, degree of pulmonary hypertension. Periprocedural mortality (14% vs 9% for HM3 vs HW; p=0.1) and most of post-operative complications rates were similar between the two groups. The overall survival at 5 years was higher in HM3 patients (64.1% vs 42.6% for HM3 vs HW, p=.004) [Figure]. The Cox-regression analysis adjusted for major confounders showed an almost doubled risk for mortality (HR 1.5 [1.2-1.9]; p=0.031), and a more than doubled risk for both ischemic stroke (HR 2.08 [1.06-4.08]; p=.033) and hemorrhagic stroke (HR 2.6 [1.3-4.9]; p=.005) in patients supported by HW. Moreover, HW patients experienced a higher rate of pump thrombosis (3.9% vs 0.5%; p<.001). Subanalysis in Bridge-to-Transplant reported similar cumulative survival and freedom from adverse events, though time to transplant was shorter in HW (32.2 vs 49.1 months; p=0.001). In Destination Therapy, 5-years cumulative survival (61.8% vs 34.5% p=0.002) and freedom from haemorrhagic stroke was lower in HW (85.5% vs 67.9%; p=0.01).
Conclusions: Although similar post-operative results, patients implanted with HW developed a higher risk of mortality and major cerebrovascular events after 5-year from the implantation when compared to HM3 patients. A consensus should be reached about the future management of all patients still supported by HW.

Figure



OS6_2 IMPACT OF THE 2018 FRENCH ALLOCATION SCHEME ON THE PROFILE OF HEART TRANSPLANTATION CANDIDATES AND RECIPIENTS: INSIGHTS FROM A HIGH-VOLUME CENTER

Guillaume Coutance*[1], Eva Desiré[1], Mickael Lescroart[1], Guillaume Lebreton[1], Shaida Varnous[1], Leprince Pascal[1]

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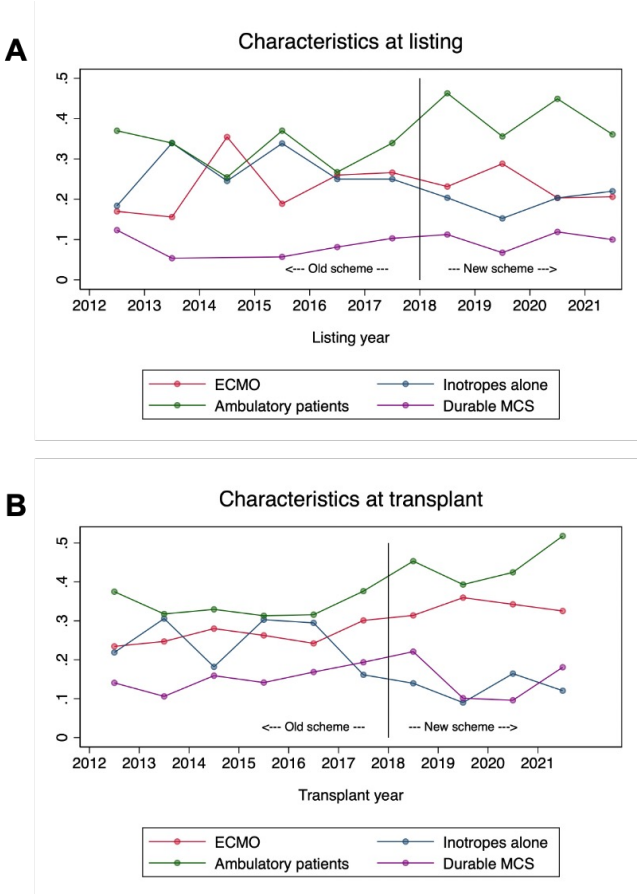
Background: In 2018, a new cardiac allograft allocation scheme based on an individual scoring system considering the risk of death both on the waitlist and after heart transplantation (HTx), was implemented in France. We aimed to assess the impact of this new scheme on the profile of HTx candidates and recipients.
Methods: In this single-center retrospective study, we included consecutive patients listed and/or transplanted between 01/01/2012 and 09/30/2021 at La Pitié-Salpêtrière Hospital. Baseline characteristics of patients were retrieved from the national CRISTAL registry and were compared according to the type of allocation scheme (before or after 2018).
Results: A total of 1098 newly listed HTx candidates and 855 HTx recipients were included. One-year post-listing and post-transplant mortality was 12.4% and 20%, respectively. At listing, the proportion of candidates on inotropes significantly declined following the scheme update (26.3% compared to 20.9%; p = 0.038), reflecting a change in medical practice (Figure 1A). At transplant, recipients had a worse kidney function (estimated glomerular filtration rate ≤ 60 mL/min/1.73 m2: old scheme = 28.6%; new scheme: 45%, p < 0.001), and were more likely to be on ECMO support (33.5% compared to 28.1%, p = 0.080) under the new scheme, reflecting the prioritization of more severe patients (Figure 1B). Post-transplant outcomes were not significantly influenced by the allocation system.
Conclusions: The implementation of the 2018 French allocation scheme had a limited impact on the profiles of HTx candidates but selected more severe patients for HTx without significant impact on post-transplant outcomes.

Figure 1



FULL ORALS

Improving outcomes of end-stage heart: instead of MCS to the long-term

OS6_3 RESULTS FROM OVER 800 TRANSPLANT RECIPIENTS ENROLLED IN THE GUARDIAN-HEART REGISTRY: CHALLENGING THE STANDARD OF CARE

Andreas Zuckermann*[1], Yasuhiro Shudo[2], Dan Meyer[3], Scott Silvestry[4], Marzia Leacche[5], Christopher Sciortino[6], Maria Rodrigo[7], Si Pham[8], Jeffrey Jacobs[9], Koji Takeda[10], Hannah Copeland[11], Andrija Vidic[12], Masashi Kawabori[13], Jacob Schroder[14], David D'alessandro[15]

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Background: The decades long gold standard for preservation of donor hearts in ice appears to be rapidly shifting to advanced hypothermic preservation. In 2022, almost one in 3 donor hearts in the US were transported in a Paragonix SherpaPak Cardiac Transport System (CTS). This controlled hypothermic technology is both FDA approved and CE Marked and has been in clinical use since 2018 preserving organ temperatures between 4 – 8°C. Real-world evidence on the clinical benefits of using CTS compared to conventional ice storage (ICE) is evaluated in the GUARDIAN-Heart Registry to assess whether improved outcomes are achieved with this technology.

Methods: Data from 877 adults at 16 US centers receiving donor hearts preserved and transported in either CTS (n=487) or ICE (n=390) between October 2015-August 2022 were analysed in the GUARDIAN-Heart registry. Propensity matching on site, donor age, transplant era, ischemic time, and baseline durable ventricular assist device (VAD) was performed to balance baseline differences to further evaluate outcomes between cohorts (see Table). Summary statistics were used for comparisons, and Kaplan Meier method was used to estimate survival.

Results: The CTS cohort demonstrated reduced severe primary graft dysfunction (PGD) compared to ICE in the unmatched cohort (p=0.08) (Table). When propensity matched, CTS had significantly lowered severe PGD compared to ICE by 60% (10.0% vs 4.0%, p=0.01), and overall MCS utilization by 37% (32.1% vs 20.1%, ICE vs CTS, respectively). Kaplan-Meier survival was similar (one year, ICE = 91.9%, SCTS = 95.6%, p=0.12). Further analysis on a larger dataset with ongoing enrolment in this live registry will be available for presentation.

Conclusions: Utilization of the Paragonix CTS for organ preservation is associated with lower rates of severe PGD. This finding continues to fundamentally challenge the decades-long status quo of using ice for transporting donor hearts.

Table: Baseline Demographics and Post-transplant Outcomes

	Overall US Cohorts			Propensity Matched Cohorts*		
	ICE	CTS		ICE	CTS	
	N = 390	N = 487	*p-value*	N = 249	N =249	*p-value*
Donor Characteristics						
Age (years)	32.3 ± 10.3	32.9 ± 10.3	0.37	32.5 ± 10.6	32.5 ± 10.3	0.99
BMI (kg/m²)	28.8 ± 6.7	28.5 ± 6.8	0.55	28.3 ± 6.7	28.9 ± 7.0	0.34
LVEF (%)	60.1 ± 6.9	60.7 ± 7.1	0.22	60.2 ± 7.0	60.5 ± 7.4	0.62
Distance to Organ (nautical miles)	**247.8 ± 248.4**	**413.6 ± 317.6**	**<0.0001**	**289.9 ± 253.0**	**350.0 ± 298.8**	**0.02**
Total Ischemic Time (minutes)	**192.1 ± 56.4**	**217.5 ± 48.5**	**<0.0001**	208.4 ± 52.9	208.1 ± 45.9	0.94
F/M Mismatch	55 / 389 (14.1%)	65 / 487 (13.3%)	0.73	32 / 249 (12.9%)	39 / 249 (15.7%)	0.37
PHM Mismatch	0.0 ± 0.2	0.0 ± 0.2	0.89	0.0 ± 0.2	0.0 ± 0.2	0.96
Most undersized (<-15%)	50 / 389 (12.9%)	58 / 487 (11.9%)	0.67	34 / 249 (13.7%)	37 / 249 (14.9%)	0.70
Era (% Post Change)	**310 / 390 (79.5%)**	**479 / 487 (98.4%)**	**<0.0001**	238 / 249 (95.6%)	241 / 249 (96.8%)	0.48
Recipient Characteristics						
Age (years)	54.0 ± 12.6	54.5 ± 13.3	0.51	53.9 ± 12.5	54.8 ± 12.8	0.46
BMI (kg/m²)	27.9 ± 4.8	27.8 ± 4.8	0.84	27.8 ± 5.0	28.1 ± 5.0	0.51
Wait List Days	181.7 ± 344.3	143.6 ± 349.1	0.11	153.9 ± 304.0	178.1 ± 367.1	0.43
LVEF at Baseline (%)	21.3 ± 12.5	20.6 ± 11.6	0.38	**22.9 ± 14.0**	**20.6 ± 11.4**	**0.04**
Implantable VAD	**149 / 390 (38.2%)**	**134 / 487 (27.5%)**	**<0.0001**	68 / 249 (27.3%)	80 / 249 (32.1%)	0.24
Temporary IABP	**80 / 390 (20.5%)**	**150 / 486 (30.9%)**	**<0.0001**	68 / 249 (27.3%)	70 / 249 (28.1%)	0.84
Temporary ECMO/VAD	42 / 390 (10.8%)	71 / 486 (14.6%)	**0.092**	30 / 249 (12.0%)	34 / 249 (13.7%)	0.59
IMPACT Score	**7.2 ± 5.1**	**7.9 ± 5.1**	**0.01**	7.6 ± 5.5	7.1 ± 5.0	0.91
Post-Transplant Outcomes						
All Post Tx MCS#	107 / 390 (27.4%)	119 / 487 (24.4%)	0.62	**80 / 249 (32.1%)**	**50 / 249 (20.1%)**	**<0.01**
New IABP Post Tx	49 / 390 (12.6%)	54 / 487 (11.1%)	>0.99	**35 / 249 (14.1%)**	**20 / 249 (8.0%)**	**0.03**
New ECMO/VAD Post Tx	44 / 390 (11.3%)	42 / 487 (8.6%)	0.22	**29 / 249 (11.6%)**	**16 / 249 (6.4%)**	**0.04**
Cardioversion	51 / 387 (13.2%)	45 / 486 (9.3%)	**0.066**	**31 / 247 (12.6%)**	**17 / 248 (6.9%)**	**0.03**
PGD	78 / 390 (20.0%)	87 / 487 (17.9%)	0.42	49 / 249 (19.7%)	39 / 249 (15.7%)	0.24
PGD Severe	40 / 390 (10.3%)	34 / 487 (7.0%)	**0.083**	**25 / 249 (10.0%)**	**10 / 249 (4.0%)**	**0.01**
30-Day Survival	382 / 390 (97.9%)	479 / 487 (98.4%)	0.65	246 / 249 (98.8%)	245 / 249 (98.4%)	0.70
In-hospital Survival	376 / 390 (96.4%)	475 / 487 (97.5%)	0.33	241 / 249 (96.8%)	245 / 249 (98.4%)	0.24
1-year Survival	338 / 368 (91.8%)	368 / 393 (93.6%)	0.34	216 / 235 (91.9%)	188 / 199 (94.5%)	0.30

* Matching performed on site, donor age, era, ischemic time, and baseline implantable VAD.
# All MCS includes MCS continued from pre-transplant, and MCS that continued throughout the post-transplant period.
Continuous variables presented as mean ± standard deviation.
Abbreviations: BMI = body mass index; CTS = (Paragonix) cardiac transport system; ECMO = extracorporeal membrane oxygenation; F/M mismatch = female to male mismatch; IABP = intra-aortic balloon pump; LVEF = left ventricular ejection fraction; MCS = mechanical circulatory support; PGD = primary graft dysfunction; PHM = predicted heart mass; Tx = transplant; VAD = ventricular assist device.

OS6_4 HEART TRANSPLANTATION FROM CONTROLLED DONATION AFTER THE CIRCULATORY DETERMINATION OF DEATH: OUR EXPERIENCE

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Background: Heart transplantation is currently the most effective treatment to improve the prognosis of patients with end-stage heart failure. In recent years, donation after circulatory death (cDCD) with regional normothermic thoracoabdominal perfusion (TA-NRP) has been developed in Spain. We present the initial experiences in heart transplantation from cDCD donors with TA-NRP at the Hospital Virgen de la Arrixaca in Murcia.

Methods: cDCD was considered in patients under 65 years of age admitted to the ICU in whom the medical team and legal representatives had made the decision for withdrawal of life support therapy (WLST) and the donation was accepted. The evaluation was performed as usually. Donor heart monitoring was performed using a Swan-Ganz catheter and continuous transesophageal echocardiography (TEE). Brain activity was monitored using the bispectral index. After declaration of death (5 minutes no touch), the 3 aortic arch vessels were clamped to exclude cerebral flow. Simultaneously, the patient was intubated and mechanical ventilation was initiated. The values of troponin I and lactate were monitored during the whole procedure.

Results: 11 procedures were performed to local recipients with excellent outcome. In all cases the heart reverted to sinus rhythm within 1 minute. Left ventricular ejection fraction at the validation, and 60 minutes after it, was optimal. The recipients had a short ICU stay and were discharged home with an excellent evolution and optimal cardiac index. Only one of them required mechanical support after transplantation, and another one finally died for a local complication, not related with the graft function.

Conclusions: Transplantation from cDCD donors represents an important source of grafts in countries with an adequate legal framework. TA-NRP may become a way to make cDCD donor heart transplantation feasible, reducing the costs of ex situ machine devices by making this procedure economically affordable.

OS6_5 MOLECULAR DIAGNOSTIC CLASSIFICATION OF HEART ALLOGRAFT REJECTION BASED ON THE TARGETED BANFF HUMAN ORGAN TRANSPLANT GENE EXPRESSION PANEL

Alessia Giarraputo*[1;2], Guillaume Coutance[1;3], Marny Fedrigo[2], Olivier Aubert[1], Jessy Dagobert[1], Blaise Robin[1], Ilaria Barison[2], Chiara Castellani[2], Fariza Mezine[1], Philip Rouvier[4], Patrick Bruneval[1], Jon Kobashigawa[5], Jignesh Patel[5], Jean-Paul Duong van Huyen[1;6], Annalisa Angelini[2], Alexandre Loupy[1]

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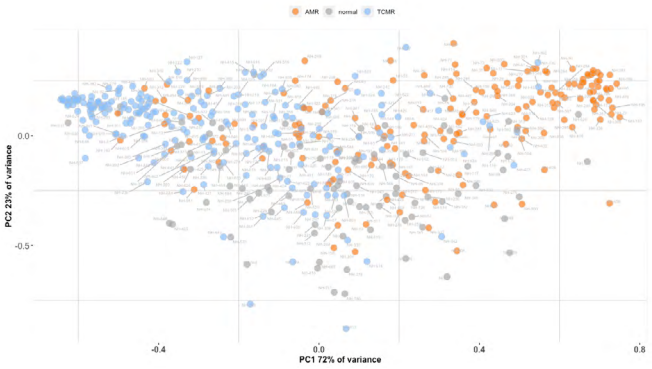
Background: Endomyocardial biopsies (EMB) gene expression profiling is a promising companion tool of the pathology diagnosis of rejection. While the routine application of pangenomic approaches is limited, targeted molecular profiling combined with reproducible formalin-fixed paraffin-embedded (FFPE) EMB-based technology has the potential to change the current paradigm of cardiac rejection diagnosis. We aimed to develop and validate targeted gene expression diagnostic system of cardiac rejection.

Methods: We performed a multicenter, retrospective study, building a reference set of 610 FFPE-EMB collected between 2011 and 2021 and representative of the landscape of rejection (antibody-mediated rejection-AMR, n=189; acute cellular rejection-ACR, n=289; non-rejection, n=114). Nanostring nCounter technology with BHOT panel, a consensus-based panel of 770 genes, was used to analyze tissue gene expression. Differential expression and elastic net approaches were applied to identify key AMR and ACR-related transcripts. A supervised machine learning model was used to build molecular classifiers of AMR and ACR. Their performance was evaluated in an independent validation set (n=117).

Results: Overall, the molecular analysis of 592 (97%) biopsies successfully passed all quality control and normalization steps. The molecular profiles of both ACR and AMR included typical transcripts reflecting the rejection-related pathophysiology. In the validation cohort, the AMR and ACR models accu-

rately identified each type of rejection. The diagnostic accuracy was 81.89% for AMR (ROC-AUC=0.844, Brier score=0.143) and 77.58% for ACR (ROC-AUC=0.812, Brier score=0.176). Principal component analysis based on the molecular scores showed the detection of 72% of variance (Figure) allowing the histo-molecular contextualization of the reference set samples according to the molecular scores.
Conclusions: We developed and validated robust molecular-based models, showing high diagnostic performance to detect heart rejection profiles in transplanted patients. These results support the clinical utility of BHOT-based diagnostic model to improve diagnostic and follow-up procedure in heart transplantation.



OS6_6 BANFF HUMAN ORGAN TRANSPLANT CONSENSUS GENE PANEL FOR DETECTING ANTIBODY MEDIATED REJECTION IN HEART ALLOGRAFT BIOPSIES

Alessia Giarraputo*[1;2], Guillaume Coutance[1;3], Olivier Aubert[1], Marny Fedrigo[2], Dina Zielinski[1], Fariza Mezine[1], Michael Mengel[4], Patrick Bruneval[1], Jean-Paul Duong van Huyen[1;5], Annalisa Angelini[2], Alexandre Loupy[1]

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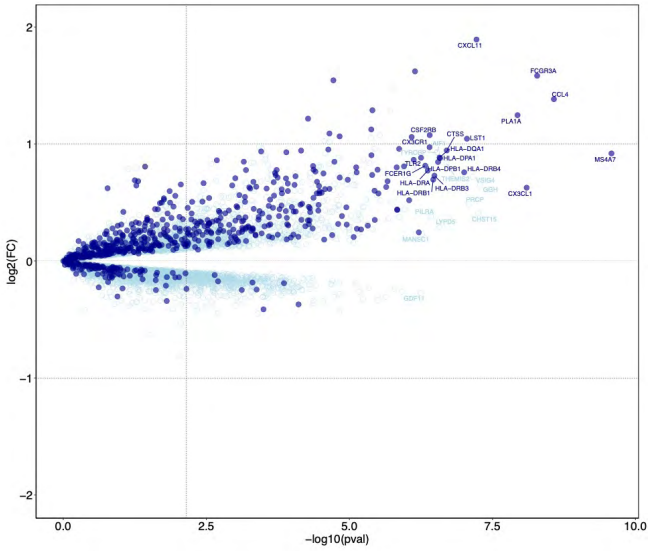
Background: Tissue-based gene expression approaches have been developed as a companion tool of routine pathology to refine the diagnosis of cardiac rejection. Whole-transcriptome profiling defined molecular phenotypes of rejection, but its clinical application remains limited by several hurdles. The consensus Banff Human Organ Transplant (BHOT) panel is developed to facilitate cost-effective and reproducible expression analysis of solid organ allografts. We aimed at validating the targeted panel as a proxy to whole-transcriptome analysis.
Methods: To assess the BHOT panel reliability in detecting gene expression pattern associated with antibody-mediated rejection (AMR), we performed *in silico* analysis and projected the BHOT panel on already published microarray data of 142 heart transplant biopsies (PMID:28148598). We compared the targeted and whole-transcriptome molecular profiles in AMR-biopsies (n=71) and non-AMR matched-control (non-rejection or acute cellular rejection, n=71) by performing differential expression, pathway, and network analyses.
Results: Out of the 30 most differentially expressed genes (FDR<0.05) between AMR and non-AMR identified in whole-transcriptome analysis, two-thirds (n=19) were included in the BHOT panel (Figure). These genes covered major immune pathways and key cells involved in the physiology of AMR, including IFNG-inducible genes, NK-cells, monocytes-macrophages, injury and B-cells. The remaining genes not targeted in the BHOT were related to unspecific immune response. Major pathways related to AMR and graft injury identified in the targeted panel were associated with: antigen processing cross presentation (q=2.86E-15), lymphoid and non-lymphoid immune interaction (q=1.00E-22), endothelial activation (q=6.80E-10), Toll-like receptor cascade (q=1.59E-10) and Immunoregulatory interaction in adaptive immune system (q=1.01E-22).
Conclusions: The targeted molecular signature of AMR based on the B-HOT panel detected relevant AMR-related genes and pathways. This study demonstrate that the targeted panel can be used as a proxy to whole-transcriptome to analyze the molecular profile of heart allograft rejection.



OS6_7 PREGNANCY AFTER HEART TRANSPLANT

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Background: The Transplantation Pregnancy Registry International (TPRI) has been collecting data for 32 years in solid organ transplant recipients.
Methods: Data are collected by the TPRI via questionnaires, telephone interviews, and review of medical records. The purpose of this study is to analyze pregnancy outcomes in heart transplant recipients (HTR) reported to the TPRI.
Results: 123 HTR (including 6 HTR from outside of North America), 208 pregnancies and 214 pregnancy outcomes (3 twin, 1 triplet pregnancy) were analyzed. Pregnancy outcomes: 149 live births (70%), 52 miscarriages, 8 terminations, 3 ectopic and 2 stillbirths. Median age at conception was 28.6 (IQR 24-32) yrs and median transplant to conception interval was 5.8 (IQR 3.4-11.1) yrs. Unplanned pregnancies were reported in 44%. Immunosuppression consisted of tacrolimus-based in 63% and cyclosporine-based in 37%. Forty pregnancies had mycophenolate mofetil exposure (MPA): 22 miscarriages, 17 live births and 1 ectopic pregnancy. Comorbid conditions during pregnancy: hypertension 48%, insulin treated diabetes 8%, infection during pregnancy 16%, cholestasis of pregnancy 6%, preeclampsia 27%, and rejection 6.9%. Of the 149 live born, median gestational age was 37 (IQR 35-38.1) weeks, and median birthweight was 2693 (IQR 2324-3005) grams; 44% were premature (<37 weeks). There were 12 (8.1%) infants with birth defects; 3 infants had MPA exposure, defects included: laryngomalacia (1), facial malformations (1), and duodenal atresia, AV canal defect, Tetralogy of Fallot (3 defects in 1 child). At a median follow-up of 6.4 yrs most children are reported healthy and developing well. Nine children inherited their mothers heart disease; 4 had heart transplants. With a median follow-up of 7.5 (IQR 3.1-13.4) yrs: 36 recipients died, 4 had reduced function, 3 were lost to follow-up, and 80 (65%) had adequate function.
Conclusions: This is the largest reported series of pregnancies in HTR to date. Pregnancy in HTR is possible with 70% reporting live births. MPA exposure continues to present significant concerns. Pre-pregnancy counselling should include discussion of fertility post-transplant, the prospect of unplanned pregnancy, inheritable cardiac conditions, MPA avoidance, risk of rejection/graft dysfunction, and long-term maternal survival.

OS6_8 LONG-TERM OUTCOMES OF COMPLEMENT INHIBITION FOR PREVENTION OF ANTIBODY-MEDIATED REJECTION IN IMMUNOLOGICALLY HIGH-RISK HEART TRANSPLANTATION

Guillaume Coutance*[1], Evan Kransdorf[2], Jon Kobashigawa[3], Alexandre Loupy[1], Jignesh Patel[3]

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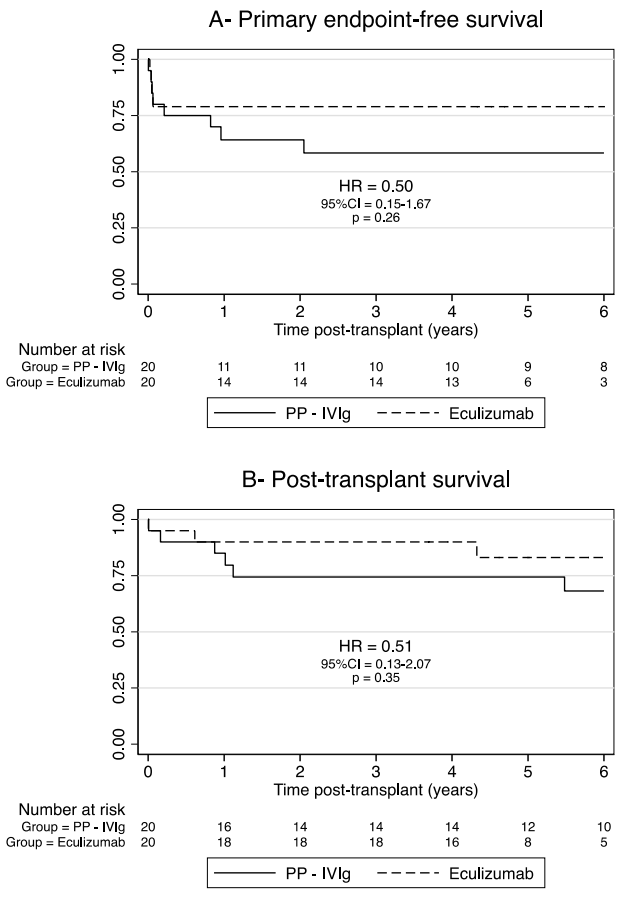
Background: Allosensitization represents a major barrier to heart transplantation (HTx). We assessed the efficacy and safety of complement inhibition at transplant in immunologically high-risk heart transplant recipients. We previously reported favorable 1-year outcomes of this strategy. The aim of the current study was to report 5-year outcomes.

Improving outcomes of end-stage heart: instead of MCS to the long-term

Methods: We performed a single-center, single-arm, open-label trial (DUET trial, NCT02013037). Patients with panel reactive antibodies (PRA) ≥70% and pre-formed donor-specific antibodies (DSA) ≥ 5,000 MFI were eligible. In addition to standard of care, patients received 9 infusions of eculizumab during the first two months post-transplant. The primary composite endpoint was antibody-mediated rejection (AMR) ≥ pAMR2 and/or left ventricular dysfunction during the first year. Secondary endpoints included hemodynamic compromise, allograft rejection and patient survival. A matched control group at equivalent immunologic risk and treated with perioperative plasmapheresis and intravenous immunoglobulins was retrieved from the Paris Transplant Group reference set (propensity score matching).
Results: Twenty patients were included in the treatment group. Median post-transplant follow-up was 4.8 years. Beyond the first year post-transplant, there were no episodes of pAMR2 or greater and no LV dysfunction. Primary endpoint free-survival was 79.0% at 3- and 5-year post-transplant. Overall survival was 90% and 83.1% at 3- and 5-year post-transplant. Beyond the first year post-transplant, one episode of pAMR1 was diagnosed and one patient had minimal de novo cardiac allograft vasculopathy. Compared to a matched-control group, we observed a non-statistically significant benefit of eculizumab with a lower incidence of primary endpoint or death (primary endpoint: HR=0.50, 95%CI=0.15-1.67, p=0.26; mortality: HR=0.51, 95%CI=0.13-2.07, p=0.35, Figure 1A and 1B).
Conclusions: We report favorable 5-year outcomes of a complement inhibition-based strategy for the management of immunologically high-risk HTx. Chronic antibody-mediated allograft injuries were uncommon. Our results support the utility of complement inhibition for immunologically high-risk heart transplantation.

Figure 1



IVIG, intravenous immunoglobulins; PP, plasmapheresis.

Molecular monitoring of lung allograft rejection

OS7_1 UTILITY OF THE BANFF HUMAN ORGAN TRANSPLANT PANEL IN DIAGNOSING ANTIBODY-MEDIATED REJECTION IN LUNG TRANSPLANT BIOPSIES

Marta Sablik[*1], **Natalia Belousova[2], Fariza Mezine[1], Dina Zielinski[1], Marc Raynaud[1], Patrick Bruneval[1], Olivier Aubert[1], Carmen Lefaucheur[1], Alexandre Loupy[1], Antoine Roux[1;2]**

[1]Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, [2]Lung Transplantation Department, Hôpital Foch, Suresnes, France

Background: Despite reaching a consensus on the definition of pulmonary antibody-mediated rejection (AMR), diagnosing AMR remains a challenge in clinical practice. Molecular phenotyping has the potential to improve the current diagnostic approach. We aimed to identify the molecular signature and capture the key functional pathways involved in pulmonary AMR using the Banff Human Organ Transplant (B-HOT) panel.
Methods: One hundred twenty-one formalin-fixed paraffin-embedded transbronchial biopsies from lung transplant recipients were included. The biopsies were classified into three categories according to ISHLT guidelines: AMR (n=42), acute cellular rejection (ACR, n=50) or non-rejection (n=29), and gene expression analysis was performed using the B-HOT panel. We performed differential expression analysis comparing AMR vs. all non-AMR biopsies. Significant differentially expressed genes (false discovery rate <0.05) were used as input for pathway analysis with ReactomePA.
Results: A total of 295 genes were differentially expressed. The top significant upregulated genes associated with pulmonary AMR demonstrated an activation of immune cascades and captured a cell injury-related profile, including cellular injury (TIMP1, S100B, TNC, HIF1A, IGF1, COL3A1, COL1A1), chemokine signalling (CXCL14, CXCL13), macrophage activation (MMP12, MS4A6A), complement activation (C3AR1), adaptive immune response (JAK3, TNFRSF9, TNFRSF18, IL2RA) and immune regulation (CD84, LILRB4, CTLA4, LAG3). Contrary to other transplanted solid organs, key endothelial transcripts (CDH13, CAV1, TEK, VEGFA, KDR, ROBO4) were down-regulated. Pathway analysis showed that the top significant AMR-associated pathways were: interleukin (specifically interleukin-4 and 13) and interferon signalling, toll-like receptor cascade, chemokine signalling, vascular wall interactions, complement cascade and lymphocyte interactions (co-stimulation CD28).
Conclusions: This study shows that the B-HOT panel was able to capture the molecular profile of AMR in lung allografts and detects previously identified pathways observed in other solid organ allografts. Multicentric international cohorts are needed to develop robust precision molecular-based diagnostic systems for pulmonary AMR.

OS7_2 USING PREDICTED INDIRECTLY RECOGNIZABLE HLA EPITOPES TO INVESTIGATE FORMATION OF DE NOVO DONOR-SPECIFIC HLA-ANTIBODIES AFTER LUNG TRANSPLANTATION

Maximilian Vorstandlechner[*1], **Lisa Kleid[2], Julia Walter[1;3;4], Christian Schneider[1;4;5], Sebastian Michel[4;5;6], Nikolaus Kneidinger[3;4], Michael Irlbeck[5;7], Rudolf Hatz[1;4], Andrea Dick[2], Teresa Kauke[1;4;5]**

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Background: Human leucocyte antigen (HLA) histocompatibility between organ donor and recipient can play a crucial role in the outcome after lung transplantation (LuTX). The development of de novo donor-specific HLA-antibodies (dnDSA) can be a risk factor for graft failure and consequently have a negative impact on long-term post-TX (graft-)survival. Mismatches can be detected both directly and indirectly by the recipient's immune system. This retrospective cohort study focuses on the prediction of dnDSA through the indirect pathway of antigen recognition by using the PIRCHE-II algorithm (predicted indirectly recognizable HLA epitopes).
Methods: Patients who underwent LuTX from 2005 to 2018 were considered for the study. Besides complete clinical records regarding underlying disease and indication for transplantation, inclusion criteria were single or double LuTX, complete donor and recipient class I and II HLA-typing (loci A, B, C, DR and DQ) prior to TX and regular post-TX-screenings for newly developed antibodies. In order to assess long-term transplant success and monitor chronic lung allograft dysfunction (CLAD), a follow-up time of at least one year was required.
Results: Overall, a total of 581 patients was included in the study. 196 patients (33,7%) showed signs of a repeatedly declining forced expiratory volume in 1 second (FEV1), eventually resulting in CLAD. Two groups were formed based

on the median value for PIRCHE-II. There was no significant difference in the two groups regarding probability of dnDSA development. However, there was a clear trend towards a reduced five-year survival rate in the group that showed a high-PIRCHE-II score and developed dnDSA post-TX (p = 0,076).
Conclusions: Taking the current shortage of donor organs into consideration, PIRCHE may be able to identify acceptable mismatches to optimize donor-recipient compatibility, help improve long-term survival and reduce the rate of graft failures. However, as pre-TX HLA-matching, in contrast to other forms of solid organ transplantation (SOT), currently plays no role in general in the allocation of lung allografts, adjustments in the PIRCHE-II thresholds may be needed in order to better reflect epitope load and DSA development.

OS7_3 TRANSCRIPTIONAL CO-ACTIVATOR BOB1 AS THE KEY REGULATOR OF PATHOGENIC LYMPHOCYTIC RESPONSES IN CHRONIC LUNG ALLOGRAFT DYSFUNCTION

Nataliya Yeremenko*[1], Aurore Foureau[1], Nicolas Sailliet[1], Adrien Tissot[1], Alexey Tomilin[2], Sophie Brouard[1]

[1]The University of Nantes, Inserm, CR2TI UMR1064, Nantes, France, [2]Institute of Cytology of the Russian Academy of Sciences, Saint-Petersburg, Russian Federation

Background: CLAD is the leading cause of mortality after lung transplantation. Emerging evidence suggests that the balance of effector and regulatory lymphocytic responses determines lung allograft outcomes favouring rejection or tolerance. However, the molecular mechanisms controlling these responses remain largely unknown. Recently we demonstrated that the expression of lymphocyte-specific transcriptional co-activator BOB1 in the lung recipients' blood predicts CLAD development. In this study, we aimed to explore the role of BOB1 in the pathophysiology of CLAD.
Methods: The imaging mass cytometry was performed on lung tissue obtained from patients with CLAD through transbronchial biopsy and stained with a panel of 36-heavy-metal-tagged antibodies. BOB1-specific inhibitors were developed through a classical medicinal chemistry approach via virtual library screening. The effect of BOB1 targeting was assessed on: 1) B-cell proliferation, apoptosis, activation, and immunoglobulin production in the model of T-dependent B-cell differentiation; 2) B-cell regulatory capacity in the co-cultures with activated effector T cells; 3) primary and secondary T-cell responses.
Results: We identified multiple immune cell subsets in the lung allograft, the target tissue of CLAD, and observed the massive infiltration of plasma cells expressing high levels of BOB1. Targeting BOB1 abrogates B-cell proliferation, activation and differentiation into antibody-secreting plasmablasts in vitro. This phenotype and the arrest of isotype-switched immunoglobulin production was accompanied by the down-modulation of plasma cell differentiation and class-switching genes, such as IRF4, PRDM1, AICDA, IgHG1, and IgHG3. In addition, targeting BOB1 suppressed proliferation and IL-17A production by T cells during recall responses. In sharp contrast, the interference with BOB1 function did not affect the regulatory function of B cells.
Conclusions: The presence of BOB1+ lymphocytes in CLAD lungs and the notion that attenuation of biological activity of BOB1 in vitro dampens activated lymphocytic responses without compromising the immunosuppressive potential, support the role of BOB1 in CLAD pathogenesis, laying a solid rationale for the investigation of its targeting in relevant experimental models in vivo.

OS7_4 VALIDATION OF A BLOOD GENE SIGNATURE TO PREDICT CHRONIC ALLOGRAFT DYSFUNCTION IN LUNG TRANSPLANTATION

Richard Danger*[1], Eugénie Durand[1], Aurore Foureau[1], Johanna Claustre[2], David Lair[1], Antoine Roux[3], Jerôme Le Pavec[4], Benjamin Coiffard[5], Benjamin Renaud-Picard[6], Jean-François Mornex[7], Claire Dromer[8], Martine Reynaud-Gaubert[9], Antoine Magnan[3], Adrien Tissot[10], Sophie Brouard[10]

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Background: Since chronic lung allograft dysfunction (CLAD) is the major limitation to long-term survival after lung transplantation, identifying patients at risk of CLAD using non-invasive biomarkers would allow to prevent lung allograft damage. We previously identified three B-cell related genes with blood expression associated with CLAD, namely *BLK*, *POU2AF1* and *TCL1A*. The purpose of this study was to validate this signature in an independent cohort of 293 lung transplanted recipients.
Methods: The expression of the 3 genes was measured by quantitative PCR at 12, 18 or 24 months after transplantation in the blood samples of lung transplanted patients of the multicenter COLT cohort. Theses samples include samples from patients with CLAD (n=56) and patients with good graft function at least 5 years after transplantation (n=102). Blood from patients with lung infection at 12 months post-transplantation (n=10) and healthy volunteers (n=10) were analysed as controls.
Results: The expression of the 3 genes measured during the second year post-transplantation was significantly decreased in blood from patients with CLAD occurring between 3 and 24 months after sample collection compared to patients with good graft function (p=0.041, 0.029 and 0.038 for *BLK*, *POU2AF1* and *TCL1A*, respectively). Gene expression was not significantly affected by lung infection. These results confirm the ability of these 3 genes to predict the development of CLAD in lung transplantation.
Conclusions: The downregulation of these three B cells-related genes suggests a B cell imbalance in favour of an alloimmune reaction. Combined with clinical parameters, these genes may help identifying patients likely to develop CLAD and to benefit from therapy to prevent development of the pathology.

FULL ORALS

Molecular monitoring of lung allograft rejection

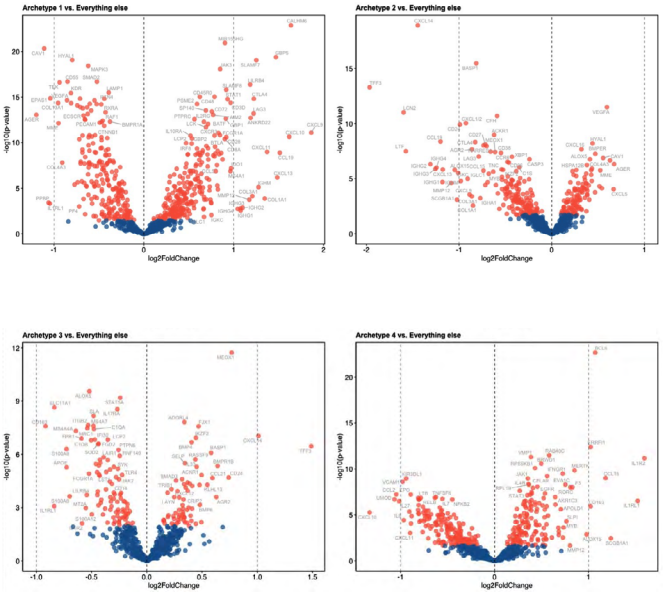
OS7_5 UNSUPERVISED ANALYSIS OF LUNG TRANSPLANT PHENOTYPES USING GENE EXPRESSION DATA

Marta Sablik*[1], Natalia Belousova[2], Fariza Mezine[1], Dina Zielinski[1], Marc Raynaud[1], Patrick Bruneval[1], Olivier Aubert[1], Carmen Lefaucheur[1], Alexandre Loupy[1], Antoine Roux[1;2]

[1]Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, [2]Lung Transplantation Department, Hôpital Foch, Suresnes, France

Background: Non-specific histopathologic findings and a lack of accurately defined phenotypes pose a barrier in diagnosing rejection in lung allografts. We hypothesized that new rejection phenotypes could be identified using probabilistic unsupervised analysis of gene expression data.
Methods: 121 formalin-fixed paraffin-embedded transbronchial biopsies were included and classified according to ISHLT criteria to three categories: antibody-mediated rejection (AMR, n=42), acute cellular rejection (ACR, n=50) or non-rejection (n=29). Histological, clinical and immunological data were gathered and biopsies were sequenced using the Banff Human Organ Transplant panel. Archetypal analysis was applied to normalized gene counts to identify distinct phenotypes. The final archetypal model was chosen using the elbow method on the residual sum of squares. We performed differential expression analysis comparing each archetype vs. all other archetypes.
Results: We identified four distinct histological, immunological and molecular archetypes. Archetype 1 (n=21 biopsies) was characterized by capillary lesions and circulating anti-HLA DSA. Differentially expressed genes captured B- and T-cells activation (CD48, CD3D, JAK3) and interferon signalling (STAT1, CXCL11). Archetype 2 (n=46) was predominantly defined by perivascular mononuclear cell infiltrates. Its upregulated transcripts were associated with cell-extracellular matrix interactions, angiogenesis (COL4A3, VEGFA) and cell injury (AGER). Archetype 3 (n=35) and archetype 4 (n=18) were histologically similar with capillary lesions, perivascular mononuclear cell infiltrates and circulating anti-HLA DSA occurring at low frequencies. Molecularly the archetypes differed with top transcripts of archetype 3 being mainly involved in cellular processes while archetype 4 captured anti-inflammatory responses (IL1R2, IL4R) and interferon signalling (IFNGR1, JAK1, STAT3).
Conclusions: Unsupervised archetypal analysis of gene expression data identified lung allograft phenotypes with distinct histological, immunological and molecular profiles. This approach has the potential to refine rejection-related diagnoses in lung allografts and improve the shortcoming of the current diagnostic classification system.

Figure 1. Volcano plots of differentially expressed genes associated with each archetype.
Dots represent individual transcripts. Red dots indicate differentially expressed genes after applying a threshold of 0.05 to false discovery rate corrected p-values.



OS7_6 ROLE OF DONOR-DERIVED CELL-FREE DNA IN CHRONIC LUNG ALLOGRAFT DYSFUNCTION. A LONGITUDINAL STUDY

Marta Arjona Peris[1], Berta Saez Gimenez[2], Cristina Berastegui García[3], Victoria Ruiz De Miguel[4], Meritxell Boada Pérez[4], Marta Zapata Ortega[1], Carlos Bravo Masgoret[1], Susana Gomez-Olles*[5], Jordi Riera Del Brio[6], Antonio Roman Broto[1]

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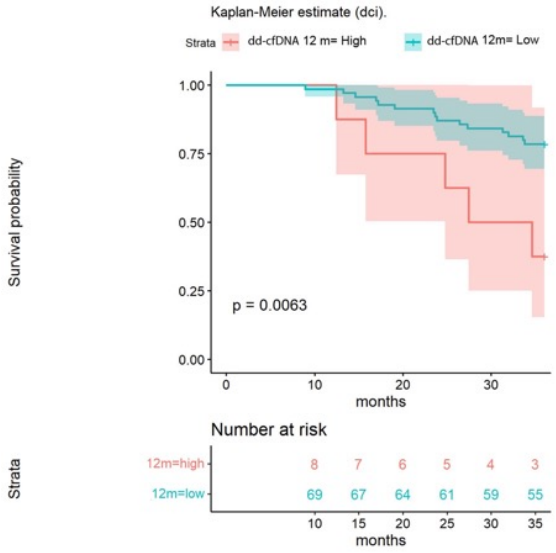
Background: Survival after lung transplantation (LT) is hampered by the development of chronic lung allograft dysfunction (CLAD). There is no treatment available to reverse CLAD once diagnosed, but early intervention could modify the progressive lung function decline. Thus, biomarkers are need for early detection of CLAD. High levels of donor derived cell-free DNA (ddcfDNA) have been described to precede acute cellar rejection and antibody mediated rejection diagnosis. The aim of this study is to assess if there is any association between ddcfDNA and chronic lung allograft dysfunction (CLAD).
Methods: This is a longitudinal study in which ddcfDNA levels were determined in 100 LT recipients at the 3rd, 6th, 9th, 12th,24th and 36th month after LT. Firstly, real-time PCR was performed to detect an informative INDEL polymorphism for each donor/recipient pair. Secondly, levels of ddcfDNA were determined by quantifying the informative INDEL by digital PCR in the plasma of the recipient. Clinical data was collected during a three years follow-up to determine infections, antibody mediated and acute cellular rejection, and CLAD.
Results: Globally, we noted an upward trend of ddcfDNA levels at 1, 2 and 3 years of follow-up when referred to 3 months. Levels of ddcfDNA were compared between CLAD and no CLAD patients at different time points, and a cut-off value of 1.86% at 12 months could identify those patients with higher probability of developing CLAD (Figure 1).
Conclusions: Determine ddcfDNA levels in plasma could be a useful non-invasive biomarker for CLAD prediction. *This study was partially funded by ISCIII ("PI17/01485"), co-funded by ERDF and SEPAR (552/2017).*



FULL ORALS

Molecular monitoring of lung allograft rejection

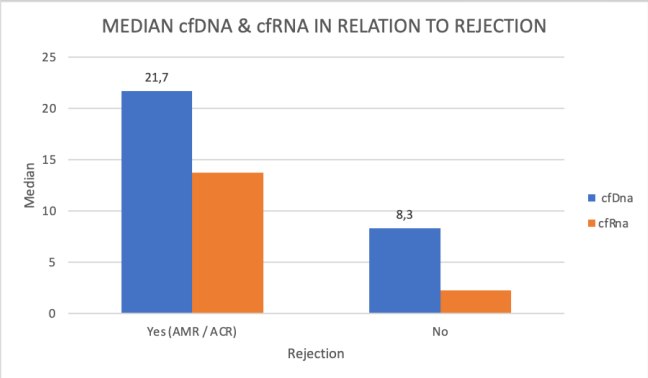
OS7_7 DONOR-DERIVED CELL-FREE DNA AND CELL-FREE RNA LEVELS USING A COST-EFFECTIVE LIQUID BIOPSY TECHNIQUE MONITORING LUNG ALLOGRAFT REJECTION

Owais Tisekar*[1], MD Moiz Lalani[1], Vijil Rahulan[1], Samuel Devi[1], Manjunath Negigowda[1], Menander M[1], Prabhat Dutta[1], Sandeep Attawar[1]

[1]Krishna Institute of Medical Sciences , Institute of Heart and Lung Transplant, hyderabad, India

Background: Donor-derived cell-free DNA (dd-cfDNA) and cell-free RNA are non-invasive tests that look for donor-specific DNA/RNA markers in recipient plasma. Next Generation Sequencing (NGS), droplet digital PCR (ddPCR), and massively multiplexed PCR (mmPCR) platforms, which are currently available to diagnose allograft rejection, are not economically viable in developing countries. To address this problem, we created a real-time PCR-based donor-derived cell-free DNA (dd-cfDNA) and cell-free RNA (dd-cfRNA) assay.
Methods: We used a novel PCR assay to measure donor-derived cell-free DNA (dd-cfDNA) and donor-derived cell-free RNA (dd-cfRNA) in 123 plasma samples from 60 lung transplant recipients to diagnose acute rejection.
Preoperative, intraoperative, and postoperative risk factors were subjected to regression analysis.
Results: The majority of the patients (61.2%) were male, with a mean age of 47.37 years (range: 14-72 years) and a BMI of 22.84. (range: 14.1- 33.7). The most common pre-transplant diagnosis was idiopathic pulmonary fibrosis (35.8%), followed by chronic hypersensitivity pneumonitis (15.4%) and connective tissue-related interstitial disease (8.9%).Our key findings are as follows:1. When compared to the stable organ (median 8.3; IQR: 0.0-40.65 ng /µl)., the dd-cfDNA level was higher in acute rejection (median 21.7 ng/l, interquartile range (IQR): -0.0- 95.65 ng/l). 2. The dd-cfRNA level was higher in acute rejection (median 13.75 ng/l, interquartile range (IQR):-0.0- 46.8 ng/l) than in stable organ (median 2.3 ng/l, IQR:-0.0- 17.3 ng/l).3. Data analysis of dd-cfDNA levels revealed a rejection sensitivity of 56.7% and specificity of 79.7%, whereas dd-cfRNA levels revealed a rejection sensitivity of 33% and specificity of 77.1%. However, the positive predictive values for dd-cfDNA and dd-cfRNA were only 28.8% and 33%, respectively, while the negative predictive values were 89.68% and 87.1%, respectively.4. Using multinomial logistic regression, we discovered that only donor ischaemia time had a statistically significant impact on dd-cfDNA or dd-cfRNA levels.
Conclusions:dd-cfRNA, like dd-cfDNA, has good negative predictive values in detecting rejection that histopathology may have missed.

Figure 1: Median cfDna & cfRna in relation to rejection



OS7_8 INDUCTION EXTRACORPOREAL PHOTOPHERESIS STIMULATES BENEFICIAL IMMUNE MODULATION IN CYSTIC FIBROSIS PATIENTS UNDERGOING LUNG TRANSPLANTATION

Ilaria Righi*[1], Claudio Fenizia[2], Claudia Vanetti[2], Lorella Torretta[1], Letizia Corinna Morlacchi[1], Valeria Rossetti[1], Lorenzo Rosso[1], Giacomo Grisorio[3], Mario Nosotti[1], Daria Trabattoni[2], Mario Clerici[4]

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Background: Chronic rejection (CR) is the leading cause of late morbidity and mortality upon lung transplantation (LuTx). Extracorporeal photopheresis (ECP) has emerged as a promising immunomodulatory treatment against rejection. We performed and in-depth investigation of the immunological effects of induction ECP in LuTx recipients with a diagnosis of cystic fibrosis (CF).
Methods: A pilot clinical trial enrolled 20 CF LuTx patients who were randomly allocated in 2 arms: standard immunosuppressive therapy alone *vs.* standard immunosuppressive therapy plus ECP (one cycle within 72 hours of transplantation followed by 5 cycles in the following 3 months). Functional activation of T and NK subpopulations as well as mRNA expression and cytokine secretion profiling were evaluated in peripheral blood and in bronchoalveolar lavage (BAL) before the first cycle and 48 hours after the end of each cycle and up to 12 months after LuTx. Clinical parameters, including respiratory volumes (e.g. FEV1), rejection episodes and infections, were analyzed as well.
Results: ECP was well tolerated with no complications nor opportunistic infections. Rejection rate was comparable in the two groups Notably, a significantly better FEV1 was observedin the ECP group overtime. Treg lymphocytes and IL10-producing NKs were significantly increased, while Th17 cells were significantly reduced in the ECP group compared to the control. Cytokine profile showed that ECP reduced pro-inflammatory cytokines (e.g. IL1b, IL6) production, increasing that of anti-inflammatory cytokines (e.g. IL10, IL1RA) both in plasma and BAL
Conclusions: Induction ECP is associated with immune modulation resulting in improved patients' respiratory performance. More extensive studies and longer follow-up are needed to verify if ECP-induced immune modulation will have a beneficial effect of organ rejection as well.

Kidney allocation to improve outcomes

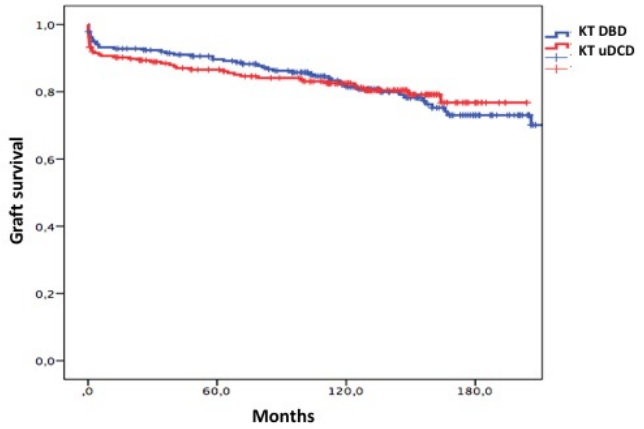
OS8_1 KIDNEY TRANSPLANTATION FROM UNCONTROLLED DONATION AFTER CARDIAC DEATH, AN OPTION WITH EXCELLENT RESULTS IN THE LONG TIME

Maria Molina*[1;2], Javier Paúl-Martínez[1], Marina Urrutia-Jou[1], Esther González Monte[2], Angel Sevillano[2], Mario Fernández-Ruiz[2], Carles Cañameras[1], Josep Riera[1], Rosana Gelpi[1], Angela Casas[1], Gregorio Romero[1], Monica Bolufer[1], Jimena Cabrera[3;4], Anna Vila-Santandreu[1], Amado Andrés[2]

[1]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [2]Hospital Universitario 12 de Octubre, Madrid, Spain, [3]Programa de Prevención y Tratamiento de las Glomerulopatías, Centro de Nefrología, Hospital de Clínicas, Universidad de la República., Montevideo, Uruguay, [4]Department of Nephrology, Hospital Evangelico., Montevideo, Uruguay

Background: Kidney transplantation (KT) from uncontrolled donation after cardiac death (uDCD) has as good results as KT from donation after brain death (DBD) after 5 and 10 years of follow-up. The results after these periods are unknown.
Methods: Unicentric retrospective cohorts study that compared 237 KT from uDCD with 237 KT from standard DBD after 5, 10 and 15 years of follow-up. We measured basal demographics from donor, recipients and donation procurement; and graft survival, patient survival and renal function.
Aim: To compare the graft survival, patient survival and renal function of KT from uDCD to KT from standard DBD after 15 years of follow-up.
Results: uDCD donors had worse renal function at the moment of procurement (creatinine 1.3±0.4 vs 0.8±0.2 mg/dL; p<0.001) and delayed graft function was more frequency (73.4% vs 46.4%; p<0.001). Thymoglobulin were administered to 92.8% of KT from uDCD vs none of KT from DBD (p<0.001). There was more acute rejection in KT from DBD (12.2% vs 24.5%; p=0.001). Graft's survival (non-censured by non-primary function or patient death) 5, 10 and 15 year after KT was in KT from uDCD 86.1%, 82.5% and 79.2% vs in KT from DBD 89.6%, 81.4% and 73% (p=0.97). Kaplan-Meier curve is shown in Figure 1. The patient's survival 5, 10 and 15 year after KT was in KT from uDCD 91.9%, 86.3% and 83.5% vs in KT from DBD 92.4%, 84.2% and 72.5% (p=0.33). Serum creatinine were similar in both groups in the different periods: 1st year (1.40 vs 1.39; p=0.83), 5th years (1.36 vs 1.41; p=0.33), 10th year (1.26 vs 1.50; p=0.23) and 15th year (1.44 vs 1.43; p=0.93).

Conclusions: The results of KT from uDCD were similar to optimum donors from DBD in the long time.



OS8_2 IS THERE A DIFFERENCE IN SURVIVAL OUTCOMES OF DUAL KIDNEY TRANSPLANTS OF DCD V/S DBD ALLOGRAFTS IN ABSENCE OF NATIONAL PATHOLOGY SERVICE?

Abdullah Khawaja[*1;1;2], Kunal Kapoor[1], Thilina Gunawardena[1], Bhavesh Devkaran[1], Ibrahim Khawaja[1], Adham El-Bakry[3], Sanjay Mehra[1], Abhishek Sharma[4], Hemant Sharma[1]

[1]Royal Liverpool University Hospital, Transplant and Vascular Access Surgery, Liverpool, United Kingdom, [2]Medway NHS Foundation Trust, General Surgery, Gillingham, United Kingdom, [3]Leeds General Infirmary, Transplant Surgery, Leeds, United Kingdom, [4]Loyola University Chicago, Chicago, United States

Is there a difference in Survival Outcomes of Dual Kidney Transplant (DKT) of Allografts Procured from DCD versus DBD Donors in absence of a Dedicated National Pathology Service. A Propensity Score Analysis of UK Transplant Registry. An Epidemiology in Transplant Study Group (ETrSG) Initiative.

Background: DKT's are generally from marginal kidneys or small-for-size kidneys that are implanted to provide optimum total nephron mass. Glomerulosclerosis-Pathology-scoring has been used globally to guide about single or dual-kidney implant. In addition, there are reported concerns that DCD transplant outcomes are inferior to DBD. Survival-outcomes of DKTs procured from DCD v/s DBD donors has not been reported.

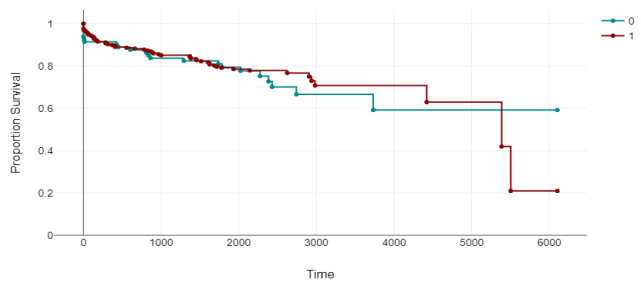
Aim: This study aims to research if there is a difference in survival-outcomes of DKT's of allografts procured from DCD versus DBD Donors in absence of a dedicated National-Pathology-Service in the UK.

Methods: In this exploratory analysis, adults who underwent DKT in the United-Kingdom between Jan 1, 2000, and 31st Dec, 2019, were identified in the NHSBT-Transplant registry, with follow-up to December 31, 2022. Post-transplantation graft survival was assessed with Cox-Regression analysis. Propensity-scores were used to control for selection bias.

Results: N= 51,961 renal transplants were reported to NHSBT during the study period of whom N= 525 underwent DKT. After confounders were controlled for with propensity-score, there were no significant differences in survival outcomes of DCD versus DBD transplants. Region of Transplant OR 1.6(1.0-2.5) p=0.02, transplant post 2011 OR 3.0(1.7-5.2) p<0.001, non-diabetic donor OR 2.1 (1.1-3.9) p=0.009 were associated with better graft survival, while DBD transplants were associated with low DGF rates OR 0.4 (0.27 - 0.59) p<.001.

Conclusions: There are equivalent Survival-Outcomes of DKT of Allografts procured from DCD versus DBD Donors. These results are admirable as UK does not have a dedicated National-Pathology Service to report pre-transplant renal biopsies.

Fig 1: Survival DBD =0 versus DCD =1 (Log Rank 0. 71)



OS8_3 ALL ECD KIDNEYS ARE EQUAL BUT ARE SOME MORE EQUAL THAN OTHERS? A POPULATION-COHORT ANALYSIS OF UK TRANSPLANT REGISTRY DATA

Kamlesh Patel[*1], Anna Brotherton[1], Felicity Evison[2], Dilan Dabare[1], Thomas Nieto[1], Adnan Sharif[1;3]

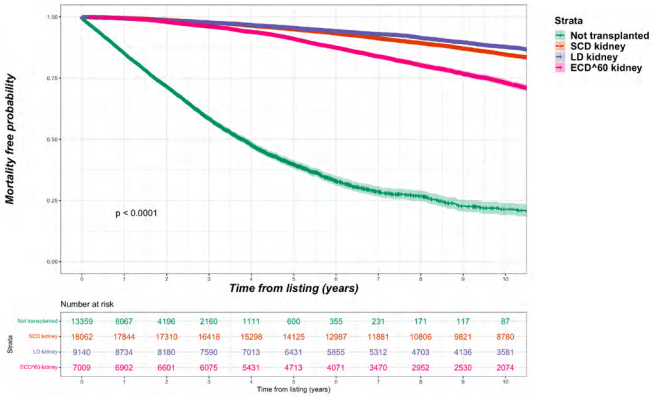
[1]Queen Elizabeth Hospital Birmingham, Department of Nephrology and Transplantation, Birmingham, United Kingdom, [2]University Hospitals Birmingham, Informatics Department, Birmingham, United Kingdom, [3]University of Birmingham, Institute of Immunology and Immunotherapy, Birmingham, United Kingdom

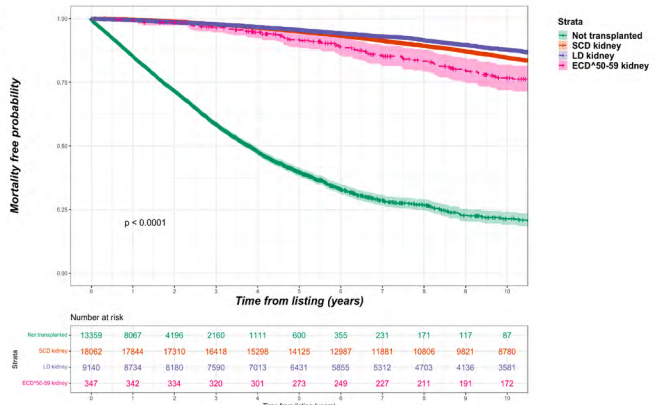
Background: Classification for expanded criteria donor (ECD) kidneys is either purely age based (deceased donor aged ≥60 years) or partially age based (deceased donor aged between 50-59 years) with the need to fulfil additional criteria (two required from the following three; hypertension; raised creatinine and/or death from stroke) - ECD^{60} and ECD$^{50\text{-}59}$ respectively. Although inferior to SCD kidneys, differential survival outcomes comparing ECD kidneys is not clear.

Methods: A retrospective cohort study was undertaken of prospectively collected registry data of all waitlisted kidney failure patients receiving dialysis in the United Kingdom. From January 1, 2000 until September 30, 2019 inclusive, all patients listed for their first single kidney transplant were included. The primary outcome was all-cause mortality. Time-to-death from listing was analysed using time-dependent nonproportional Cox regression models, with survival analysis conducted according to the intention-to-treat principle. We explored adjusted models factoring for age (at listing), sex, ethnicity, cause of kidney failure and treatment type. All analyses were done using R statistical software (version 4.2.2).

Results: A total of 47,917 waitlisted kidney failure patients formed the study cohort, of whom 34,558 (72.1%) received a kidney transplant (living donors; n=9,140, standard criteria donor; n=18,062 and ECD; n=7,356). From the ECD recipient group, 7,009 were classified based upon donor aged ≥60 (ECD^{60}) while 347 were classified based upon donor aged 50-59 and additional criteria met (ECD$^{50\text{-}59}$). Compared to SCD, both ECD^{60} (Hazard Ratio 1.126, 95% CI 1.093-1.161) and ECD$^{50\text{-}59}$ (Hazard Ratio 1.228, 95% CI 1.113-1.356) kidney recipients had increased association for all-cause mortality. However, compared to dialysis, both ECD^{60} (Hazard Ratio 0.194, 95% CI 0.187-0.201) and ECD$^{50\text{-}59}$ (Hazard Ratio 0.218, 95% CI 0.197-0.241) kidney recipients have significantly lower all-cause mortality.

Conclusions: ECD kidneys, regardless of definition, provide equivalent and superior survival benefits in comparison to remaining waitlisted.





FULL ORALS

Kidney allocation to improve outcomes

OS8_4 IMPACT OF DECEASED DONOR ACUTE KIDNEY INJURY (AKI) ON RENAL TRANSPLANT OUTCOMES

Mikhail Nozdrin[*1], **Maria Irene Bellini**[2], **Vassilios Papalois**[3]

[1]Queen's Hospital, London, United Kingdom, [2]Sapienza University of Rome, Roma, Italy, [3]Hammersmith Hospital, London, United Kingdom

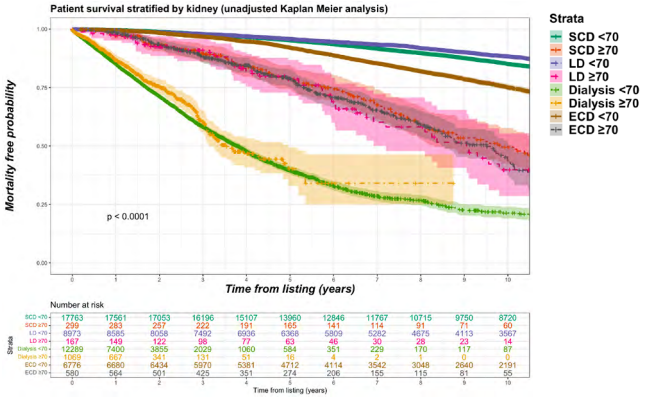
Background: Donor AKI is a common reason for discarding deceased donor kidneys due to uncertainty regarding transplant outcomes. Our study compared the post-transplant kidney function, patient and graft survival in recipients of kidneys from deceased donors with and without AKI.
Methods: Propsero, Medline, Embase, Cochrane and Web of Science were searched. NHBLI tools were used by two independent researchers for risk of bias assessment. Analysis was performed in Revman 5.4. 2984 studies were identified by the search, 34 met the inclusion criteria and were analysed in the study. There were a total of 103,529 kidney transplants analysed, 97,165 (94%) with and 6,364 (6%) without donor AKI.
Results: There was no significant difference between recipients of grafts from donors with terminal serum creatinine >2.0 mg/dl and <2.0 mg/dl in 1 year patient survival (RR: 0.99, CI: 0.96-1.02, P=0.52), as well as in 1 year (RR: 1.01, CI: 0.98-1.03, P=0.61) and 5 year (RR: 0.99, CI: 0.94-1.04, P=0.63) graft survival. There was no significant difference in 1 year post-transplantation serum creatinine between recipients of grafts with donor terminal serum creatinine >2.0 mg/dl and <2.0 mg/dl (Mean difference (MD): -0.01, CI: -0.09-0.07, P=0.84). Delayed graft function (DGF) was the only parameter significantly worse in recipients of grafts from donors with terminal serum creatinine >2.0 than to non-AKI recipients (RR: 1.89, CI: 1.64-2.17, P<0.01). In studies that compared the severity of AKI stage using the AKIN criteria, there was no significant difference in 1 year post-transplantation serum creatinine even between recipients of grafts from the most severe AKI stage (AKIN3) and the non-AKI group (AKIN0) (MD: -0.01, CI:-0.17-0.16, P=0.92).
Conclusions: Donor AKI is associated with a higher incidence of DGF but has no effect on post-transplant patient and graft survival and, based on this analysis, should not be a sole reason for discarding kidneys.

OS8_5 DO WAITLISTED KIDNEY TRANSPLANT CANDIDATES AGED ≥70 YEARS HAVE A SURVIVAL BENEFIT POST-TRANSPLANTATION?

Benjamin Anderson[*1], **Anna Brotherton**[1], **Kamlesh Patel**[1], **Felicity Evison**[2], **Dilan Dabare**[1], **Thomas Nieto**[1], **Adnan Sharif**[1;3]

[1]Queen Elizabeth Hospital Birmingham, Department of Nephrology and Transplantation, Birmingham, United Kingdom, [2]Queen Elizabeth Hospital Birmingham, Informatics Department, Birmingham, United Kingdom, [3]University of Birmingham, Institute of Immunology and Immunotherapy, Birmingham, United Kingdom

Background: Survival benefits for older kidney transplant candidates remains a contentious issue, with those aged ≥70 years often advised transplantation benefits are more quality rather than quality of life. However, data to support this statement is conflicting. The aim of this study was to analyse survival for waitlisted kidney transplant candidates aged ≥70 years.
Methodology: A retrospective cohort study was undertaken of prospectively collected registry data of all waitlisted kidney failure patients receiving dialysis in the United Kingdom. From January 1, 2000 until September 30, 2019 inclusive, all patients listed for their first kidney-alone transplant were included. Stratification for age at listing was done at 70 years. The primary outcome was all-cause mortality, with survival analysis conducted according to the intention-to-treat principle. Time-to-death from listing was analysed using adjusted nonproportional hazard Cox regression models, with transplantation handled as a time-dependent covariate. All analyses were done using R statistical software (version 4.2.2).
Results: A total of 47,917 waitlisted kidney failure patients formed the study cohort, of whom 34,558 (72.1%) received a kidney transplant. At listing only 4.4% (n=2,115) of transplant candidates were aged 70-years or over, of whom half never got transplanted (50.5%, n=1,069). Expanded criteria donor (ECD) was the commonest allograft (27.4%, n=580), followed by standard criteria donor (SCD) (14.1%, n=299) and least common from living donors (7.9%, n=167). Transplant recipients had different baseline demographics compared to those who do not receive transplants. Unadjusted mortality rate was 30.9% (n=653). In a time-dependent nonproportional hazard Cox regression model, compared to remaining on dialysis any kidney transplant provided survival benefit for waitlisted candidates aged ≥70 years; LD – HR 0.44 [95% CI 0.36-0.54]; SCD – HR 0.35 [95% CI 0.30-0.41]; ECD – HR 0.43 [95% CI 0.37-0.50].
Discussion: Any kidney allograft provides survival benefit for waitlisted kidney transplant candidates aged ≥70 years versus dialysis. While confounding by residual selection bias cannot be ruled out, our data supports encouragement of kidney transplantation as an option to consider for suitable older kidney failure patients.

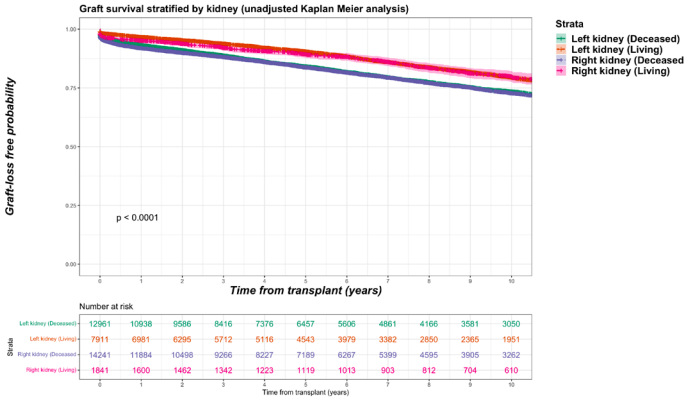


OS8_6 GRAFT-RELATED OUTCOMES COMPARING LEFT VERSUS RIGHT KIDNEYS: A POPULATION COHORT ANALYSIS

Raja Rashid[*1], **Charlotte Stephens**[1], **Adnan Sharif**[1;2]

[1]Queen Elizabeth Hospital Birmingham, Department of Nephrology and Transplantation, Birmingham, United Kingdom, [2]University of Birmingham, Institute of Immunology and Immunotherapy, Birmingham, United Kingdom

Background: A recent meta-analysis demonstrated right kidneys have inferior early outcomes, with higher rates of delayed graft function (DGF), technical failure and graft thrombosis (although differences are small in absolute terms), but long-term graft survival is equivalent. However, a contemporary population-cohort analysis exploring this question has not been undertaken
Methods: A retrospective cohort study was undertaken of prospectively collected registry data of all kidney transplant recipients in the United Kingdom from January 1, 2000 until September 30, 2019 inclusive. Outcomes studied included short-term and long-term graft outcomes. Time-to-graft loss was modelled using weighted estimation of Cox regression to account for non-proportional hazards, with covariate adjustment. All analyses were done using R statistical software (version 4.2.2).
Results: A total of 37,251 kidney transplant recipients formed the study cohort, of whom 21,068 received a left kidney and 16,183 received a right kidney. There were 9,874 and 27,377 living and deceased donors respectively, with right kidneys forming 18.9% of living donor and 52.3% of deceased donor kidneys. After deceased donor transplantation, there was no difference between left and right kidneys in rates of DGF (27.3% versus 26.7%, p=0.262) and a clinically negligible difference in primary non function rates (2.6% versus 3.2%, p=0.003). After living donor transplantation, there was a clinically negligible difference between left and right kidneys in rates of DGF (5.1% versus 7.0%, p=0.002) and primary non function (1.0% versus 2.2%, p<0.005). There was a statistically significant but clinically negligible difference in 1-year creatinine (129 umol/L versus 130 umol/L, p=0.034) or 3-month rejection rates (14.6% versus 13.6%, p=0.010) comparing left to right kidneys respectively. In an adjusted weighted Cox regression model, receiving a right versus left kidney had no impact on long-term death-censored graft survival (Hazard Ratio 1.12, 95% CI 0.94-1.33, p=0.199).
Conclusions: Left versus right kidneys make no difference with regards to long-term graft survival, although early complications are slightly higher with right kidneys especially in the context of living donor kidney transplantation.



FULL ORALS

Kidney allocation to improve outcomes

OS8_7 DECISION MAKING ABOUT LIVING DONOR KIDNEY TRANSPLANTATION: IN A MULTI-ETHNIC PATIENT POPULATION

Ahmed Ahmed[*1;2], Anna Winterbottom[3;4], John Stoves[5], Shenaz Ahmed[4], Sunil Daga[1;3]

[1]University of Leeds, Leeds, United Kingdom, [2]St James's University Hospital , Nephrology, Leeds, United Kingdom, [3]St James's University Hospital, Nephrology , Leeds, United Kingdom, [4]Leeds Institute of Health Sciences (LIHS), Leeds, United Kingdom, [5]Bradford Teaching Hospitals NHS Foundation Trust, Nephrology , Bradfors, United Kingdom

Background: Decision-making about living donor kidney transplant (LDKT) is challenging for people with advanced kidney disease (AKD). Fear of risks, insufficient knowledge and health literacy, religious beliefs, and complex family dynamics are cited as reasons for not choosing LDKT. With the aim of improving informed decision-making and experience of care, our study examined the decisional needs of people with AKD in a diverse population in the United Kingdom.
Methods: Semi-structured interviews with people with AKD from two kidney units, West Yorkshire, United Kingdom were conducted. Purposive sampling (N=30) ensured people from diverse ethnic (n=19 minority ethnic group), gender balance (female -16) and socially disadvantaged groups (n=19). In relation to transplantation, participants from waiting list (13) and those who had a kidney (only) transplant within the last two years (7 received LDKT and 9 DDKT) participated. Data were analysed using thematic analysis and managed using NVivo software.
Results: Three themes were identified. **Knowledge**: about benefits of LDKT, donor work-up process, financial implication, and long-term outcomes. Knowledge gaps were predominantly identified among those with low education and socially deprived areas irrespective of their ethnic groups. **Family and social matters:** post-transplant relationship concerns, guilt around potential transplant failure, community perception of organ donation, fear of isolation and compromised opportunities for marriage and starting a family for female. **Deliberation and validation**: need to clarify religious views, deliberation around fate and religion as well as cultural norms, desire to meet others in receipt of transplant of a similar background. Needs related to religion and culture were only identified among older minority ethnic groups.
Conclusions: While ethnicity has been identified as a significant factor associated with transplantation decision preference, it appears to intersect with other factors such as age, gender, social deprivation, and education levels. These findings and those of a parallel study exploring kidney health professionals' views, will inform the development of a transplant decision support intervention for people with advanced kidney disease from diverse ethnic backgrounds in UK kidney units.

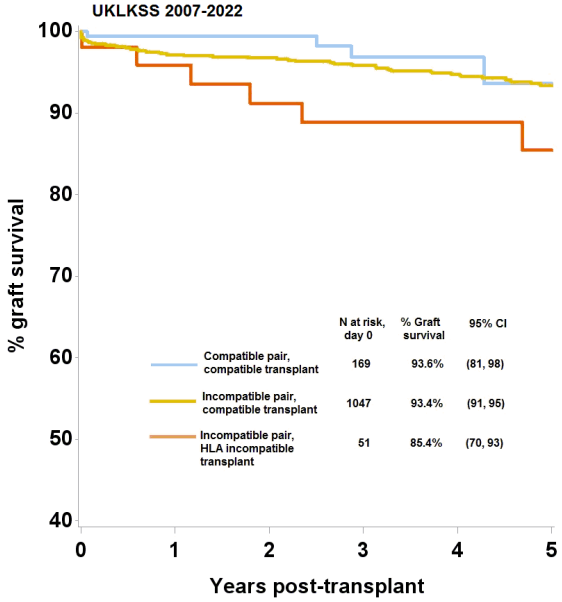
OS8_8 THE UK LIVING KIDNEY EXCHANGE PROGRAMME – PUSHING BOUNDARIES TO OPTIMISE TRANSPLANT POSSIBILITIES

Rachel Johnson[1], Matthew Robb*[1], Lisa Mumford[1], Lisa Burnapp[2]

[1]NHS Blood and Transplant, Bristol, United Kingdom, [2]NHS Blood and Transplant, London, United Kingdom

Background: Non-directed altruistic donation (NDAD) and living kidney exchanges between incompatible pairs first became legal in the UK in 2006, with the first transplants happening in 2007. The UK Living Kidney Sharing Scheme (UKLKSS), which seeks to find transplants for patients with willing but incompatible living donors, has grown incrementally since 2007, to the sophisticated programme that exists today.
Methods: This study highlights the benefits of the UKLKSS, which started by only facilitating 2-way exchanges (ie between 2 pairs), but grew to allow 3-way exchanges (2009), NDAD transplant chains (2012 for chains giving 2 transplants and 2015 for chains giving 3 transplants). Innovatively, the scheme also includes compatible pairs (seeking to improve age gap or HLA mismatch) and routinely facilitates both ABO incompatible (ABOi) and HLA incompatible (HLAi) transplant exchanges. The latter has been possible since 2012 by permitting registration of modified blood groups and unacceptable antigens to enable incompatible transplantation, where safe in the UKLKSS context.
Results: To the end of 2022, the UKLKSS has enabled a total of 1684 living donor (LD) transplants through 188 2-way exchanges (376 transplants, 22%), 185 3-way exchanges (555 transplants, 33%), 177 short chains (354 transplants, 21%) and 133 long chains (399 transplants, 24%). There have been 195 transplants for recipients registered in a compatible pair. There have also been 8 ABOi transplants, 61 HLAi transplants and one both ABOi and HLAi. The recipients of antibody incompatible transplants included 13 who waited over 2 years for a transplant in the UKLKSS. Overall, death-censored graft survival rates for all recipients receiving a transplant via the UKLKSS are 93.1% at 5 years (95%CI 91-95), with a breakdown by pair and transplant compatibility shown in Figure 1.
Conclusions: The UK Living Kidney Sharing Scheme has become one of the most innovative and mature schemes in Europe. In the last 5 years it has contributed 21% (2.6pmp) of the 4311 LD kidney transplants in the UK (12.8pmp). The scheme is continuously reviewed and improvements implemented to maximise the number of transplant opportunities. The scheme is the largest in Europe and its success has led to increasing numbers of LD transplants in the UK with excellent post-transplant outcomes.

Figure 1 - Five year death-censored graft survival, transplants in UKLKSS 2007-2022



Kidney immunology and HLA mismatch analysis

OS9_1 ASSOCIATION OF PIRCHE-II SCORES WITH KIDNEY ALLOGRAFT ANTIBODY-MEDIATED REJECTION: A POPULATION-BASED STUDY

Zeynep Demir[*1], Esteban Cortes Garcia[1], Agathe Truchot[1], Gillian Divard[1], Matthias Niemman[2], Kevin Louis[1], Olivier Aubert[1], Marc Raynaud[1], Arnaud Del Bello[3], Alexandre Hertig[4], Julien Hogan[5], Olivia Boyer[6], Carmen Lefaucheur[1], Alexandre Loupy[1]

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Background: Predicted Indirectly Recognizable Human Leucocyte Antigen Epitopes-II (PIRCHE-II) score have shown associations with kidney rejection, but its value in large prospective unselected cohorts has not been assessed so far.
Methods: We included consecutive ABO-compatible kidney recipients from a large prospective deep phenotyped cohort (NCT03474003), between 2004 and 2017 in 6 transplant referral centers in France. The total HLA-derived mismatched peptides epitopes and HLA-locus specific peptides epitopes (HLA-A, -B, -C, -DR, -DQ), that could be respectively presented by the recipient's HLA-DRB1 molecules were calculated using the PIRCHE-II algorithm. Pre-transplant circulating Anti-HLA DSA were considered positive for MFI≥ 1,400 (STAR 2022 recommendations). The measured outcome was the occurrence of biopsy-proven antibody-mediated rejection (ABMR). The associations of clinical, immunological baselines parameters with the outcome were assessed using uni- and multivariate Cox models.
Results: A total of 5,839 patients with pairs of donors and recipients were included. The median follow-up time post-transplantation was 7.3 years (IQR: 4.5-10.7). Preformed DSA were present in 423 patients (7.2%). ABMR occurred in 1,092 (18.7%) patients. The presence of preformed circulating anti-HLA DSA (p<0.001), PIRCHE-II score (p=0.002), HLA-DRB1 antigen mismatches (p<0.001), re-transplantation (p<0.001), and induction with anti-thymocyte globulins (p<0.001) were significantly associated with occurrence of ABMR. Independent immune determinants of ABMR occurrence included the presence of preformed both Class I and Class II anti-HLA DSA (HR 3.24 [2.75-3.83], p<0.001), PIRCHE-II score (1.05 [1.03-1.07], p <0.001), and re-transplantation (HR 1.68 [1.45-1.95], p<0.001). The association between ABMR and PIRCHE-II score was mainly driven by PIRCHE-II scores for HLA-DRB1 (1.11 [1.06-1.15], p<0.001), and HLA-DQB1 (1.04 [1.01-1.07], p=0.018) respectively.
Conclusions: In a large multicentric and unselected cohort of kidney recipients, we found that PIRCHE-II scores are significantly associated with ABMR, suggesting that its potential role to risk stratify patients for rejection at a population level.

OS9_2 NON-HLA RECIPIENT GENOTYPES ASSOCIATE WITH INCREASED RISK OF ANTIBODY-MEDIATED KIDNEY GRAFT REJECTION

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Background: Donor-recipient mismatches in *HLA* genes have long been associated with a poorer kidney graft survival. However, *HLA* mismatches alone do not explain long-term graft function decline. We ran a genome-wide survival study (GWSS) on a large monocentric cohort of kidney transplant recipients in order to characterize non-HLA genetic factors associated with biopsy-proven antibody mediated rejection (ABMR), the main complication causing graft loss.
Methods: The KiT-GENIE French genetic cohort comprises 1687 European recipients for kidney transplants performed since 2002. After whole-genome genotyping and imputing further genetic polymorphisms (SNP) with the TopMed reference panel, we performed a genetic survival study on >8.2M SNPs for time to ABMR (103 cases vs 1584 controls). Cox proportional hazards models were notably adjusted for *HLA* allelic mismatches and fit to assess the association between non-HLA recipients' genotypes and ABMR. P-values below the genome-wide multiple testing Bonferroni correction threshold ($P<5x10^{-8}$) were considered significant.
Results: We identified six statistically significant associations in chromosomes 1 ($p= 1.20x10^{-9}$, HR=5.82), 4 (2 independent signals with $p=4.77x10^{-9}$, HR=4.68 and $p=3.48x10^{-8}$, HR=6.18), 7 ($p= 3.82x10^{-9}$, HR=6.02), 10 ($p=1.79x10^{-8}$, HR=5.24) and 17 ($p=3.33x10^{-9}$, HR=5.24). Interestingly, the chs1 signal is located near the promotor of *RTCA*, which was repeatedly associated with kidney function, and *RTCA* gene expression was two-fold lower in acute rejection biopsies than in controls (n=6 vs 5, $p=4.5x10^{-6}$). The chs17 intronic SNP lies within *ASIC2* encoding a sodium channel that could play a role in kidney morphology and regulation, as supported by *ASIC2* overexpression in chronic kidney disease biopsies vs. normal renal biopsies (n=48 vs 5, $p=3.4x10^{-11}$).
Conclusions: Our genome-wide survival analysis in a large homogeneous monocentric cohort of kidney transplant recipients revealed six non-HLA loci associated with ABMR. External validation in independent cohorts and functional explorations will be performed to better characterize the molecular pathways involved in ABMR. We will further investigate the impact of donor genotypes and donor-recipient mismatches on ABMR to capture the complex interactions at stake during rejection events.

OS9_3 IMPACT OF HLA EVOLUTIONARY DIVERGENCE AND EPLET MISMATCHES ON KIDNEY ALLOGRAFT REJECTION AND OUTCOME: A POPULATION-BASED STUDY

Zeynep Demir*[1], Esteban Cortes Garcia[1], Agathe Truchot[1], Gillian Divard[1], Kevin Louis[1], Olivier Aubert[1], Marc Raynaud[1], Arnaud Del Bello[2], Alexandre Hertig[3], Julien Hogan[4], Olivia Boyer[5], Alexandre Loupy[1], Carmen Lefaucheur[1]

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Background: As a surrogate of HLA diversity, the HLA evolutionary divergence (HED) between individual HLA alleles have been suggested as a potential metric to correlate with allo-immune response but has not been evaluated so far in large prospective cohorts. We sought to determine the impact of HLA related immunogenicity measurements on kidney allograft rejection and allograft loss.
Methods: We included consecutive ABO-compatible kidney transplanted patients from a comprehensive and prospective cohort (NCT03474003), between 2004 and 2017 in 6 transplant centers in France. The donor and recipient HED was calculated using the physicochemical Grantham distance for class I (HLA-A, HLA-B, HLA-C) and class II (HLA-DRB1, HLA-DQB1) HLA alleles and for their respective loci. Class I and II HLA eplet mismatches (MM) were calculated by using HLAMatchmaker® software. HLA immunogenicity was assessed at the time of transplantation. The primary outcome was the occurrence of ABMR and the secondary outcome was allograft loss. The associations of clinical, immunological baselines parameters with the outcome's measures were assessed.
Results: A total of 5,839 recipients were evaluated. The median follow-up time post-transplant was 7.3 years (IQR: 4.5-10.7). Preformed DSA were present in 854 patients (14.6%). ABMR occurred in 1,092 (18.7%) patients and graft loss occurred in 1,149 (20%) patients. The independent immune determinants of ABMR were the presence of preformed anti-HLA DSA both class I and class II (HR 3.77 (3.22-4.4), p<0.0001), HLA class II eplet MM (1.02 (1.01-1.05), p <0.001) while class I and II HED of both donor and recipient showed no independent association with risk. Among the immunological determinants of long-term allograft outcome, only the presence of anti-HLA DSA was independently associated with risk (HR 1.59 (1.32-1.92), p<0.001)
Conclusions: In a large multicentric and qualified prospective unselected cohort of kidney recipients, the presence of class I and II anti-HLA DSA as well as class II HLA eplet MM were independent immunological predictors of ABMR. HED did not show any significant association with ABMR. Both pretransplant HLA eplet MM as well as HED did not show independent association with long-term allograft failure suggesting their inability to risk stratify patients at a population level.

OS9_4 ALLOIMMUNE RISK STRATIFICATION IN KIDNEY TRANSPLANTATION - DEVELOPMENT AND VALIDATION OF A NOVEL HLA MOLECULAR MISMATCH ALGORITHM

Hannah Charlotte Copley*[1;2], Chris Wiebe[3], Jon Jin Kim[1;4], Miriam Manook[1], Eleanor Williams[5], Irina Mohorianu[5], Christiane Kling[6], Dietrich Kabelitz[6], Andrew Leach[2], Peter Nickerson[3], Vasilis Kosmoliaptsis[1]

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Background: Alloimmune risk stratification to guide personalised recipient care requires prognostic biomarkers and is an unmet need in kidney transplantation.
Methods: Using three molecular HLA mismatch (molMM) algorithms, Amino-Acid-Mismatch-Score (AAMS), Electrostatic-Mismatch-Score (EMS3D) and NetMHCIIpan we assessed model discrimination for predicting de novo donor-specific-antibody (dnDSA) at the individual HLA level in an experimental sensitisation dataset (patients receiving standardised donor lymphocyte injections, mismatched HLA n=665). Derivation of risk thresholds for HLA-DR/DQ mismatch was performed and externally validated in two extensively phenotyped kidney transplant cohorts (Manitoba, n=856, Denver n=404), and in the NHSBT kidney transplant registry (2000-2020, n=27,028).
Results: External validation (Manitoba cohort) of experimentally-derived HLA-DR/DQ molMM risk thresholds showed all algorithms had similar performance for dnDSA prediction at the single HLA level (HLA-DQ AUC 0.78-0.80; HLA-DR AUC 0.76-0.81). AAMS and EMS3D showed improved risk stratification at the patient level (incremental hazard increase from low to medium to high risk groups for HLA-DR+DQ dnDSA) vs NetMHCIIpan (p=NS for medium vs. high risk groups). A novel algorithm combining AAMS and EMS3D further improved discrimination (Figure 1), identifying a larger cohort at very low risk of Class-II dnDSA (Table 1). In multivariate analysis, this algorithm demonstrated correlation with primary alloimmune events (dnDSA p<0.001, TCMR p<0.001, ABMR p=0.0049) and all-cause graft loss (p=0.0038). Validation in an ethnically diverse cohort (Denver) confirmed the dnDSA risk association (p<0.0001), and in the NHSBT registry showed a significant association with all-cause graft loss (p<0.001).
Conclusions: We describe a novel molMM algorithm incorporating information from HLA sequence and tertiary structure, that may be used as prognostic biomarker of primary alloimmunity risk, and to enrich prospective clinical trials in kidney transplantation.

Table 1. Low Risk Patient Stratification (HLA-DR/DQ dnDSA development) by model (Manitoba Kidney transplant cohort).

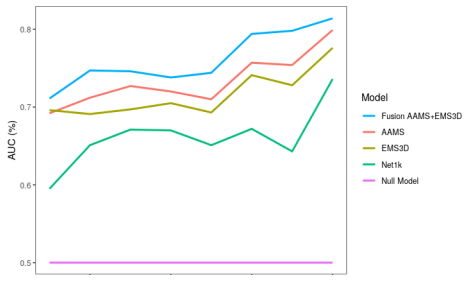
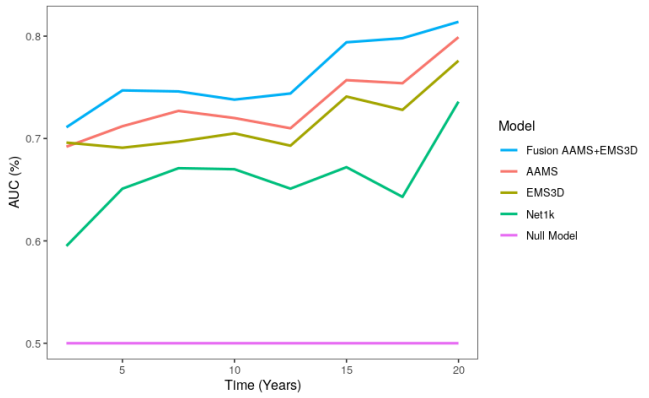


Figure.1. Time-dependent discrimination performance for HLA-DR/DQ dnDSA prediction in Manitoba Kidney transplant cohort.



OS9_5 NON-A1/NON-A1B TO B BLOOD GROUP DECEASED DONOR KIDNEY TRANSPLANT: A LARGE AND SUCCESSFUL SINGLE CENTER EXPERIENCE

Hasan Khamash*[1], Caroline Jadlowiec[1], Kunam Reddy[1], Pooja Budhiraja[1], Raymond Heilman[1]

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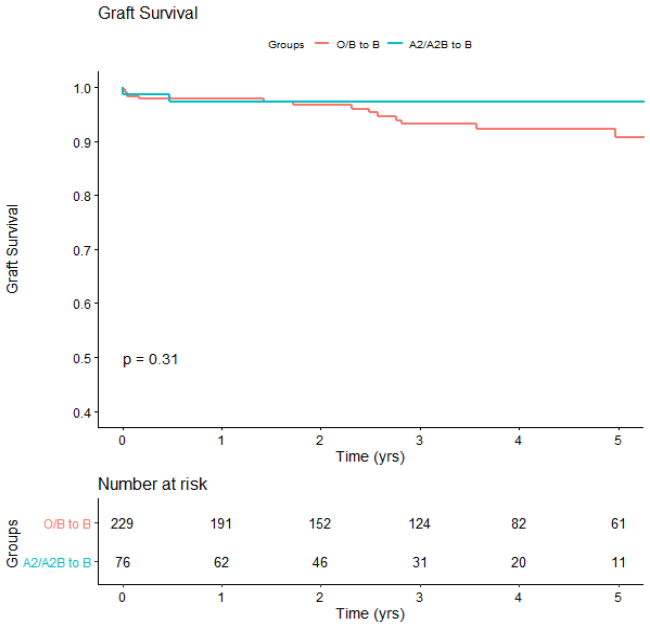
Background: Blood type B candidates wait longer for deceased donor kidney transplant (DDKTXs) than Blood types A and AB and are clustered more in disadvantaged minorities populations especially black race. To address that the kidney allocation system (KAS) was implemented in December 2014 allowing the allocation of DDKTXs from non-A1/non-A1B donors to blood type B candidates who have acceptable anti-A titers. This process was left to the different transplant centers to opt in for and implement.
Methods: Retrospective single center data review including all blood type B recipients of deceased donor kidney alone transplants since the implementation of KAS 4/30/2022 and follow-up through 9/1/2022. All blood type B candidates undergo anti-A titer check by the tube method at evaluation to establish candidacy for non-A1 listing. Initially acceptable anti-A titers were kept at or below 1:8 and subsequently gradually increased to 1:64 in 2017. Our titers are higher than the previously published data as we do not utilize dithiothreitol to neutralize IgM. Titers are checked every 3 months while on the waitlist, at day of transplant and 2 days after. Within this group we compared outcomes between recipient of blood type B/O to B and A2/A2B to B.
Results: We identified 305 blood type B recipients and out of those 76 received non-A1/non-A1B. The non-A1/non-A1B group was more likely to be transplanted faster, avoid dialysis and receive an organ from outside of the local OPO. There were similar cold ischemia times and delayed graft function rates. Estimated GFR was slightly low at 4 months and 1 year but did not translate to worse graft outcomes at 5 years in fact those were similar. There was only 1 AMR episode in the non-A1/non-A1B group that was related to HLA antibodies. Anti-A titers were mostly (79%) similar or reduced posttransplant.
Conclusions: In select blood type B candidates, transplants from a non-A1/non-A1B deceased donors offer opportunities for shorter waiting while maintaining excellent outcomes. Despite the benefits, this option continues to be underutilized evident by stagnant transplant rates due to the lack of or the suboptimal implementation by transplant centers.

Groups	B/O to B (N=229)	A2/A2B to B (N=76)	p value
Qualifying Time Median (mo)	39.6	27.7	< 0.001
Listing Time Median (mo)	8.4	4.4	0.008
Preemptive to dialysis n(%)	37 (16.2%)	22 (28.9%)	0.015
Regional/National Donor n(%)	107 (46.7%)	49 (64.5%)	0.007
Recipient Black Race n(%)	38 (16.6%)	13 (17.1)	0.918
KDPI Ref Population 2017 Median (%)	44%	50%	0.051
KDPI>85% n(%)	20 (8.7%)	11 (14.5%)	0.152
Cold Ischemia Time Median (hrs)	20.1	19	0.963
Delayed Graft Function n(%)	124 (54.1%)	45 (59.2%)	0.442
HLA Mismatches Median	4	5	0.006
CKD-EPI GFR at 4 mo ml/min (non-race based)			0.035
Mean (SD)	57.7 (22.8)	50.6 (17.3)	
Median (Q1, Q3)	53.9 (40.4, 73.7)	50.5 (40.8, 58.7)	
CKD-EPI GFR at 1 yr ml/min (non-race based)			0.003
Mean (SD)	62.7 (22.9)	51.5 (17.6)	
Median (Q1, Q3)	59.6 (47.7, 78.2)	52.19 (39.5, 64)	
Rejection in the first Yr n(%)	24 (10.5%)	13 (17.1%)	0.125
Cellular Rejection including borderline n	21	12	
Antibody Mediated Rejection/Mixed n	3	1	



OS9_6 ANTI-HLA I IGG FC AGALACTOSYLATION DRIVES DIRECT ENDOTHELIAL CELL ACTIVATION VIA IFNa PATHWAY

Anaïs Beyze*[1], Vincent Pernin[2], Nicole Bec[3], Anthony Chauvin[1], Christian Larroque[1], Moglie Le Quintrec[1]

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Background: Antibody-mediated rejection (ABMR) is the first cause of kidney graft loss. ABMR is mainly caused by IgG directed against the graft HLA antigens (Donor-Specific Antibody, DSA). Binding of DSA to the graft endothelial HLA proteins leads to intracellular signalling pathways causing an inflammatory endothelial profile with secretion of cytokines and chemokines. Exploring DSA characteristics leading to endothelial inflammation is crucial to explain why some DSA positive patients develop ABMR while other do not. IgG are glycoproteins with an oligosaccharide attached to the Fc fragment. The composition of this oligosaccharide is a clue to understand the difference in IgG effector functions. We hypothesize that anti-HLA antibodies Fc glycosylation influence direct endothelial cell activation and thus occurrence of ABMR.
Methods: We analysed DSA Fc glycosylation of kidney grafted patients using mass spectrometry. In vitro, endothelial cells were exposed to a monoclonal anti-HLA I antibody whose glycosylation had been previously modified and cytokine and chemokine secretion was analysed.
Results: In a cohort of 54 DSA positive patients, agalactosylation of IgG1 DSA was associated with ABMR. In vitro, exposition of endothelial cells to an at least 50% agalactosylated anti-HLA I IgG1 causes CXCL10 and CXCL11 secretion while exposition to galactosylated or siaylated forms do not. Interestingly, IFNa secretion was also found highly superior when cells were exposed to agalactosylated forms. Blocking the IFNa pathway using a neutralizing anti-IFNa antibody, a blocking anti-IFNAR antibody or a JAK1/2 inhibitor completely blocked CXCL10 and CXCL11 secretion.
Conclusions: Anti-HLA I IgG1 agalactosylated at more than 50% generates IFNa secretion after ligation to endothelial HLA I proteins. This IFNa production has an autocrine and paracrine effect leading to the production of the chemokines CXCL10 and CXCL11 by endothelial cells.

OS9_7 MULTIPARAMETER MASS SPECTROMETRY DECIPHERS SPECIFIC CIRCULATING NATURAL KILLER TCELL SUBSETS PROTECTING KIDNEY TRANSPLANT PATIENTS FROM CMV INFECTION

Laura Donadeu*[1], Thomas Jouve[2], Sofia Bin[3], Susan Hartzell[3], Alba Torija[1], Delphine Kervella[1], Weijia Zhang[3], Zeguo Sun[3], Luis Sanchez[3], Nestor Toapanta[4], Irina Torres[4], Maria Meneghini[1;4], Jose Zuñiga Vergara[1;4], Francesc Moreso[4], Paolo Cravedi[3], Oriol Bestard[1;4]

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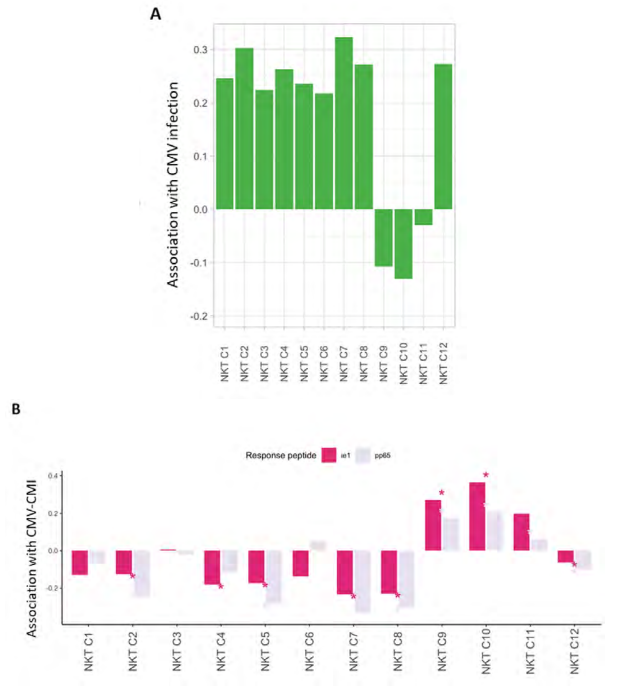
Background: Cytomegalovirus (CMV) infection still unpredictably occurs in a significant number of kidney transplant (KTR) patients conferring poorer patient and graft outcomes. Deciphering the role of the immune system driving protection against CMV is key for immune-risk stratification and to establish guided preventive strategies.
Methods: In 112 prospectively collected PBMC samples from 28 CMV seropositive KTR at 4 different time points recruited in a RCT: pre-transplantation, 15-days (D15), 3-months (M3) and 12-months (M12) posttransplant, we simultaneously assessed a CyTOF (Cytometry by Time Of Flight) extended T-cell phenotype and CMV-specific functional cell-mediated immunity (CMV-sp CMI) against IE1 and pp65 antigens using an IFN-γ ELISPOT. In a semi-supervised CyTOF analysis, we assessed combined specific T-cell subsets phenotype clusters in meta-clusters significantly correlating with protective anti-viral CMI and prevention of CMV infection. We validated these data in an independent KTR cohort.
Results: Among the 28 patients, 12 developed CMV infection at a median time of 2.38 (IQR 1.25-3.50) months. KTR developing CMV infection showed significantly lower CMV-sp CMI frequencies both prior (p=0.004) and at 15-day after transplant (p=0.006) than those KTR that did not. Semi-supervised cell-cluster analysis revealed that while CMV(tetramer-stained)-specific T-cell numbers associated with high functional CMI and clinical protection (R=0.555 p<0.001), global CD3+CD4+CD56+ NKT-cell numbers (NKT) highly associated with CMV reactivation. However, 3 specific NKT-cell meta-clusters, sharing the CD11b surface marker, directly correlated with both protected CMI responses and low CMV replication events (Figure 1). These findings were validated in an external KTR cohort showing a higher expression of CD11b-NKT cells in patients not developing CMV infection as compared to those that did not (p=0.042).
Conclusions: Using a multidimensional deep phenotype characterization by CyTOF, we demonstrate the specific functional role of certain specific cell subset phenotypes that may not be observed when using traditional flow cytometry analysis. We describe a novel NKT-cell subset, expressing the CD11b surface marker, having a protective and functional role preventing CMV infection in KTR.



OS9_8 SPATIAL PROFILING OF THE KIDNEY ALLOGRAFT UNRAVELS A CENTRAL ROLE OF FCYRIII+ INNATE IMMUNE CELLS IN REJECTION

Baptiste Lamarthée*[1;2], Jasper Callemeyn[1], Yannick Van Herck[3], Asier Antoranz[4], Priyanka Koshy[4], Claire Tinel[1;2], Francesca Bosisio[4], Maarten Naesens[1]

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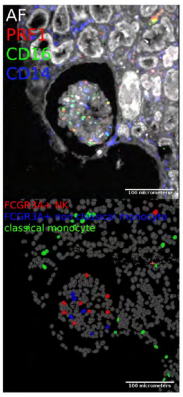
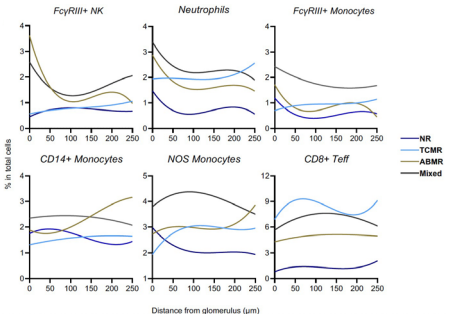
Background: How the immune system participates to kidney transplant rejection has not been fully elucidated. Using transcriptomics, we previously reported that NK cells and monocytes are key players in kidney transplant rejection. Here, we examined spatial localization and interactions at single-cell resolution between these two cell types and all other cells present in the graft using multiplex immunofluorescent staining.
Methods: We performed Multiple Iterative Labeling by Antibody Neodeposition (MILAN) technic on 18 different transplant biopsies, with a representative mix of clinicopathological phenotypes: 3 antibody-mediated rejection (DSA+ ABMR), 5 DSA-negative cases with microvascular inflammation (DSA- MVI), 2 mixed rejection, 4 T-cell mediated rejection (TCMR), 1 borderline changes, and 3 stable cases (NR). The cell identities were determined using a broad panel of 36 phenotypic markers after digital reconstruction.
Results: We mapped 555,479 cells to 17 phenotypes including 5 types of renal epithelial cells (PT cells, AQP1+ tubule cells, CD138+ tubule cells, distal tubule cells and AQP1+ PanCK+ tubule cells), 9 immune cell subtypes: 3 myeloid (macrophages, CD1c+ dendritic cells [DC] and S100+ DC), 5 lymphoid (B cells, CD4 regulatory T cells (Tregs), FcγRIII+ NK cells, CD4 effector T cells (Teff) and CD8 Teff) and an MPO+ neutrophil subtype. Importantly, FcγRIII+ NK cells, neutrophils, FcγRIII+ monocytes and CD8+ Teff proportions mainly correlated with inflammation associated to transplant rejection. Compartmentalization analysis indicated that FcγRIII+ NK cells and FcγRIII+ monocytes infiltrate vascular compartment. In addition, neighbourhood analysis unravelled a strong and significant enrichment of FcγRIII+ NK cells next to FcγRIII+ monocytes in ABMR or mixed rejection biopsies, but not in TCMR or NR biopsies. In contrast, CD14+ monocytes were mainly surrounded by CD8 T cells in TCMR.
Conclusions: Our study provides new insights in the role of the different innate immune cell populations and their interactions with the kidney structural cells at the protein level. FcγRIII+ and CD14+ monocytes act as the dominant "communication hubs" within the allograft, mainly communicating with FcγRIII+ NK cells in vascular compartment and CD8 T cells in interstitial compartment, respectively.





OS10_1 IMPACT OF DESENSITIZATION THERAPY WITH ISATUXIMAB ON HLA-SPECIFIC MEMORY B CELLS AND PLASMA CELLS IN HIGHLY SENSITIZED PATIENTS

Alba Torija*[1], Delphine Kervella[1], Laura Donadeu[1], Maria Meneghini[2], Elena Crespo[1], Francesc Moreso[2], Josep Maria Cruzado[3], Rico Buchli[4], Flavio Vincenti[5], Amarpali Brar[5], Anat Tambur[6], Mark Stegall[7], Helen Lee[8], Markus Dudek[8], Giovanni Abbadessa[8], Oriol Bestard[1;2]

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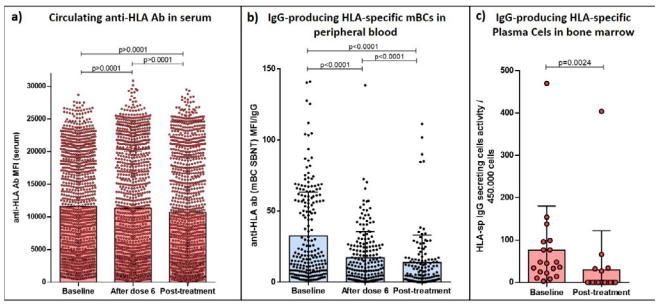
Background: HLA sensitization is a main barrier for successful kidney transplantation. Anti-HLA antibodies (Ab) are produced by HLA-specific (HLA-sp) plasma cells (PCs) and peripheral memory B cells (mBCs). Targeting plasma cells through an anti-CD38 monoclonal antibody (mab) may reduce titers of anti-HLA antibodies.
Methods: 10 of 23 highly sensitized patients recruited in the anti-CD38 mAb isatuximab desensitization clinical trial (NCT04294459) with available paired samples were analyzed at baseline, after dose 6 and one week after last (8th) dose, for changes in anti-HLA Ab and circulating HLA-sp mBCs using SAB assays on serum and polyclonally expanded mBCs culture supernatants and with a HLA-sp B-cell Fluorospot assay. Multidimensional spectral Flow cytometry immunophenotyping was also performed in 16/23 PBMC samples prior and after therapy, and in 4 patients bone marrow (BM) aspirates were obtained at the same time-points to analyze HLA-sp IgG-producing PC frequencies and changes in cell subset numbers.
Results: Serum HLA-specific Ab MFI values were progressively and significantly reduced over time until last follow-up (p<0.0001) (Figure 1a). Moreover, isatuximab significantly reduced the secretion of circulating HLA-specific IgG from mBCs (p<0.0001) (Figure 1b). BM-residing IgG-producing HLA-specific PCs were also significantly reduced (75.6±104 and 29.6±92, p=0.0024) (Figure 1c). Multidimensional spectral immune-phenotyping revealed a drastic reduction of peripheral CD38+ B cells (CD19+), class switched memory B cells (CD19+CD27+IgD-) and plasmablast (CD19+CD24-) (p<0.0001, for all cell subsets), whereas circulating class-switched CD38- mBC increased (p<0.0001). In the bone marrow, percentages of LLPC (CD20-CD38+CD138+) were also reduced after therapy. Isatuximab also suppressed CD38+ Tregs from the circulation (p<0.0001).
Conclusions: These findings support the capacity of isatuximab to reduce the burden of sensitization in highly immunized patients, decreasing serum anti-HLA antibody levels by targeting HLA-sp mBCs and HLA-sp PCs from both peripheral blood and the bone marrow.



OS10_2 DARATUMUMAB DESENSITIZATION BEFORE KIDNEY TRANSPLANTATION – A PILOT STUDY

Marie Matignon*[1], Nizar Joher[1], Caroline Pilon[2], Emmanuelle Boutin[3], Jean-Luc Taupin[4], José Cohen[2], Florence Canoui-Poitrine[3], Vissal David Kheav[4], Maryvonnick Carmagnat[4], Philippe Grimbert[1]

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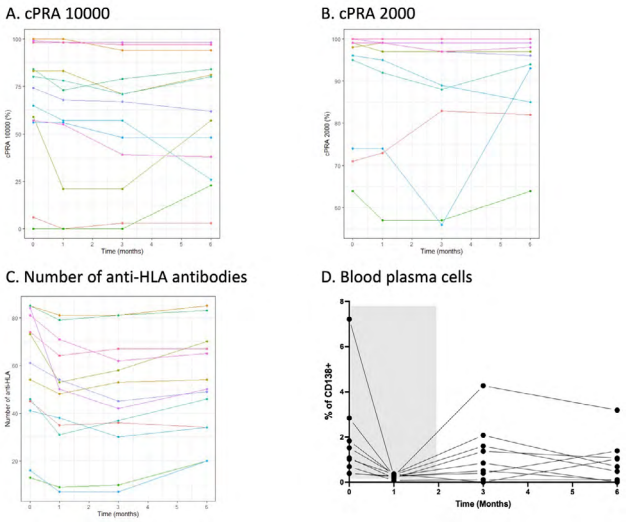
Background: Sensitized patients have lower access to kidney transplantation (KT). We conducted a pilot study to desensitize awaiting KT patients with the anti-CD38 antibody Daratumumab.
Methods: Our monocentric, open label, phase I/II study included adults awaiting KT with calculated panel reactive antibodies (cPRA) ≥95 % for ≥3 years. Dose-escalation step included patients treated with 4 weekly increasing doses. Expansion cohort enrolled patients treated with 8 weekly doses of 16 mg/kg daratumumab.
Primary endpoints were safety of daratumumab (serious adverse events (SAE)) and 6-months evolution of cPRA in expansion cohort. We calculated cPRA for two anti-HLA antibodies mean fluorescence intensity (MFI) thresholds: 2000 and 10000.
Results: Dose-escalation step included 9 patients with no SAE reported.
Expansion cohort included 13 patients (Table 1) with no SAE and 27 AE in 9 patients (69%), mainly reaction to infusion (n=22 (81.5%)). One patient died because of stroke within 5 months not related to daratumumab infusion.
Within 6 months, cPRA 10000 decreased significantly (62 [38-84] vs. 74 [57-84]; P=0.02) while cPRA 2000 remained stable (97 [93-99] vs. 99 [95-100]; P=0.28). Maximum effect was reached after three months (P<0.001 and P=0.07 respectively) (Figure 1). Number of anti-HLA decreased significantly from 61 [45-81] to 50 [34-67] (P<0.001). Plasma cells (CD138+) decreased significantly after one month from 1.08% [0.238-3.535] to 0.28% [0.196-0.337] in PBMCs. Gammaglobulins decreased significantly from 10 [9-16] to 6 [5-8] g/L (P<0.001) with no infectious event reported beside one COVID.
Conclusions: Daratumumab desensitization before KT significantly decreases cPRA and number of anti-HLA antibodies especially 3 months after an 8-weeks treatment without significant secondary effects.

Table 1: characteristics of the patients included in the expansion cohort

Patients	N=13
Age, years, median [IQR]	48.7 [41.0-49.1]
Sensitization risk factors	
Prior kidney transplantation, N (%)	12 (92.3)
Transfusion, N (%)	3 (23.1)
Immunological characteristics	
cPRA - threshold 2000	99 [95-100]
cPRA - threshold 10 000	74 [57-84]
Anti-HLA antibodies, median, [IQR]	61 [45-81]
Class I, median, [IQR]	43 [32-56]
Class II, median, [IQR]	17 [7-29]

Figure 1: sensitization evolution within 6 months



OS10_3 EARLY RESULTS OF ATTAIN (ITN090ST): DARATUMUMAB & BELATACEPT FOR HLA DESENSITIZATION IN KIDNEY TRANSPLANT CANDIDATES WITH 100% CPRA

Flavio Vincenti*[1], Sindhu Chandran[2], Rajalingam Raja[3], Thomas Martin[3], Stalinraja Maruthamuthu[3], Shreya Mall[3], Cynthia Breeden[4], Kristen Mason[5], Doan Nguyen[6], Frances Lee[7], Juliete Silva[4]

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Background: Despite high allocation priority, <10% of kidney transplant candidates with calculated panel reactive antibody (cPRA) 100% are able to find a compatible donor. Current HLA desensitization strategies are ineffective due to antibody rebound. Adding costimulation blockade to plasma cell (PC) depletion prevents antibody rebound in NHP by countering nodal B cell and Tfh expansion. We hypothesized that a similar approach in humans could improve success with HLA desensitization.

Methods: ATTAIN is a pilot, phase I/II trial of daratumumab, a CD38 mAb used in multiple myeloma, plus belatacept, a high affinity CTLA4-Ig, to desensitize kidney transplant candidates with cPRA ≥99.9%. Enrolled subjects receive daratumumab (6 doses: 8 mg/kg) and Belatacept (4 doses: 10 mg/kg) over 10 weeks with blood and bone marrow assessments pre-and post-treatment. The primary efficacy endpoint is a composite of (1) elimination of ≥1 HLA antibody specificity, (2) ≥50% reduction in the MFI of ≥3 HLA antibody specificities, or (3) kidney transplant from a previously incompatible donor. Target accrual is 15, enrolled in 2 cohorts (5+10).

Results: Cohort 1 (n=5, mean age 44, 60% with previous transplant) has been enrolled and treated, with 5-31 weeks follow-up to date. The treatment was tolerated well in all 5 patients. Three of 5 participants met the primary efficacy endpoint and 5 of 5 had >50% bone marrow PC depletion. It was accompanied by decrease of both CD19+CD38hiCD138- short-lived PC (SLPC) and CD19+CD38hiCD138+ PC subsets with maintenance of CD19-CD38+CD138+ PC population which contains the long-lived PC (LLPC) subsets. Moreover, circulating CD19+CD27-IgD+CD38+CD24+ transitional B cells were also decreased all 5 patients. One patient received a kidney transplant from a previously incompatible deceased donor and is doing well at 7 months post-transplant without rejection or rebound of HLA antibodies.

Conclusions: Daratumumab and belatacept may provide effective desensitization for kidney transplant candidates with cPRA 100% by depleting PC from existing marrow and blood PC subsets. ATTAIN (NCT04827979) is a trial conducted by the Immune Tolerance Network and sponsored by NIAID (award UM1AI109565).

OS10_4 A PILOT STUDY EVALUATING DUAL CO-STIMULATION BLOCKADE WITH DAZODALIBEP (HZN4920) AND BELATACEPT FOR PROPHYLAXIS OF KIDNEY ALLOGRAFT REJECTION

Allan Kirk[1], Jun Shoji[2], David Wojciechowski[3], Jim Kim[4], Wenjing Xu[5], Todd Wilson[5], Flavio Vincenti*[2]

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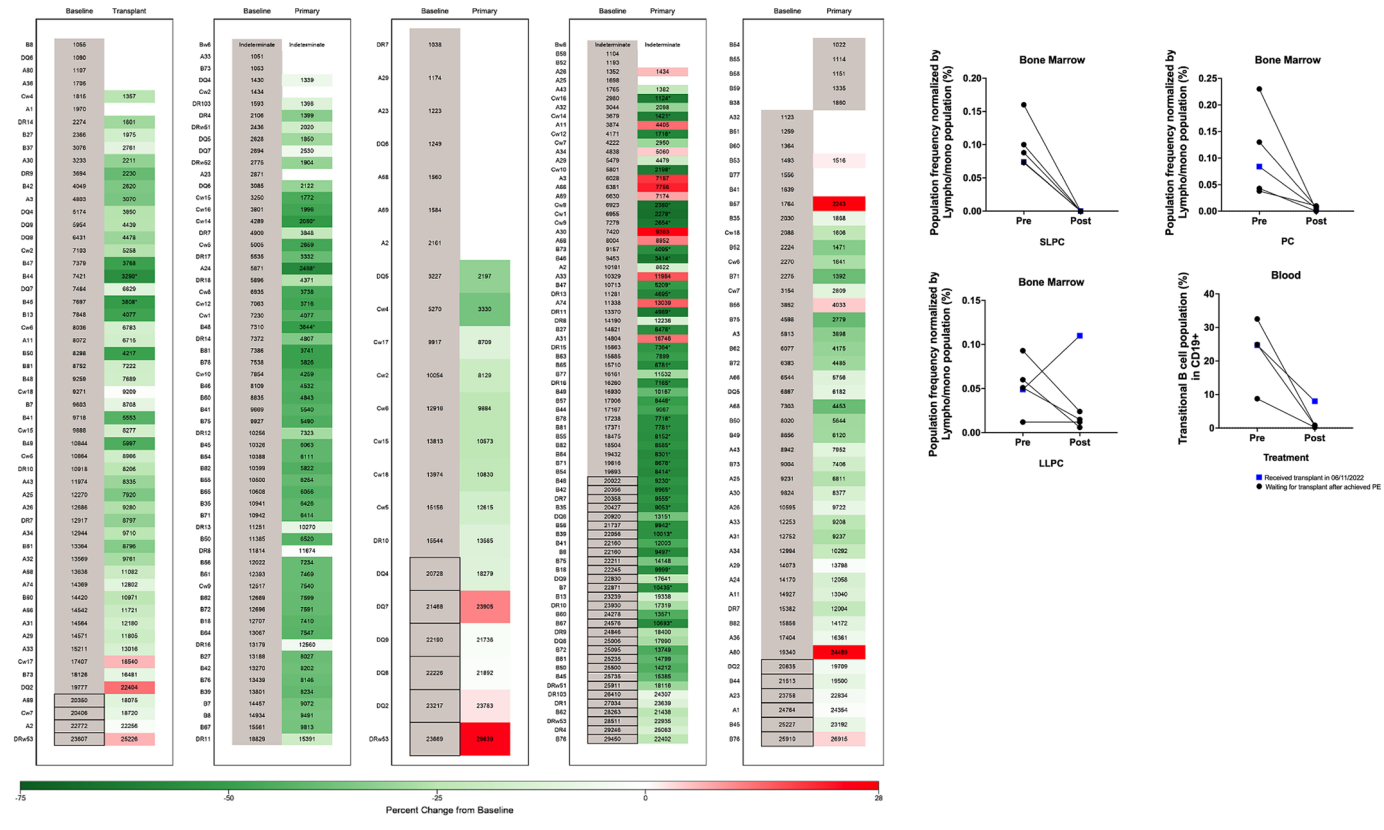
Background: Dual co-stimulation blockade (CoB) of the CD28-CD80/86 and CD40-CD40L pathways to prevent kidney allograft rejection has been demonstrated in non-human primate studies. However, this preclinical approach has never been tested in human subjects. The purpose of this study (NCT04046549) was to test dual CoB, combining dazodalibep (DAZ), a non-antibody biologic antagonist of CD40L, with belatacept (Bela), a CTLA-4-Fc fusion protein, as the sole maintenance antirejection therapy in adults undergoing kidney transplantation.

Methods: This was a Phase 2a, single-arm, open-label, pilot study in adults of low immunologic risk undergoing a first kidney transplant. Participants (pts) received lymphocyte depleting induction (thymoglobulin) and corticosteroids, followed by intravenous DAZ+Bela initiated the day after surgery and repeated every 2–4 weeks post-transplantation. The primary endpoint was the incidence of composite efficacy failure (treated biopsy-proven acute rejection of grade 1A or higher, graft loss or death) 24 weeks post-transplant. Secondary endpoints included the incidence of composite efficacy failure, antibody-mediated rejection (ABMR), and treated acute rejections at Week 48. Safety was also evaluated. All data reported here represents an interim analysis.

Results: Twenty-three pts underwent kidney transplant and received DAZ+-Bela, and 20 pts (age 21–70, 80.0% male) were included in the efficacy evaluable set. Graft and pt survival were 100%. Both drugs were well tolerated; one pt discontinued DAZ+Bela due to an adverse event (AE; neutropenia), and 60% stayed on study therapy at least 48 weeks. The incidence of composite efficacy failure was 5/20 (25%) at Week 24 and 48. The mean (SD) eGFR of pts at Week 48 was 71.3 (12.7) mL/min/1.73^2. There were 3/20 (15.0%) ABMRs and 6/20 (30.0%) treated acute rejections by Week 48 (five diagnosed within 12 weeks). The most frequently reported AEs (≥4 pts) were COVID-19, anaemia, BK virus infection, hypophosphataemia, and leukopenia. Nine pts experienced ≥1 serious AE and seven experienced ≥1 AE of special interest.

Conclusions: This is the first clinical study of dual CoB blockade in organ transplantation. DAZ+Bela was safe and well tolerated, and prevented rejection in most pts.

Figure 1. A. Change in HLA antibodies with treatments. B. Change in blood and bone marrow PC subsets with treatment.



OS10_5 A PHASE I/IIA TRIAL OF AUTOLOGOUS REGULATORY T CELL THERAPY TOGETHER WITH DONOR BONE MARROW INFUSION IN KIDNEY TRANSPLANTATION

Rainer Oberbauer[1], Moritz Muckenhuber[1], Jasmin Mucha[1], Roman Reindl-Schwaighofer[1], Andreas Heinzel[1], Gabriela A. Berlakovich[1], Nina Worel[1], Michael Wolzt[1], Thomas Lion[2], Matthias Edinger[3], Thomas Wekerle*[1]

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Background: In preclinical models combining Treg therapy with donor bone marrow (BM) transplantation leads to mixed hematopoietic chimerism and tolerance without myelosuppressive recipient conditioning, avoiding the adverse effects of irradiation or cytotoxic drugs.
Methods: A single center, controlled, first-in-human phase I/IIa trial is conducted in HLA-mismatched living donor kidney transplant recipients. In vitro expanded polyclonal recipient Tregs and MNC-separated donor BM cells are administered within 3 days after transplant, tocilizumab is injected s.c. for the first 3 weeks. No irradiation or cytotoxic drugs are given. Immunosuppression (IS) consists of thymoglobulin, belatacept, sirolimus and steroids. Starting at 6 months, sirolimus and steroids are gradually withdrawn in stable study group patients. A parallel control group receives the same IS, but no Tregs, BM or tocilizumab. Total leukocyte donor chimerism and safety are co-primary endpoints. Immune monitoring accompanying the trial includes NGS of the TCR repertoire, flow cytometric leukocyte subset analysis, scRNAseq and protocol biopsies including transcriptomic analysis (at 6, 12, 24, 36 and 60 months).
Results: Eight patients have been enrolled and treated so far (5 in the study group, 3 in the control group; out of the predetermined sample size of 6 per group). One additional patient was enrolled but not treated as Treg manufacturing failed. Treg (1.1-1.5x10^7 cells/kg) and BM cell (0.7-1.9x10^8 nucleated cells/kg) infusions were well tolerated. The study group developed low levels of total leukocyte donor chimerism (<1%) in the first weeks post-transplant, whereas no chimerism was detectable in the control group. The study group shows a favorable clinical course, with GFRs of 55-74 ml/min/1.72m² at latest follow-up (median follow-up 20 months) and no safety signals were observed. IS reduction has been completed in one patient currently maintained on belatacept monotherapy q8 weeks and is in progress in all other patients. Protocol biopsies at 12 months were clear.
Conclusion: Combined Treg therapy and BM transplantation is safe and feasible in living donor kidney transplantation and induces low-level chimerism. Results from immune monitoring assays will provide insight into the immunomodulatory effect of this protocol.

OS10_6 LONG-TERM OUTCOMES AFTER CONVERSION TO A BELATACEPT-BASED IMMUNOSUPPRESSION IN KIDNEY TRANSPLANT: A MATCHED COHORT STUDY

Gillian Divard*[1], Charlotte Debiais-Deschamps[1], Olivier Aubert[1], Radu Vadanici[2], Christophe Legendre[1], Carmen Lefaucheur[1], Alexandre Loupy[1]

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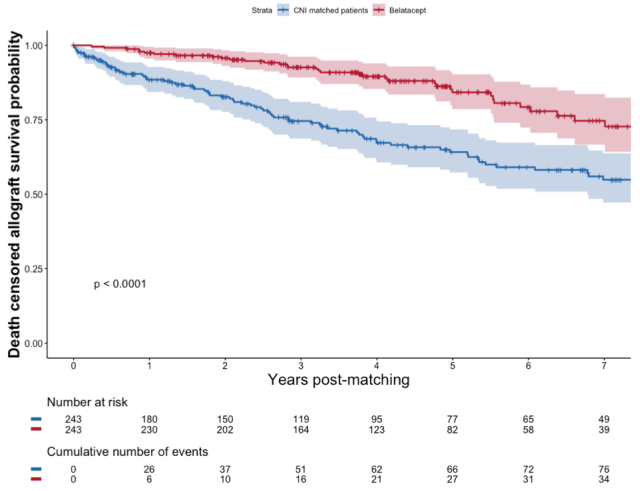
Background: Conversion to a belatacept based immunosuppression is currently the most promising Calcineurin inhibitors (CNI) avoidance strategy in kidney transplantation. However, there is a lack of evidence on long-term efficacy and safety outcomes. This study aims to investigate the long-term outcomes of patients converted to belatacept after transplant and compared them with matched patients treated with a CNI-based immunosuppression.
Methods: Kidney transplant recipients from two French academic transplant canters were recruited. We used a propensity score to match, patients at time of the biopsy which indicate the conversion to belatacept to control patients under a CNI regimen with a biopsy after transplant. We used 11 parameters associated with graft survival for the matching, 4 at baseline (recipient age, prior transplant, donor type, dgf) and 7 at time of the biopsy (time after transplant, eGFR, proteinuria, DSA and Banff scores cv, ah, IFTA). Transplant outcomes defined by graft and patient survival, as well as safety outcomes were compared between the matched patients.
Results: Among the 311 patients converted to belatacept after transplant, 243 patients were matched to 243 patients treated and maintained under CNI (control). All matching parameters were well balanced before intervention between the 2 groups with a mean age of 54.7±15.1years, a median time of 1.0 [0.3-2.7] years after transplant, a mean eGFR of 33.0±13.3 ml/min/1.73m², and 30.9% of positive DSA in the belatacept group. After a mean follow-up time after conversion of 5.4±3.4 years, 43 (17.7%) patients lost their graft and 39 (16.0%) patients died in the belatacept group. After conversion to belatacept, graft survival was significantly improved compared with matched patients' under CNI p<0.0001. Furthermore, patients converted to belatacept showed lower death rate (p<0.001). The safety outcomes show similar rate of rejection, cardiovascular events, and cancer, while a higher rate of CMV disease was observed among the belatacept treated patients (p<0.01).
Conclusions: This study confirms that conversion to belatacept post-transplant is associated with improved long term graft outcomes and acceptable safety. Conversion to belatacept after transplant should be considered as a valuable therapeutic option in kidney recipients.

Figure 1: Death censored allograft survival between matched patients after conversion to a belatacept regimen and CNI control group (ratio 1:1).

The blue line is the death censored allograft survival of the matched patients from the CNI control group and the red line is the death censored allograft survival of the matched patients from the belatacept cohort.



OS10_7 EFFECTIVENESS OF THE TREATMENT OF ANTIBODY MEDIATED REJECTION: A REAL-WORLD EVIDENCE STUDY

Gillian Divard*[1], Sofia Naser[1], Solaf Alawadhi[1], Charlotte Debiais-Deschamps[1], Ivana Juric[2], Maria Cristina Ribeiro de Castro[3], Nassim Kamar[4], Juliette Gueguen[5], Marta Crespo[6], Olivier Aubert[1], Alexandre Loupy[1], Carmen Lefaucheur[1]

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Background: Antibody-mediated rejection (AMR) is the leading cause of long-term graft failure in kidney transplant recipients (KTR). However, the current standard of care treatment is mainly based on small observational studies. The aim of this study was to provide real world evidence of the effectiveness of AMR treatment in kidney transplant recipients.
Methods: This multicenter prospective cohort study included all patients who presented a first clinical antibody-mediated rejection (active of chronic active) between 2007 and 2020 in four French, two European and one south American centers. AMR cases were reassessed using the latest Banff 2019 classification. All demographic, clinical, biological, immunological, histological and AMR treatments were collected at time of rejection and during the follow-up up to death, graft loss or lost to follow-up. The AMR treatments were separated into several group: no specific treatment, standard of care (SOC), monotherapy or alternative treatment association.
Results: A total of 537 patients were included, with mostly a diagnosis of active AMR (n=383, 71.3%). The AMR occurred in a median time of 16.1 [1.5-58.3] months post-transplantation, mean eGFR was 29.1 (18.4) ml/min/1.73m2, median proteinuria was 0.5 [0.2-1.4] g/g, 386 (76.1%) had positive anti-HLA DSA. In the first 3 months post AMR, 249 (46.4%) patients received a standard of care treatment after AMR, 123 (22.9%) received no specific treatment, 86 (16.0%) received a monotherapy and 79 (14.7%) an alternative treatment association. After a mean follow-up time of 4.1 (3.3) years post AMR, 267 (49.7%) patients experienced graft failure. The absence of specific AMR treatment was highly associated with graft failure (p<0.01) while the association of SOC AMR treatment with graft survival was protective (p=0.04).
Conclusions: This study reports the largest cohort of AMR with treated and untreated patients. Antibody-mediated rejection has a severe prognosis that frequently leads to graft failure. This study provides evidence that the standard of care treatment improved transplant outcomes after antibody mediated rejection.

FULL ORALS

Innovations in kidney immunosuppression

OS10_8 RESULTS OF THE TRIBUTE RADOMIZED TRIAL: TREATMENT WITH BORTEZOMIB OF LATE ANTI-BODY-MEDIATED REJECTION DUE TO DE NOVO DSA

Renaud Snanoudj*[1], Alice Koenig[2], Fabienne Marquant[3], Sophie Caillard[4], Nadia Arzouk[5], Christophe Legendre[6], Michel Delahousse[7], Hakim Mazouz[8], Nassim Kamar[9], Vincent Pernin[10], Marie Matignon[11], Laurent Mesnard[12], Caroline Elie[3], Magali Giral[13], Valérie Dubois[14], Karine Autain-Renaudin[15]

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Background: The current treatment of antibody-mediated rejection (ABMR) after kidney transplantation (KT), based on plasmapheresis, steroids and intravenous globulins is inconstantly efficient. There have been so far very few randomized trials on its treatment. The role of proteasome inhibitors in addition to the current strategy has not been explored in a controlled trial.
Methods: We included kidney transplant recipients with a clinical or infra-clinical biopsy-proven ABMR (defined by a score g+ptc ≥2), occurring more than three months after KT and due to de novo DSA. They were randomized to receive 5 plasma exchanges, 4 monthly courses of intravenous globulins, steroids, and 2 cycles of IV bortezomib (BTZ arm) or no further treatment (CTRL arm). The primary endpoint combined at one year the reduction of immunodominant (ID) DSA MFI > 50% and the stabilization or improvement of histological lesions compared to the inclusion biopsy (Δ(g+ptc)≤1 and Δcg < 1).
Results: 60 patients were randomized (30 in each arm in the ITT analysis, 20 (BTZ) and 19 patients (CTRL) for the per protocol (PP) analysis). ABMR occurred at a mean delay of 76 months after KT in each arm. The median MFI of the ID DSA was 17130 (BTZ arm) and 11230 (CTRL arm). 23% of patients had cg lesions associated to microvascular inflammation. In the ITT analysis, 40.0 % of patients (BTZ arm) and 33.3% (CTRL arm) reached the coprimary endpoint (p=0.59). There was no difference between the 2 arms, whatever the type of ABMR, clinical or infra-clinical. In the PP analysis, this success rate was 50.0% and 42.1%, respectively (p=0.62). Regarding separately the two endpoints at one year, 56.7% (BTZ) and 46.7% (CTRL) experienced a reduction > 50% of the MFI of the ID DSA, and 56.7% of patients in each arm experienced a stabilization/improvement of histological lesions. The mean reduction of ID DSA MFI was 60% in each group at one-year post-treatment. One patient lost his graft in each group during the one-year follow-up, and none died. The slope of eGFR decrease was similar. The rate of infectious AE was similar in the 2 groups.
Conclusions: This randomized controlled trial did not show any benefit of adding bortezomib to the current strategy to treat ABMR caused by de novo DSA. The next step will be to characterize the half of patients who experienced a successful treatment of their ABMR.

Kidney biomarkers to the rescue

OS11_1 ASSESSMENT OF DONOR-DERIVED CELL-FREE DNA (DD-CFDNA) IN KIDNEY TRANSPLANT RECIPIENTS WITH INDICATION BIOPSY

Louise Benning*[1], Annette Fink[2], Markus Rudek[1], Claudius Speer[1], Christian Nußhag[1], Christoph Mahler[1], Florian Kälble[1], Martin Zeier[1], Caner Süsal[3], Christian Morath[1], Thuong Hien Tran[2]

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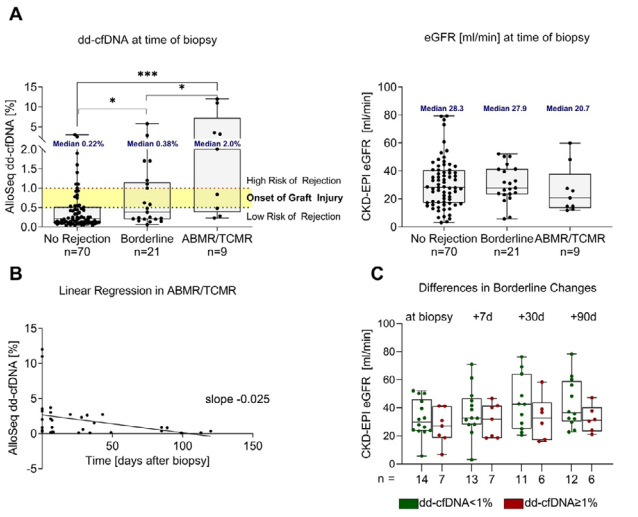
Background: Donor-derived cell-free DNA (dd-cfDNA) is released into the circulation upon allograft injury in kidney transplant recipients (KTR).
Methods: Starting in November 2020, we enrolled 100 KTR with indication biopsy in this prospective single-center trial to assess dd-cfDNA at time of biopsy as well as 7, 30 and 90 days post biopsy. Levels of circulating dd-cfDNA were measured using the AlloSeq dd-cfDNA assay (CareDx).
Results: The analytic sample included 325 dd-cfDNA measurements from 100 patients. 30/100 (30%) biopsies were graded as different types of rejection, whereof 5/30 (16.7%) patients showed signs of antibody-mediated rejection (ABMR), 21/30 (70%) borderline changes, and 4/30 (13.3%) signs of T-cell-mediated rejection (TCMR) in the graft. At time of biopsy, patients with ABMR or TCMR had significantly higher levels of dd-cfDNA than patients without any signs of rejection in the graft (*P*<0.001), whereas eGFR did not differ significantly between the two groups (*P*>0.99, Figure 1A). Levels of circulating dd-cfDNA were with a median (IQR) of 2.0% (0.38 – 7.25) highest in patients with ABMR or TCMR, compared to the 0.38% (0.20 – 1.15) in patients with borderline changes and 0.22% (0.11 – 0.52) in patients with no signs of rejection (Figure 1A). Following anti-rejection treatment, dd-cfDNA decreased in most patients with ABMR or TCRM (pooled slope -0.025, Figure 1B), possibly indicating response to therapy. Patients with Borderline changes and dd-cfDNA levels <1% at time of biopsy showed a trend towards increasing eGFR following corticosteroid pulse therapy whereas patients with higher dd-cfDNA levels (>1%) showed unchanged or even subsequent eGFR decline (Figure 1C).
Conclusions: dd-cfDNA significantly discriminates between KTR with signs of rejection in the graft and KTR with other pathology. Decreasing levels of dd-cfDNA reflect response to anti-rejection treatment. Higher dd-cfDNA levels in patients with borderline changes may help to identify patients at risk that may profit from intensified therapy.



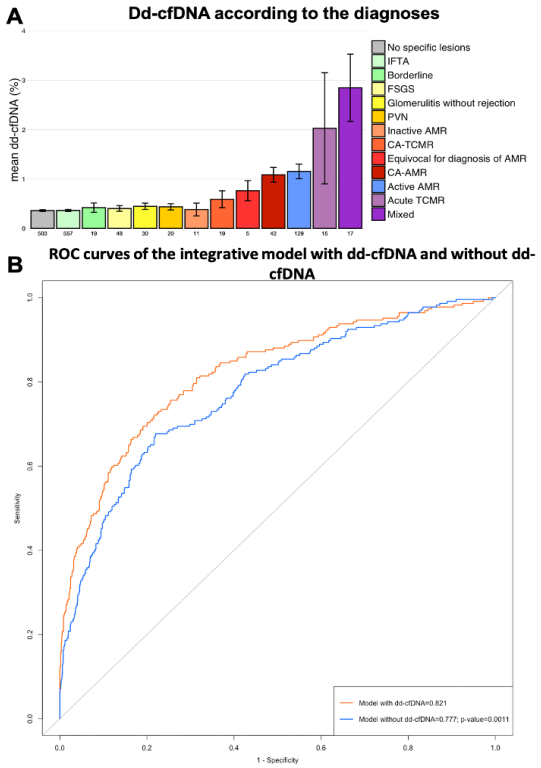
OS11_2 MULTIDIMENSIONAL RISK ASSESSMENT OF KIDNEY ALLOGRAFT REJECTION USING DONOR DERIVED CELL-FREE DNA

Cindy Ursule-Dufait*[1], Olivier Aubert[1;2], Romain Brousse[1], Juliette Gueguen[1], Maud Racape[1], Christophe Legendre[1;2], Dany Anglicheau[1;2], Carmen Lefaucheur[1;3], Alexandre Loupy[1;2]

[1]Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, [2]Kidney Transplant Department, Necker Hospital, Paris, France, [3]Kidney Transplant Department, Saint Louis Hospital, Paris, France

Background: Post-transplantation patient care requires development and validation of non-invasive biomarkers to improve allograft monitoring and prevention from unnecessary biopsies. Reports have suggested the association of donor derived cell-free DNA (dd-cfDNA) with allograft rejection. However, there is no proof of its added value on standard of care in large, unselected and deep phenotyped cohorts.
Methods: We enrolled 1134 kidney transplant recipients having concomitant evaluation of allograft histology, anti-HLA DSA and functional parameters between April 2013 and June 2018 in the derivation cohort, representing 1415 biopsies. Dd-cfDNA was measured in plasma at the time of the biopsy. Diagnoses were performed using Banff 2019 criteria. 171 AMR, 34 TCMR and 17 mixed rejections occurred. Parameters associated with rejection were assessed using uni- and multivariable logistic regression. We then developed a risk model using the variables that were independently associated with kidney rejection. The validation cohort comprised 1929 evaluations including 499 evaluations in one Belgian center and 1430 evaluations in nine North American centers.
Results: Higher levels of dd-cfDNA were observed for AMR and TCMR or both compared to other diagnoses (Figure 1A). Dd-cfDNA incrementally increased with Banff acute lesions without significant increase for chronic lesions. In multivariable analysis, the variables independently associated with rejection were anti-HLA DSA (P<0.0001), dd-cfDNA (P<0.0001), eGFR (P<0.033), proteinuria (P=0.016), and previous history of rejection (P<0.0001). Dd-cfDNA remained independently associated with kidney allograft rejection in validation cohorts from Belgium (P =0.0006) and North America (P<0.0001). Discrimination of the model without dd-cfDNA was 0.777 and 0.821 with its inclusion, showing its added value (Figure 1B). The good discrimination performances of the model with dd-cfDNA were also confirmed in the validation cohorts from Belgium (AUC: 0.815) and North America (AUC: 0.826).
Conclusions: We here demonstrate the independent and added value of dd-cfDNA in addition to conventional features to predict rejection. This first integrative system shows improved performance for patient monitoring and could help physicians in decision-making process.

Figure 1: dd-cfDNA results according to the diagnoses and ROC curve of the model with dd-cfNDA



OS11_3 DETECTION OF KIDNEY ALLOGRAFT REJECTION USING BLOOD BIOMARKERS: RESULTS OF THE EUROPEAN MULTICENTER PROSPECTIVE EU-TRAIN TRIAL (NCT03652402)

Valentin Goutaudier*[1], Maud Racape[1;2], Esteban Cortes Garcia[1;2], Gillian Divard[1;2], Marc Raynaud[1;2], Rusan Ali Catar[2;3], Richard Danger[2;4], Sophie Brouard[2;4], Magali Giral[2;4], Pierre-Antoine Gourraud[2;4], Jean Villard[2;5], Klemens Budde[2;3], Christophe Legendre[1;2], Oriol Bestard[2;6], Olivier Aubert[1;2], Carmen Lefaucheur[1;2], Alexandre Loupy[1;2]

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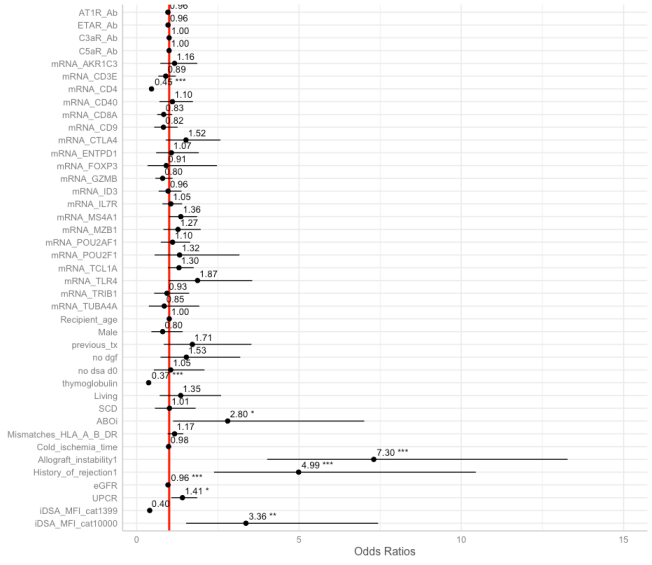
Background: There is an unmet need for clinically validated biomarkers to non-invasively detect kidney allograft rejection in routine care. In this study, we aimed to investigate the additional value, beyond standard of care patient management, of 24 candidate blood biomarkers in a large, prospective, and unselected cohort of kidney transplant recipients.
Methods: We prospectively monitored 412 consecutive patients who received a kidney allograft at 9 European transplant centers between November 2018, and June 2020, for standard of care clinical, biological, immunological, and histological parameters. Twenty-four biomarkers including 20 blood mRNA (AKR1C3, CD3E, CD4, CD40, CD8A, CD9, CTLA4, ENTPD1, FOXP3, GZMB, ID3, IL7R, MS4A1, MZB1, POU2AF1, POU2F1, TCL1A, TLR4, TRIB1, TUBA4) together with anti-ATI1R, anti-ETAR, ant-C3aR, and anti-C5aR antibodies, were assessed in blood samples collected at the time of protocol (M3, M12) and clinically indicated biopsies in the first-year post-transplant. We assessed the value of the biomarkers to detect allograft rejection, as compared to standard of care patient monitoring.
Results: 816 post-transplant biopsies were included (625 [76.59%] protocol, 191 [23.41%] clinically indicated). The prevalence of overall rejection (AMR, TCMR and mixed) in the first-year post-transplant was 6.37%. Twenty-three (95.8%) of the 24 biomarkers did not show any statistical association with the primary outcome (allograft rejection) (**Figure 1**). Only CD4 mRNA showed a significant association (p< 0.001). When adjusted on standard of care patient monitoring parameters including history of rejection, ABO-incompatibility, type of induction therapy, allograft instability, eGFR, urine protein-to-creatinine ratio, and circulating anti-HLA DSA, none of the 24 candidate biomarkers was independently associated with overall allograft rejection, as well as with AMR, TCMR and mixed rejection.
Conclusions: In this large, prospective, and unselected cohort of kidney transplant recipients with a systematic non-invasive biomarker assessment in the first-year post-transplant, none of the 24 candidate blood biomarkers had an additional clinical value to detect kidney allograft rejection.

Figure 1. Forest plot of the determinants of kidney allograft rejection.



OS11_4 DSA-NEGATIVE MICROVASCULAR INFLAMMATION IN KIDNEY TRANSPLANT BIOPSIES: GENE EXPRESSION COMPARISON WITH NATIVE AND TRANSPLANT KIDNEY CONTROLS

Anna Buxeda*[1;2], Ivy Fixsen[1], Ian Gibson[3], Christopher Wiebe[4], Peter Nickerson[4], Patricia Campbell[1], Natalia Polanco[5], Marta Crespo[2], Benjamin Adam[1], Michael Mengel[1]

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Background: Microvascular inflammation (MVI) in kidney transplant (KT) biopsies from patients without detectable anti-HLA donor-specific antibodies (DSA) presents a diagnostic and therapeutic dilemma. This study aimed to further understand the significance of these changes by characterizing their molecular phenotype compared to other native and transplant kidney biopsies.
Methods: The NanoString B-HOT panel (770 genes) was used to measure the expression of six literature-derived gene sets in 195 archival FFPE kidney biopsies from four centers, including transplant biopsies with MVI (g+ptc>1) but no detectable DSA (MVI, n=47), antibody-mediated rejection with DSA (ABMR, n=42), pure T-cell mediated rejection without DSA (TCMR, n=25), mixed MVI and TCMR without DSA (MVI+TCMR, n=47), normal implant biopsies (Normal, n=11), and native kidney biopsies with either endocapillary proliferative glomerulonephritis (GN, n=12) or minimal change disease (MCD, n=11). The evaluated gene sets included transcripts previously associated with ABMR, DSA (DSAST), endothelial injury (ENDAT), TCMR, early injury, and late injury. Gene expression was compared between groups using principal component and class comparison analyses.
Results: Principal component analysis demonstrated significant molecular overlap between sample groups (Figure 1A). However, gene set analysis showed lower expression of ABMR-related, DSAST (Figure 1B), and ENDAT gene sets in DSA-negative MVI compared to ABMR. DSAST and ENDAT gene set expression was similar between MVI, MVI+TCMR, and TCMR groups; but higher than native biopsies (p≤0.002). TCMR and early injury gene set expression was higher in TCMR than all other groups (p≤0.002), except MVI+TCMR. Late injury gene set expression was lower in MVI compared to ABMR, MVI+TCMR, and TCMR groups (p≤0.031); but higher than the Normal and MCD groups (p≤0.016).
Conclusions: These results suggest that DSA-negative MVI displays a lower expression of ABMR-related genes than ABMR, but similar to MVI+TCMR and higher than native kidney biopsies with or without glomerulonephritis. Further work is underway to evaluate the potential role of non-HLA DSA and recognition of missing self in these cases.

Figure 1A

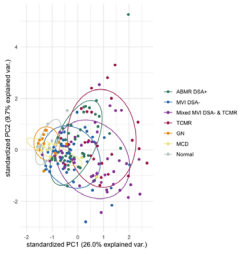
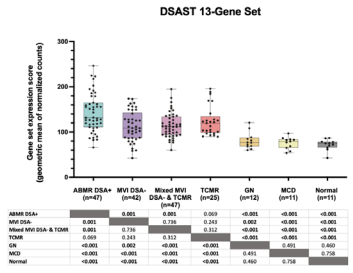


Figure 1B



OS11_5 AGE-MODULATED PROTEOMIC SIGNATURES OF DONOR KIDNEY BIOPSIES ASSOCIATE WITH BELOW-MEDIAN 12 MONTH OUTCOMES

Philip Charles*[1], Sarah Fawaz[1], Rebecca Vaughan[1], Roman Fischer[1], Benedikt Kessler[1], Edward Sharples[1], Alberto Santos[2], Rutger Ploeg[1], Maria Kaisar[1]

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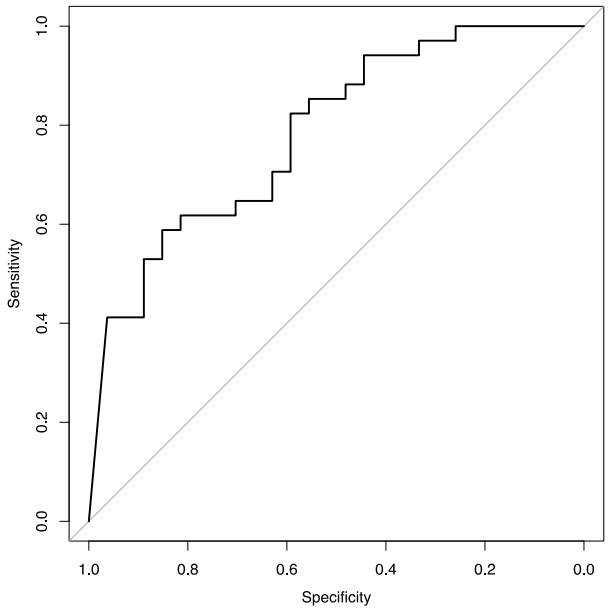
Background: Clinical factors such as donor age aid kidney transplantation decisions limited predictive value; older donors with potentially good function are not utilised, while inferior organs are transplanted with suboptimal outcomes. More granular prediction models, based on deep resolution assessment and understanding of damage processes, could substantially reduce graft dysfunction risk. Here, we studied the predictive value of subclinical markers in the proteomes of kidney pretransplant biopsies
Methods: Kidney biopsies (n=185; Donors after Brain Death n=100, Donors after Circulatory Death n=85) were provided by the UK QUOD biobank, selected from donors where both kidneys were transplanted and had similar posttransplant outcomes. Biopsies were analysed by deep mass spectrometry proteomic profiling. Protein data were analysed in an integrative model combining donor/recipient demographic and clinical measurements vs ranked 12-month eGFR. 2/3 of the data were used for analysis and model training, sampling equally across each eGFR tertile. Final prediction ROC AUC was calculated against the holdout set.
Results: We quantified 2984 protein groups. Analysis of the data via iterative Prediction Rule Ensemble machine learning shortlisted 235 proteins associated with 12-month eGFR, including CST3, VTN, APOE and other proteins associated with complement activation and metabolic regulation; and further regularised multiadaptive regression spline (MARS) modelling suggested most terms (164/235) showed evidence for donor age interaction. We used a final MARS analysis to summarise our shortlist as a prediction model for below-median outcomes (12 month eGFR < 50). The final parameters were a) donor age multiplied by CST3 and b) VIM. This summary model achieved a ROC AUC of 0.80 in our holdout test set (Fig. 1).
Conclusions: Our work suggests donor organ proteomic signatures can refine current models of graft dysfunction. The biological themes of the identified candidates reinforce known immuno-metabolic mechanisms of kidney injury but raise interesting possibilities for further work. Furthermore, our results strongly suggest that for any studies of subclinical molecular indicators regarding kidney transplant outcomes, donor age-moderated weighting should be considered as a matter of course.

Fig 1: Prediction of below median outcome (eGFR < 50) in test set



OS11_6 OVERALL ACTIVITY AND CHRONICITY INDICES OF KIDNEY TRANSPLANT BIOPSIES: VALIDATION ON NEW DATA

Thibaut Vaulet*[1], Priyanka Koshy[2], Karolien Wellekens[1;3], Jasper Callemeyn[1;3], Tim Debyser[1], Dirk Kuypers[1;3], Elisabet Van Loon[1;3], Maarten Naesens[1;3]

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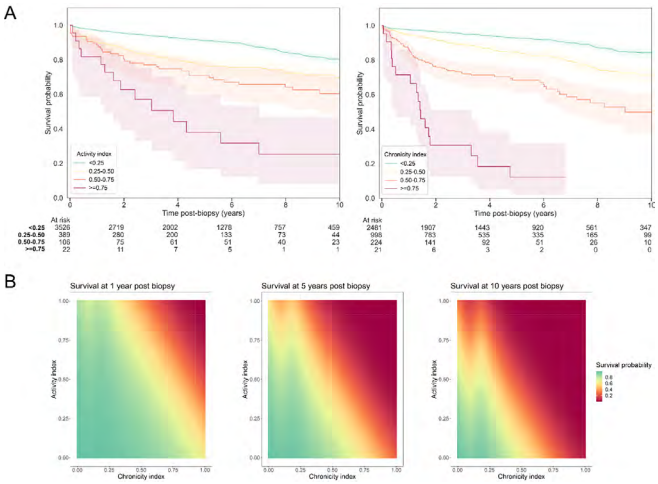
Background: New activity and chronicity indices have been recently proposed as global histological scoring for kidney transplant biopsies. These scores summarize the degree of inflammation and the chronic damages in simple numbers which, next to the Banff rejection diagnoses, can serve as additional study endpoints and clinical predictors. This study aims to validate their clinical relevance on novel data.
Methods: The activity and chronicity indices (from 0 to 1) were calculated on 4043 new biopsies from 1617 patients using our freely available online platform rejectionclass.eu.pythonanywhere.com. Missing values were imputed with k-nearest neighbors (k=5) and rounded to the closest integer. The association with graft failure was estimated with Cox-models with robust covariance matrix estimation to account for repeated biopsies. The need for interactions and/or non-linear variable transformation (with restricted cubic splines) was assessed with Wald tests. The discrimination performance was assessed with C-index corrected for optimism. The indices were arbitrarily discretized in four groups with the following thresholds: [0.25,0.5,0.75] for visual purpose with Kaplan Meier curves. Restricted mean survival time (RMST) were computed at 5 years for practical numerical comparisons.
Results: Both indices validated the previously observed association with graft-failure (HR activity: 1.65 (1.51-1.80); p<0.001, HR chronicity 1.64 (1.56 -1.74), p<0.001). The discretization in arbitrary strata also demonstrated strong association (**Fig. 1A**). For each stratum, the $RMST_{5\ years}$ is 4.74, 4.26, 4.02, 3.08 years and 4.79, 4.53, 3.88, 2.00 years for the activity and chronicity indices, respectively. We confirmed the absence of correlation between both indices (Pearson R=0.005, p=0.27). This was also reflected in the lack of significant interaction term in the model. A Cox model with only the two indices had an optimism-corrected C-index of 0.72. The predicted survival probabilities at 1, 5 and 10 years post biopsy are displayed in **Fig. 1B.**
Conclusions: Activity and chronicity indices of kidney transplant biopsies constitute two independent and validated scoring tools in complement of the current Banff classification. We are now investigating ways of simplifying the scores for easier clinical usage.



OS11_7 ASSESSING REJECTION WITH MACHINE LEARNING BASED ON BIOPSY ELEMENTARY LESIONS AND CLINICAL INFORMATION

Marc Labriffe*[1;2], Jean-Baptiste Woillard[1;2], Wilfried Gwinner[3], Jan-Hinrich Braesen[4], Dany Anglicheau[5;6;7], Marion Rabant[8], Priyanka Koshy[9], Maarten Naesens[10;11], Pierre Marquet[1;2]

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Background: Banff classification may be difficult to apply in practice and surveys showed it is poorly reproducible among professionals, for several reasons: there are many terms, some of which not consensual, with exceptions, some elementary lesions may be difficult to assess (missing information), and the clinical context is not formally considered. We investigated whether it can be improved using automated classification tools.
Methods: Several retrospective datasets from three European transplantation centers (Leuven, Hannover, and Paris Necker) were used for training and validation of two algorithms: Gradient Boosting (XGBoost) and decision tree. SHapley Additive exPlanations (SHAP values) were used to enhance the individual interpretability of each result.
Results: Models were built for the diagnoses of: antibody-mediated rejection (ABMR), T cell-mediated rejection (TCMR), interstitial fibrosis and tubular atrophy (IFTA), glomerulonephritis (GN), and for the distinction between acute and chronic forms of ABMR and TCMR. Performances were excellent with XGBoost in the three different datasets with ROC curve AUC (95%CI) of: 0.97 (0.92–1.00), 0.97 (0.96–0.97), and 0.95 (0.93–0.97) for ABMR; 0.94 (0.91–0.96), 0.94 (0.92–0.95), and 0.91 (0.88–0.95) for TCMR; >0.96 (0.90–1.00) with all three for IFTA.
Conclusions: In this study, we set up and validated machine learning algorithms to improve and automate the interpretation of kidney graft biopsy elementary lesions, also considering a few clinical data.

FULL ORALS

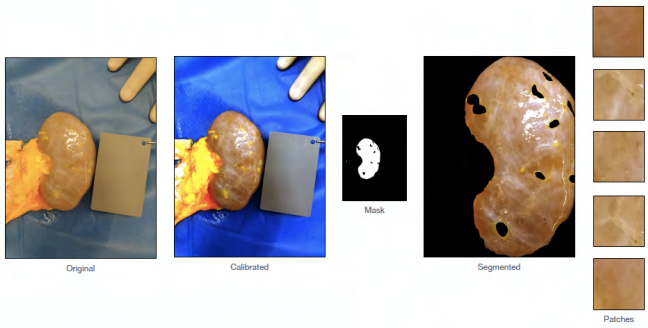
Kidney biomarkers to the rescue

OS11_8 KIDNEY COLOR: ARTIFICIAL INTELLIGENCE IMAGE PROCESSING TO IMPROVE KIDNEY TRANSPLANT OUTCOMES PREDICTION

Enric Miret Alomar*[1], Concepción Gómez Gavara[2], Gemma Piella[3], Nicolau Farré Saurí[4], Miguel Angel Cordobés Aranda[3], Daniel Esono Ferrer[3], Javier Vazquez Corral[5], Marc Perez Rodriguez[3], Alonso Narvaez Barros[1], Enrique Trilla Herrera[1]

[1]Hospital Vall d'Hebrón, Urology and kidney transplantation, Barcelona, Spain, [2]Hospital Vall d'Hebrón, Liver Transplantation, Barcelona, Spain, [3]Universitat Pompeu Fabra, Information and Communication Technologies, Barcelona, Spain, [4]Visionem Labs, Barcelona, Spain, [5]Universitat Autònoma de Barcelona, Image processing and computational vision, Barcelona, Spain

Background: Kidney transplant (KT) preimplantational predictors, such as kidney donor risk index (KDRI), can have a limited accuracy due to the lack of information from the graft itself. Transplant surgeon preimplantational graft evaluation is always performed, but the opinion may vary between centres and surgeons. Artificial intelligence training with machine learning can process, classify, and segment images. With enough information, it is possible to develop algorithms to predict patterns. Our aim was to train an algorithm on backbench images from cadaveric donor kidneys in order to predict delayed graft function (DGF). By developing a rapid, robust, accurate, and cost-effective method to assess kidney donors, we may improve the prediction of standardized models such as KDRI and support the surgeon in deciding whether to accept or discard the graft.
Methods: This is a unicentric prospective study on grafts from cadaveric donors that were successfully transplanted with at least one follow-up week. After back-bench surgery and before cold static preservation, we obtained images with last generation mobile phone cameras from both graft sides with a grey scale calibration card. Data from donors was collected, and surgeons completed a questionnaire including kidney color, roughness, atheroma arterial plaques and cortical fat adherence. Image processing steps were: Image color calibration, kidney cortex and perinephric fat masking and segmentation, patch extraction and color+texture features computation. A random forest classifier was trained to predict DGF.
Results: Our initial dataset includes 139 kidney transplants. 38 kidneys developed DGF. KDRI, fat percentage, kidney color, cortical surface roughness and ostium atheroma plaques were the predictors finally included in our model. ROC curve AUC was 0.957 to predict DGF.
Conclusions: Machine learning image processing may improve the prediction of posttrasplant graft function. This first experience can help in decision-making and allocation in kidneys from other centres. Validation from multicentre data is needed.



Kidney medical complications

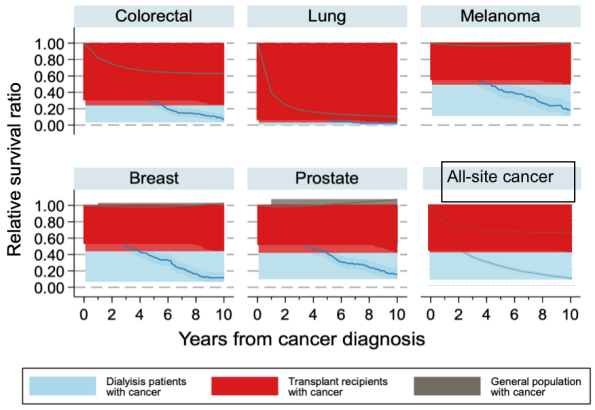
OS12_1 AUSTRALIAN AND NEW ZEALAND CANCER RELATIVE SURVIVAL IN END-STAGE RENAL KIDNEY PATIENTS: A RETROSPECTIVE COHORT STUDY

Laia Oliveras*[1], Brenda Rosales[2], Nuria Montero Perez[1], Edoardo Melilli[1], Josep Maria Cruzado[1], Angela Webster[2], Nicole De La Mata[2]

[1]Hospital Universitari de Bellvitge, Nephrology Department, L'Hospitalet de Llobregat, Spain, [2]Sydney School of Public Health, University of Sydney, Sydney, Australia

Background: Cancer survival in the general population has improved over time. Kidney failure population have a higher incidence of cancer with increased mortality. Relative survival following cancer diagnosis can provide more insight into the excess mortality directly or indirectly attributed to cancer in the kidney failure population.
Methods: We estimated and compared the relative survival for dialysis patients, kidney transplant recipients and general population with cancer in Australia and New Zealand from 1980 to 2019. The general population was reference group for background mortality, matching on sex, age, calendar year and country. We used Poisson regression to quantify the excess mortality between these three groups with cancer.
Results: We included 4,089 dialysis patients and 3,253 kidney transplant recipients with an incident cancer. Dialysis patients were older, had a higher proportion of indigenous people and had more comorbidities than kidney transplant recipients. The kidney failure population had lower 5-year relative survival: 0.25 (95%CI: 0.23-0.26) for dialysis, 0.55 (95%CI: 0.53-0.57) for kidney transplant and 0.670 (95%CI: 0.669-0.670) in the general population with cancer (Figure 1). At any given time, dialysis patients had a 2.10 times higher adjusted excess mortality compared to the general population with cancer (2.10, 95%CI: 2.02-2.18), whereas kidney transplant recipients had no excess mortality (1.02, 95%CI: 0.97-1.08). Relative survival and excess mortality varied by cancer site: lung had the lowest relative survival rates, while kidney failure population with melanoma, breast and prostate cancers had the highest excess mortality. There were also sex differences: women had greater relative survival.
Conclusions: Relative survival was lower among the kidney failure population with incident cancer compared to the general population with cancer, for all-site and particularly for melanoma, breast and prostate cancer. Decreased survival may be due to poorer access to, more harm or less efficacy of treatments.

Figure: All-site cancer and cancer-type relative survival ratios



OS12_3 CAUSES OF DEATH IN KIDNEY TRANSPLANTATION, A PARADIGM SHIFT?

Thomas Beaudrey*[1], François Séverac[2], Sébastiewn Loewert[1], Martin Planchais[3], Coralie Poulain[4], Dominique Bertrand[5], Yannick Le Meur[6], Marie Pascale Morin[7], Valérie Chatelet[8], Antoine Thierry[9], Jean-Philippe Rerolle[10], Anne Elisabeth Heng[11], Philippe Gatault[12], Fanny Buron[13], Emmanuel Morelon[13], Laeticia Albano[14], Antoine Sicard[14], Christophe Masset[15], Magali Giral[15], Bruno Moulin[1], Sophie Caillard[1]

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Background: Cardiovascular diseases have traditionally been the leading cause of mortality in kidney transplanted patients but are now reported to be overtaken by infections and cancers. There are few data in the literature concerning risk factors for mortality. We conducted a retrospective observational study in a multicentric cohort to describe the distribution of causes of death in kidney transplant recipients and to analyse the risk factors for mortality at the time of transplantation.
Methods: We included all patients transplanted between 01.01.2008 and 31.12.2014 in two French databases (ASTRE and DIVAT). We studied deaths that occurred with a functioning graft or within six months after graft failure. Our primary endpoint was the distribution of causes of death. We then analysed patient survival using competing risks analysis to identify risk factors for mortality, considering graft failure as a competing event.
Results: Of the 4878 kidney transplant recipients included in ASTRE database, the median age was 54 years. Among them, 1022 (20.9%) died during the follow-up. Mean patient survival was 97.2% at 1 year after transplantation, 89.9% at 5 years, and 73.6% at 10 years. We accounted for 262 deaths (25.6%) from infectious causes (mainly from community-acquired infections, including 102 lung infections, 10.0%), 223 deaths (21.8%) from neoplastic causes (including 51 lung cancers, 5.0%), and 198 deaths (19.4%) from cardiovascular causes (including 55 sudden cardiac deaths, 5.4%). The cause was unknown for 184 recipients (18.0%). Risk factors for mortality were age of recipient, time on dialysis, expanded criteria donor, smoking, cardiovascular comorbidities, diabetic and vascular nephropathy, negative HBV serology, previous transfusion history, delayed graft function and use of cyclosporine. We then defined an easy-to-use mortality risk score using data available at the time of transplantation. Our results were validated in 2057 patients of DIVAT database.
Conclusions: This work allowed us to highlight a paradigm shift in the causes of death in kidney transplant patients, infections and cancers being now ahead of cardiovascular diseases. Risk factors and our new score could provide better understanding of the mortality risk in kidney transplant recipients.

OS12_4 CURRENT STATUS OF PREGNANCY AND DELIVERY AFTER RENAL TRANSPLANTATION IN JAPAN

Yuki Nakagawa*[1;1], Taiki Ogasa[1], Takeshi Ashizawa[1], Keisuke Saito[1], Shuji Isotani[1], Shigeo Horie[1]

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Background: Pregnancy and childbirth in renal transplant patients are not without risk, even if renal function is preserved after kidney transplantation. The incidence of gestational hypertension in renal transplant patients is reported to be 25-31%, premature delivery 50%, and cesarean section 65%. Pregnancy and childbirth carry many risks, even for healthy individuals. Transplant patients also face a variety of risks, including the burden on the kidneys due to increased circulating blood volume, the risk of teratogenicity due to immunosuppressive and antihypertensive drugs, the risk of rejection during pregnancy, and mental illness due to changes in hormonal balance. We report on the current status of pregnancy and delivery after kidney transplantation in Japan.
Methods: 453 post-transplant pregnancies from January 1990 to December 2021 (age; 32.0±9.18(8-41)) (426 living donor kidney transplants, 29 donated kidney transplants): Group A. Controls were 6,908 nonpregnant patients; Group B, and 137 patients who became pregnant and gave birth before transplantation: Group C.
Results: (1) Cr at conception 1.19±0.54 (0.5-3.9), age at conception 33.5±10.07 (22-43) **(2)** Pregnancy period after transplantation was 3.8 years (1-18 years). There was no difference between Group A, which had pregnancies and deliveries after transplantation, and Group C, which had pregnancies and deliveries before transplantation. (10th grade implantation rate: 86% vs. 82.7% P=0.98) **(3)** Cr > 1.5 at conception was significantly worse than Cr ≤ 1.5 in terms of transplantation kidney prognosis. (10th year implantation rate 82.5% vs. 97.3% P<0.001) **(4)** There was no significant difference in the retention of transplanted kidney depending on the presence or absence of hypertension at conception (10th year retention rate: 86.5% vs. 86.5%). (10th year retention rate: 86.1% vs. 83.3% P=0.413) **(5)** Factors related to transplant kidney prognosis in post-transplant pregnancy and delivery were Cr at gestation (Cr≤1.5 vs. Cr>1.5) and Cr 1 year after delivery (Cr≤1.5 vs. Cr>1.5). Cr at 1 year after delivery (Cr≤1.5 vs Cr >1.5), and proteinuria after delivery (yes vs no).
Conclusions: Renal transplantation allows for a safe pregnancy and delivery of a child with good indication and management.

OS12_5 CANCER INCIDENCE AMONG ITALIAN KIDNEY TRANSPLANT RECIPIENTS OVER A 25-YEAR PERIOD

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Background: Solid organ transplant recipients have an augmented risk of developing several cancers. We investigated this risk in kidney transplant (KT) recipients in Italy in the last 25 years (1997-2021).
Methods: Cohort study of 11,418 patients undergoing KT in 17 Italian centers. The period at risk (person-years, PYs) was calculated from 30 days after KT to date of malignancy, death, return to dialysis or last follow-up. The risk of cancer was compared to the general population of the same age and sex was through standardized incidence ratios (SIR) and relative 95% confidence intervals (CI) and Poisson regression was used to assess trends over three periods (1997–2004/2005–2012/2013–2021).
Results: Overall, out of 85,209 PYs (median follow-up 7.1 years, IQR: 3.9-10.6) 1646 post-transplant malignancies (PTM) were diagnosed (931 excluding non-melanoma skin cancers – NMSC), with an overall incidence rate/1000 PYs ranging from 15.5 in 1997-2004 to 21.0 in 2013-2021. As compared to the general population, KT recipients have a 2.25-fold increased risk of developing a PTM (95% CI: 2.14-2.36) and SIR=7.16 for NMSC (SIR=1.47 for all cancers but NMSC). Significantly increased SIRs were found for several virus-related malignancies including Kaposi sarcoma (KS - SIR=75.8), non-Hodgkin lymphoma (NHL - SIR=4.4), lip (SIR=21.4), salivary gland (SIR=5.5), while among other virus unrelated cancers, high risks emerged for tumours of the kidney (SIR=5.4), lung (SIR=1.3), testis (SIR=2.6) and melanoma (SIR =1.7). A decreasing magnitude over time of all cancers (SIR=2.54 in 1997–2004 and SIR=1.99 in 2013–2021; P_{trend}<0.01) was observed. A decline in SIRs was observed specifically for NHL and KS, though only the KS trend retained statistical significance after adjustment (from 189.2 to 20.2; p<0.01).
Conclusions: Despite decreased KS risk, cancer remains a serious adverse event among KT recipients. Study findings indicate the need to endure and strengthen cancer preventive actions in KT recipients.

Figure 1. Standardized incidence ratios (SIR) and 95% confidence intervals (CI) for major cancer sites. Abbreviations: NHL, non-Hodgkin lymphoma; NMSC, nonmelanoma skin cancer; obs/exp, observed/expected; PTLD, posttransplant lymphoproliferative diseases. In bold results statistically significant (p<0.05)

Cancer site (ICD-10 codes)	No. of cancer cases obs/exp	SIR (95% CI)
All	1646/731.7	**2.25 (2.14-2.36)**
All but NMSC	931/631.8	**1.47 (1.38-1.57)**
NMSC (C44)	715/99.9	**7.16 (6.64-7.70)**
Solid tumors	703/576.9	**1.22 (1.13-1.31)**
Kidney (C64)	107/20.0	**5.35 (4.38-6.46)**
Prostate (C61)	99/88.6	1.12 (0.91-1.36)
Bronchus and lung (C34)	99/75.7	**1.31 (1.06-1.58)**
Breast (C50)	60/67.1	0.89 (0.68-1.15)
Colon-rectum-anus (C18-21)	59/77.1	**0.76 (0.58-0.99)**
Bladder (C67, D09.0, D30.3, D41.4)	57/49.4	1.15 (0.87-1.49)
Head and neck (C00-14, C30-32)	42/28.6	**1.47 (1.06-1.98)**
Lip (C00)	19/0.9	**21.42 (12.90-33.45)**
Salivary glands (C07-08)	4/0.7	**5.46 (1.49-13.99)**
Skin melanoma (C43)	30/17.5	**1.71 (1.15-2.44)**
Stomach (C16)	27/22.3	1.21 (0.80-1.76)
Thyroid gland (C73)	19/16.7	1.14 (0.69-1.78)
Corpus uteri (C54-55)	13/11.2	1.17 (0.62-1.99)
Pancreas (C25)	13/16.6	0.78 (0.42-1.34)
Testis (C62)	8/3.1	**2.59 (1.12-5.10)**
Liver (C22)	7/22.4	**0.31 (0.13-0.65)**
Mesothelioma (C45)	6/3.3	1.84 (0.67-4.00)
Other connective and soft tissue (C49)	5/3.2	1.57 (0.51-3.67)
Esophagus (C15)	4/4.8	0.84 (0.23-2.15)
Ovary (C56)	4/6.6	0.61 (0.17-1.56)
Brain (C71)	4/9.6	0.42 (0.11-1.07)
Unspecified sites (C76-80)	11/6.4	1.71 (0.86-3.07)
PTLD (C81-96)	129/46.7	**2.76 (2.31-3.28)**
NHL (C82-85, C96)	96/22.0	**4.37 (3.54-5.34)**
Leukaemia (C91-95)	18/12.8	1.41 (0.84-2.23)
Multiple myeloma (C90)	11/7.9	1.39 (0.69-2.48)
Hodgkin's lymphoma (C81)	4/3.0	1.32 (0.36-3.38)
Kaposi's sarcoma (C46)	99/1.3	**75.76 (61.58-92.24)**

OS12_6 VOLUMETRIC BONE MINERAL DENSITY, BONE MICRO-ARCHITECTURE EVOLUTION AFTER KIDNEY TRANSPLANTATION: A 1-YEAR RESULTS OF A PROSPECTIVE COHORT STUDY

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Background: Bone loss and mineral abnormalities are frequent in kidney transplant recipient (KTR). Currently, the clinical management of bone abnormalities includes the use of bone biopsy, surrogates' biochemical markers and imaging technique (Dual Energy X-ray (DEXA)). The high-resolution peripheral quantitative computed tomography (HR-pQCT) provides noninvasive information on bone microarchitecture and a quantitative measurement of the volumetric density of trabecular and cortical bone. The goal of our study is to evaluate the evolution of bone micro-architecture using HR-pQCT compared to standard technique (DEXA) in a kidney transplanted cohort.
Methods: All patients referred for a single kidney transplant at our centre were eligible for inclusion (NCT04713774). Participants underwent baseline, 3-months and 1-year biomarkers analysis, BMD measurements by DXA and HR-pQCT images of the distal radius and distal tibia were obtained using the XtremeCT device.
Results: 31 patients were prospectively included for the 1-year analysis. Median age was 60.4 [49.9 – 65.4]. Bone turn over biomarkers shows significant decrease between D0 and 1-year, PTH from 211.7 ng/l vs 56.7 (p<0.0001), P1NP 185 ug/l vs 59.1 ug/l (p=0.036). We observed a significant reduction of BMD by DEXA at the hip site between D0 and 1-year, respectively 0.843g/cm^2 and 0.820 g/cm^2 (p=0.025) with a non-significant increase at lumbar site. The HR-pQCT analysis demonstrated a significant reduction of the total, and trabecular BMD between D0 and 1-year, respectively 256.2 mg HA/ccm vs 255.6 mg HA/ccm (p=0.037). Correlations were observed between BMD in DEXA and HR-pQCT at 1-year but less at 3-months. PTH level correlates to cortical porosity evaluated by HR-pQCT. Formation biomarkers variations significantly correlated with several HR-pQCT parameters modulations such as trabecular homogeneity.
Conclusions: It is essential to be able to accurately assess the modification of BMD within time, ideally by non-invasive techniques. HR-pQCT is able to evaluate the decrease of BMD at trabecular site rapidly post transplantation (3 months, when no change on trabecular structure have been observed by DEXA. Correlation between both technics appears at 1-year. Bone biomarkers modulation show a promising association with HR-pQCT parameters.

OS12_7 ALLOGENEIC IMMUNITY HELPS SUSTAIN EFFECTIVE BK-VIRUS IMMUNE RESPONSES AND PREVENTS BK VIRUS-ASSOCIATED NEPHROPATHY

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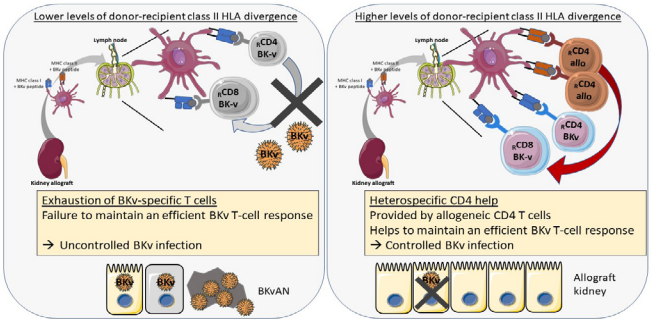
Background: BK-virus (BKv) associated nephropathy (BKvAN) emerged as a major complication in renal transplantation, affecting up to 10% of kidney transplant recipients and leading to graft loss in more than 50% of cases. If BKv T-cell response plays a crucial role in the control of BKv infection, the mechanisms involved remain unknown.
Methods: We prospectively characterized BKv T cells in a cohort of 100 kidney transplant recipients with different BKv reactivation levels (without BKV, viruria, viremia or BKvAN).
Results: Patients with BKvAN had a severe impairment of BKv CD8 T-cell functionality, such as proliferative, cytokine and cytotoxic capacities (p<0.05). We observed a gradual loss of functional BKv T cells according to BKv reactivation levels (p<0.0001), an inverse correlation between T-cell functionality and plasmatic BKv load, and an overexpression of lymphocyte inhibitory receptors (PD1, CTLA4, TIGIT and TIM3) (p<0.05). This phenotype suggested an exhaustion of BKv T cells in patients with BKvAN. This lymphocyte impairment was associated with a low level of donor-recipient class II HLA divergence, suggesting a key role of allogeneic CD4 help. In a context of higher levels of donor-recipient class II HLA divergence, allogeneic CD4 T cells can provide heterospecific help to sustain BKv T-cell responses. In *in vitro* experiments, the replacement of syngeneic CD4 T cells with allogeneic HLA-mismatched CD4 T cells restores BKv CD8 T-cell responses.
Conclusions: We observed an exhaustion of BKv CD8 T cells in patients with BKvAN. This lymphocyte exhaustion could lead to a defective BKv T-cell response, unable to provide a protective immune response against BKv reactivation. Our results suggest that in kidney transplant recipient, allogeneic CD4 T cells may provide a heterospecific help to maintain an effective BKv CD8 T-cell response in kidney transplant recipients, improving the control of BKv replication in the kidney allograft.



FULL ORALS

Kidney medical complications

OS12_8 TIME-DEPENDENT VARIATIONS IN BK POLYOMAVIRUS GENOME FROM KIDNEY TRANSPLANT RECIPIENTS WITH PERSISTENT VIREMIA

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Background: BK polyomavirus (BKPyV) is a small human DNA virus that can remain inactive for long periods within its host. In kidney transplant recipients, BKPyV reactivation can lead to nephropathy.
BKPyV genome can be roughly divided into a protein-coding region and a non-coding control region (NCCR). Twelve subgroups and two different forms of BKPyV have been described, respectively, based on the genetic variability of the major capsid protein VP1 and the NCCR.
In this work, we studied BKPyV genetic diversity and the changes that occur over time in kidney transplant recipients with persistent viremia.
Methods: The study was based on samples collected from a retrospective cohort of 394 kidney transplant recipients with viremia. BKPyV genome was analyzed from samples collected in the first months (range 75 – 139 days) and after longer post-transplant periods (range 339-1479 days) from patients with persistent viremia. BKPyV genome was obtained by next-generation sequencing and was characterized based on the entire protein-coding region and the NCCR. BKPyV sequences were compared per patient in order to identify the genomic changes over time.
Results: We were able to obtain 150 BKPyV sequences in samples collected in the first months and 45 – in samples collected later after transplantation. Per-patient comparison of BKPyV sequences showed NCCR changes in both urine and plasma samples. In urine samples, the mutation frequency did not exceed 18.5% and reached a higher value of 50% in plasma samples. Comparison of the entire BKPyV protein-coding region showed amino acid changes in urine and plasma samples in 37.5% and 34.6% of the cases, respectively. Amino acid changes were mainly found in the VP1 protein, with a frequency of 66.6% in both sample types. Most of the identified VP1 changes were located in the receptor-binding BC-loop (77.7%). Comparison of amino acid variations with those observed in samples collected in the first months after transplantation showed that amino acid changes were associated with both the introduction of a new amino acid and the reverse switch to the original one.
Conclusions: Our results suggest that BKPyV genome can accumulate mutations over time in kidney transplant recipients with persistent BKPyV viremia. This should be taken into account when developing future antiviral drugs and vaccines.

Biomarkers in Liver transplantation

OS13_1 LIVER IMMUNOSUPPRESSION FREE TRIAL (LIFT): OUTCOMES OF THE FIRST BIOMARKER-GUIDED IMMUNOSUPPRESSION WITHDRAWAL TRIAL IN LIVER TRANSPLANT RECIPIENTS

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Background: *LIFT* (NCT024989977) was a prospective multicenter immunosuppression withdrawal (ISW) trial in adult liver transplant (LT) recipients, with the primary objective to determine if the use of a 5-gene transcriptional liver tissue biomarker of operational tolerance (Bohne F et a. J Clin Invest 2012), assessed prior to ISW, accurately predicted the outcome of ISW.
Methods: Adult LT recipients were randomized 1:1 either to: 1) non-biomarker-based ISW (Arm A); or 2) biomarker-based ISW (Arm B). Inclusion criteria included: ≥3 years post-transplant (≥6 years if age ≤50 years old), no history of autoimmunity or recent episodes of rejection, normal allograft function, and no significant histological abnormalities. All patients allocated to Arm A initiated ISW, while in Arm B only biomarker-positive patients underwent ISW (Arm B+) with biomarker-negative patients remained on the same IS doses. Primary endpoint was successful ISW with maintenance of normal allograft status, as assessed by liver biopsy and liver tests 12 and 24 months after stopping IS.
Results: Between 11/2015 and 5/2019, 116 eligible patients were randomized to either ISW (n=82, Arm A and B+) or maintenance (n=34, Arm B-). 67.5% (54) of patients initiating ISW developed rejection, 26.3% (21) successfully discontinued IS, and 16.3% (13) met the histological criteria of operational tolerance 12 months after ISW. 24 months after ISW, 21% (17) patients were considered not to require IS, 19% (15) of whom met operational tolerance histology criteria. The diagnostic performance of the biomarker test was poor (95% confidence interval of the positive predictive value did not exclude 50%).
Conclusions: ISW proved to be feasible and safe but was successful in a much lower proportion of subjects than originally estimated. A liver-tissue transcriptional biomarker test, previously evaluated in a population of LT recipients with a much higher prevalence of operational tolerance, was not accurate in predicting the success of ISW.

OS13_2 MOLECULAR SIGNATURES OF REJECTION IN LIVER TRANSPLANT BIOPSIES USING THE BANFF HUMAN ORGAN TRANSPLANT GENE PANEL

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Background: Histologic assessment does not allow an accurate diagnosis of rejection in liver transplantation. The Banff Human Organ Transplant consensus gene panel (BHOT) was developed for reproductible molecular diagnosis in solid organ transplantation, but its application and relevance in liver transplant (LT) biopsies has not been investigated so far. We aimed to assess specific molecular signatures of rejection in LT biopsies.
Methods: We evaluated all LT biopsies with concomitant investigation of circulating anti-HLA DSA from pediatric and adult recipients transplanted between 2010 and 2020 in 3 French centers. Recurrence of initial liver disease, active HBV and/or HCV viremia were excluded. After extracting RNA from FFPE biopsies, the samples were sequenced using the BHOT gene panel with the Nanostring® technology. Differential gene expression (DGE) analysis was performed to assess specific molecular signature with 2 class comparisons based on histology diagnosis: in one versus everything else (EE) approach, coupled with functional pathway analysis (PA).
Results: A total of 253 biopsies (171, 67.6% performed for cause indication) from 189 patients were evaluated. The median time post-transplant was 1.29 years (IQR: 0.43-3.31). Anti-HLA DSA were positive for 114 (45.1%) biopsies. TCMR was diagnosed in 75 biopsies (29.6%); fibrosis in 33 (13%), ABMR in 3 (1.2%) and 22 (8.7%) biopsies were C4d positive. Liver TCMR-associated transcripts were significantly related to IFNγ signaling and inducible (CXCL10, CXCL11, IDO1) and to activated effector T cells (CTLA4, IFNγ, ICOS, BTLA). PA highlighted biological process related to interleukins and IFNγ signaling, lymphoid and no-lymphoid cells interaction. Fibrosis was significantly associated with transcripts related to oxidative stress (MET, FN1, ARG), cell-extracellular matrices interaction, angiogenesis (ERG, BMPER). No significant differences were found in DGE analyses of C4d positive biopsies vs EE, nor of DSA positive vs EE.
Conclusions: Using for the first time the BHOT panel in liver graft biopsies, we highlighted meaningful molecular signatures associated with TCMR with transcripts resemble universal mechanism, and fibrosis. Larger cohort of biopsies is being analyzed to establish molecular identification within more phenotypes.

OS13_3 EX SITU REPERFUSION INJURY/INFLAMMATION: IMMUNO-MOLECULAR PROFILING OF HUMAN LIVERS DURING NORMOTHERMIC MACHINE PERFUSION

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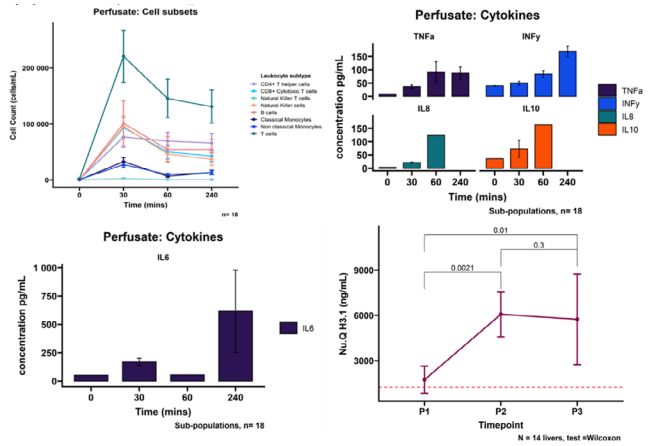
Background: Ex-situ reperfusion inflammation/injury (ERI) is an increasingly recognised phenomenon affecting donor livers preserved with normothermic machine perfusion (NMP). Higher-risk livers and DCDs are particularly vulnerable and ERI can manifest as poor graft function ex situ, with organ discard or post-transplant IRI occurring despite NMP. The immuno-molecular basis of ERI has yet to be described. This study aimed to characterise the immuno-molecular profile of circulating perfusate following ex situ reperfusion during NMP.
Methods: Perfusate samples from (n= 18 livers) in the Consortium for Organ Preservation in Europe (COPE) Liver trial and (n= 14) UK 'back to base' liver trials were included in this study. All livers were perfused using packed red cells and a colloid, with no leukocytes, platelets or complement in the starting perfusate. Serial perfusate samples were analysed for immune cells using flow cytometry, cytokines (Luminex panel) and inflammatory endogenous alarmins (chromatin-associated molecular patterns (CAMPs)) which consist of molecules such as nucleosomes and neutrophil extracellular traps (NETs) using ELISA-based measurement.
Results: NMP initiated an efflux of passenger immune cells from the donor liver into the perfusate that peaked at 30mins, then fell and plateaued by 240mins. Cytotoxic CD8+ Tcells and NK cells were the most abundant cells in the efflux, with lower levels of monocytes detected. Inflammatory cytokines progressively rose through perfusion, with IL-6 (pro-inflammatory) rising the most within 4 hours. CAMPs significantly increased in the perfusate (Nucleosomes p=0.02, NETs p=0.03) upon reperfusion to a peak at 60 mins with Nucleosomes falling significantly and NETs plateauing thereafter.
Conclusions: This is the first study to specifically characterise the immuno-molecular features of ERI, highlighting the role of immune cells, inflammatory cytokines and CAMPs in creating an inflammatory milieu within the perfusate. Donor livers susceptible to ERI may require targeted interventions to improve graft function ex situ and reduce organ discard or post-transplant preservation reperfusion injury-related complications.

Fig. Immune cells, cytokines and CAMPs during NMP. Dashed line = levels in severe sepsis.



OS13_4 BILE PROTEOME REVEALS BILIARY REGENERATION DURING NORMOTHERMIC PRESERVATION OF HUMAN LIVERS

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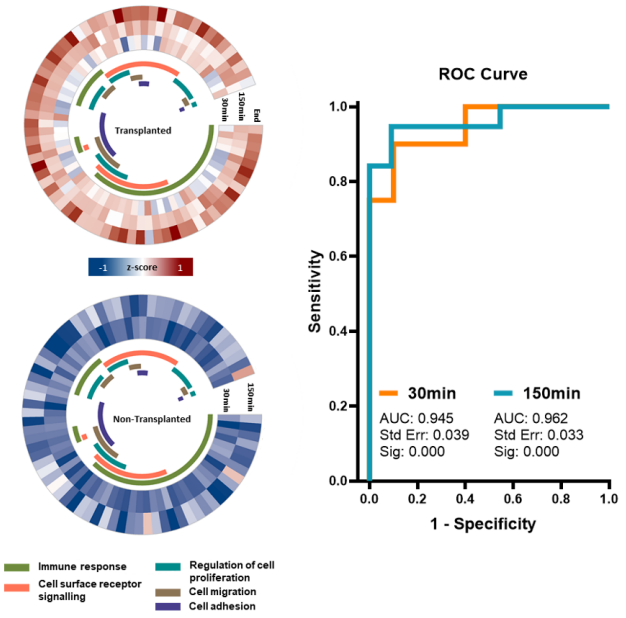
Background: Normothermic machine perfusion (NMP) after traditional static cold storage is increasingly used for preservation and assessment of human donor livers prior to transplantation. Biliary viability assessment during NMP reduces the risk of post-transplant biliary complications. However, understanding of molecular changes in the biliary system during NMP remains incomplete. Here we present an in-depth, unbiased proteomics analysis of bile collected during NMP of human livers.
Methods: A total of 56 human donor livers undergoing clinical NMP viability assessment using pre-established viability criteria were included in this study. Untargeted proteomics was performed on a retrospective discovery cohort of 31 livers. Results of predictive value were then validated in an independent, prospective cohort of 25 clinical NMP livers using the same proteomic approach. Gene ontology of identified proteins was used for pathway analysis.
Results: In the discovery cohort, a total of 2346 unique proteins were identified. Longitudinal analysis between start of NMP and viability assessment revealed a large number of significantly expressed proteins (p<0.05, >2-fold change) implicated in the flush-out of ischemia-reperfusion injury induced cell debris, and upregulation of intracellular signalling and secretion proteins. Transplanted livers showed significant upregulation proteins involved in cellular proliferation, migration, cellular signalling and the immune response at 30mins NMP, when compared to non-transplanted livers, and was maintained throughout the perfusion. Receiver operating characteristic-area under the curve analysis to predict cholangiocellular viability and successful, biliary complication-free transplantation identified a panel of 3 proteins yielding a c-statistic of 0.962 at the time of viability assessment. The validation cohort of 25 livers reproduced the performance of this diagnostic model, with a c-statistic of 0.910.
Conclusions: Proteomics of human bile reveals upregulation of regenerative pathways in viable livers during NMP. Our findings present a large and novel data set of biliary proteins which pave the way for future studies on the mechanisms of ischemia-reperfusion injury, ischemic cholangiopathy and biliary preservation in liver transplantation.



OS13_5 MMP9 CORRELATES TO WORSE ISCHEMIA REPERFUSION INJURY AND IS PARTIALLY AMELIORATED BY NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION

Abraham Den Dekker[*1;2], Sadr Shaheed[2], David Nasralla[2], Peter Friend[2], Maarten Tushuizen[1], Bart van Hoek[1], Rutger Ploeg[2], Ian Alwayn[1], Maria Letizia Lo Faro[2]

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Background: Matrix metalloproteinase-9 (MMP-9) is a collagenase that breaks down the extracellular matrix. In liver ischemia reperfusion injury, it allows leukocytes to enter liver parenchyma and thereby modulates tissue injury. Liver-selective inhibition of MMP-9 decreased ischemia reperfusion injury (IRI) in a rodent model. In humans, normothermic machine perfusion (NMP) is a potential medium to deliver therapies during the preservation period prior to liver transplantation (LT). Therefore, in this study we aimed to investigate MMP-9 levels and their correlation with IRI during and after NMP compared to traditional static cold storage (SCS), as the basis for further interventional studies.
Methods: Perfusate and recipient plasma samples (collected prior to and 1h after transplant) from n=40 LTs were selected from the Consortium for Organ Preservation in Europe (COPE) Liver NMP trial cohort (NMP n=30, SCS n=10). Samples were matched for donor and recipient demographics and analysed by enzyme linked immunosorbent assay (ELISA).
Results: MMP-9 increased in plasma after reperfusion in NMP (p=0.002) but more so in SCS (p=0.001), with fold changes of 4 and 9, respectively (p<0.001, fig 1). During NMP, perfusate MMP-9 decreased throughout perfusion with a fold change of 0.14 (p<0.001) and was higher overall in grafts with steatosis (p<0.001). The fold change of perfusate MMP-9 was negatively correlated to cholestatic markers in perfusate during NMP and in recipient plasma post-transplant (table 1). Elevated plasma MMP-9 levels were correlated to early allograft dysfunction (p=0.016), model for early allograft function, and their components; liver transaminases (AST, ALT) and INR (table 1). Post-reperfusion syndrome (p=0.05), post-transplant renal function (table 1) and need for renal replacement therapy (p<0.001) were also associated with elevated plasma MMP-9 concentrations.
Conclusions: Multiple risk factors and outcomes related to liver IRI are correlated to MMP-9 in LT, making it a potential therapeutic target during preservation. Liver NMP decreased overall levels of recipient plasma MMP9 when compared to SCS, providing a potential platform for further intervention.

Figure 1 Comparison of plasma MMP-9 concentrations between preservation types (NMP vs SCS}. Box and whisker plot showing the comparison of log2 plasma M M P -9 concentrations pretransplant and 1-hour post-reperfusion of the liver in recipients following either NMP or SCS preservation. In NMP and SCS MMP-9 significantly increased after transplant, however, in SCS this increase was significantly higher. *2-way ANOVA. **Paired student t-test.

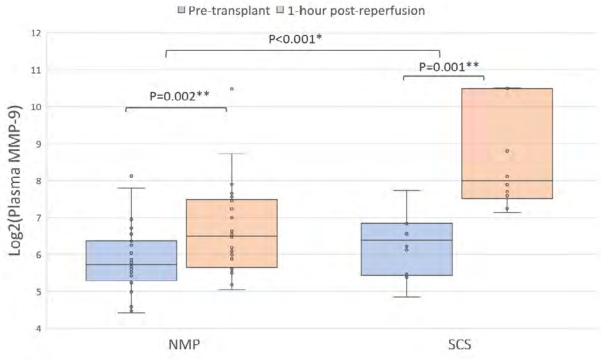

Table 1 Spearman´s Rho correlations between fold change plasma/perfusate MM-9 and continuous clinical outcomes

	Foldchange MMP-9 plasma (PI2/PI1)		Foldchange MMP-9 perfusate (Pe3/Pe1)	
Recipient	**Spearman's Rho**	**p**	**Spearman's Rho**	**p**
MEAF	0.518	0.002	NS	
AST mean day1-7	0.495	0.001	NS	
ALT mean day 1-7	0.560	<0.001	NS	
INR mean day 1-7	0.427	0.006	NS	
Bilirubin mean day 1-7	NS		-0.392	0.032
GGT mean day 1-7	NS		-0.468	0.018
Serum creatinine mean day 1-7	0.369	0.019	NS	
Perfusate				
Bilirubin Pe3	NS	NS	-0.549	0.034
Alk phos Pe1	NS	NS	-0.612	0.015
Alk phos Pe3	NS	NS	-0.579	0.024
GGT Pe1	NS	NS	-0.645	0.009
GGT Pe3	NS	NS	-0.646	0.009
GGT Pe3-Pe1	NS	NS	-0.536	0.04

Alk Phos: alkaline phosphatase, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, INR: international normalized ratio, MEAF: model for early allograft function, NS: not significant.

OS13_6 GRAFT-DERIVED CFDNA MONITORING IN PLASMA & BILE DURING EX-VIVO NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION: A PROMISING OBJECTIVE TOOL

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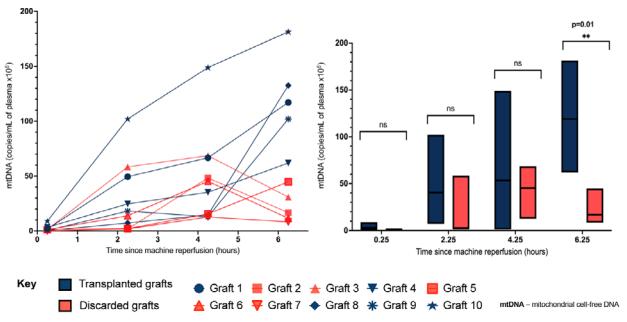
Background: *Ex-vivo* normothermic machine perfusion (NMP) is an organ preservation technique that enables an extended assessment of graft suitability prior to liver transplantation (LT). The various existing protocols used during NMP, incorporating conventional biochemical tests and perfusion parameters, vary significantly in their assessment of organ suitability for LT when applied to the same grafts. Graft-derived cell-free DNA (gdcfDNA) analysis is an emerging tool for monitoring graft health post-transplantation. We investigated the feasibility of monitoring gdcfDNA during NMP for LT in a prospective, observational cohort study.
Methods: Serial plasma and bile samples were collected during NMP for 10 consecutive grafts, at 15 minutes post-machine reperfusion and then 2-hourly intervals. Digital PCR was used to quantify mitochondrial cell-free DNA released from the graft at each timepoint.
Results: Five grafts were viable for transplantation, there were no cases of primary non-function or death in the recipients. gdcfDNA was successfully quantified in all bile and plasma samples (n>100). In plasma, gdcfDNA levels climbed post-machine reperfusion until 4.25 hours (median concentration 2.25 hours = 15.98 x 10^6 copies/mL, 4.25 hours = 40.21 x 10^6 copies/mL). gdcfDNA concentrations then diverged significantly when comparing the *viable* and *non-viable graft* groups (6.25 hours, median viable: 117.15 x 10^6 copies/mL *vs* median non-viable: 16.72 x 10^6 copies/mL). The difference in gdcfDNA concentrations between the two groups was statistically significant and levels correlated in *all cases* with the viable/non-viable outcome (**Figure 1**). There was a trend of gradual decline in bile gdcfDNA levels from viable grafts post-machine reperfusion. Discarded grafts showed more variable patterns in bile gdcfDNA levels.
Conclusions: gdcfDNA analysis during NMP is a feasible and promising objective tool to inform organ viability assessment during NMP for LT. Plasma gdcfDNA levels declined over time in non-viable grafts; possibly related to metabolic failure or microcirculatory collapse due to more severe ischaemic-reperfusion injury. gdcfDNA quantification in bile during NMP offers the alluring prospect of providing an objective means to assess the degree of biliary injury associated with organ procurement.

Figure 1.



OS13_7 BILE ACID ANALYSIS DURING NORMOTHERMIC MACHINE PERFUSION CAN REFINE LIVER GRAFT ASSESSMENT PRIOR TO TRANSPLANTATION: A PROOF-OF-CONCEPT STUDY

Guillaume Rossignol[*1;2;3], Xavier Muller[1;3], Thomas Brunet[4], Yohann Clement[4], Jean Yves Mabrut[1;3], Kayvan Mohkam[1;2;3]

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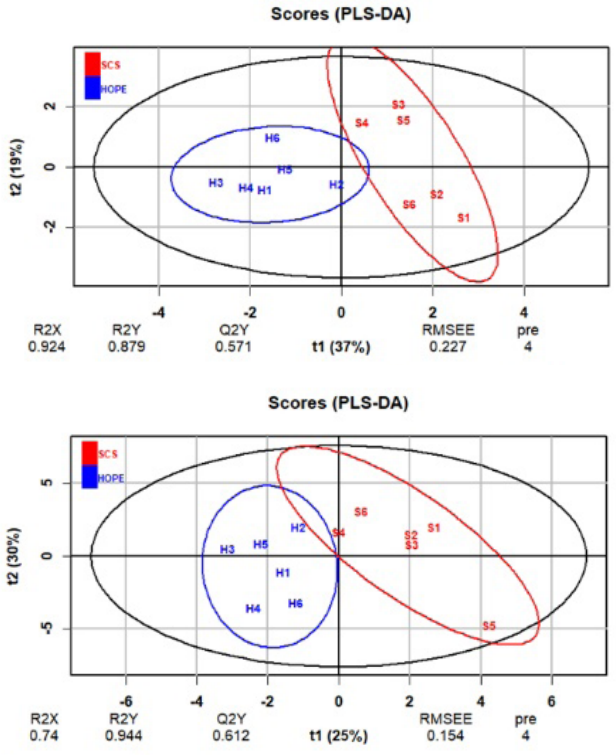
Background: Bile biochemistry serves as liver graft viability marker during normothermic perfusion (NMP). However, bile acids (BA) which are key for liver regeneration and liver injury have not yet been analyzed during NMP.
Methods: In a validated porcine model of donation after circulatory death, BA pool was analyzed in 2 different injury groups: Liver grafts underwent static cold storage for 6 hours (SCS-group; n=6) +/- 2h of hypothermic oxygenated perfusion (HOPE-group; n=6). After 2h of NMP, BA were analyzed semi-quantitatively with liquid chromatography/mass spectrometry. Validated biochemical viability criteria during NMP (transaminase release, lactate clearance, pH…) were also assessed. Partial Least Square Discriminant Analysis (PLS-DA) based on routine biochemical data alone or with additional BA analysis was used to differentiate both groups.
Results: A total of 16 main primary and secondary BA were identified. Univariate analysis of each BA did not differ among groups whereas overall BA pool was able to disclose each injury group in PLS-DA. Cholic, Tauromurocholic, TauroUrsoDeoxycholic, GlycoHyoDeoxyCholic and Glycocholic Acid were the main discriminant BA. Transaminase release (63 vs 114 UI/L/100g; p=0.004) and lactate clearance rate (83 vs 17%; p=0.02) was also able to differentiate both groups. Combining BA with biochemical data improved group discrimination when compare to biochemical viability criteria alone (Q2=0.612 vs Q2=0.571).
Conclusions: Combining BA analysis during NMP with biochemical viability criteria enabled a better discrimination between two different injury groups in a porcine model of DCD liver grafts. BA may thus refine graft selection especially in grafts with “borderline” biochemical viability profiles.

Figure 1: PLS-DA analysis based on biochemical viability criteria and bile acids in SCS and HOPE group. R2 values represents goodness-fit-measure and Q2 values estimated the predictive ability of the model. Panel A exhibits PLS-DA analysis based on biochemical viability criteria alone, with good discrimination between both groups (Q2Y=0.571, pR2Y=0.15). Panel B exhibits PLS-DA analysis based on biochemical viability criteria alone and bile acids, with better discrimination between both groups (Q2Y=0.612, pR2Y=0.05)



OS13_8 ANALYSIS OF THE BILE METABOLOME TO SEARCH FOR POTENTIAL BIOMARKERS OF QUALITY OF THE LIVER WITH PARTICULAR EMPHASIS ON BILE ACIDS

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Background: Background: The constantly growing demand for transplant organs forces transplantation centres to improve organ preservation methods and better use of suboptimal grafts. Although machine perfusion methods have a beneficial effect on organs compared to static cold storage (SCS), new methods of graft quality assessment before transplantation are still being sought. This study focused on searching for biliary metabolites that could be biomarkers of changes in transplanted livers, with particular emphasis on the analysis of bile acids.
Methods: The studies were performed on a porcine model without (0 min) or with induced moderate (30, 60, 90 min) liver warm ischemia. Bile samples produced by organs subjected to SCS or normothermic ex vivo liver perfusion (NEVLP) collected during the peri-transplant period were analyzed. Sample preparation was performed using thin-film solid-phase microextraction (TF-SPME). The LC-HRMS platform was used to search for potential biomarkers, while targeted analysis of bile acids was performed on a triple quadrupole mass spectrometer.
Results: The chemometric analysis showed a separation indicating differences in the metabolomic patterns of the bile samples based on the time interval they were collected. The preservation method used affected the level of such metabolites as lysophosphatidylcholines (LPC) and bile acids, including glycocholic acid, glycoursodeoxycholic acid, tauroursodeoxycholic and taurocholic acid. It was observed that 30 min ischemia affects the metabolomic profile of bile produced by the organ subjected to SCS (including changes in the level of oxidized bile acids and 5-methoxyindoleacetic acid), while in the NEVLP group, the alterations were seen after 90 min ischemia (mainly LPC level). In addition, the optimized and validated method of bile acid analysis allowed for the precise determination of concentrations of these metabolites in studied samples.
Conclusions: This study identified metabolites worth considering as potential markers of changes occurring in preserved grafts and optimized method for bile acid analysis, which may contribute to the development of new diagnostic tools assessing the organ’s condition in the future.

Acknowledgments: This study was funded by National Science Centre, grant Opus No. 2021/41/B/NZ5/00860

Defining risk and optimizing selection

OS14_1 WHERE TO DRAW THE LINE IN EX-SITU SPLIT LIVER TRANSPLANTATION FOR ADULT RECIPIENTS? A BENCHMARKING ANALYSIS

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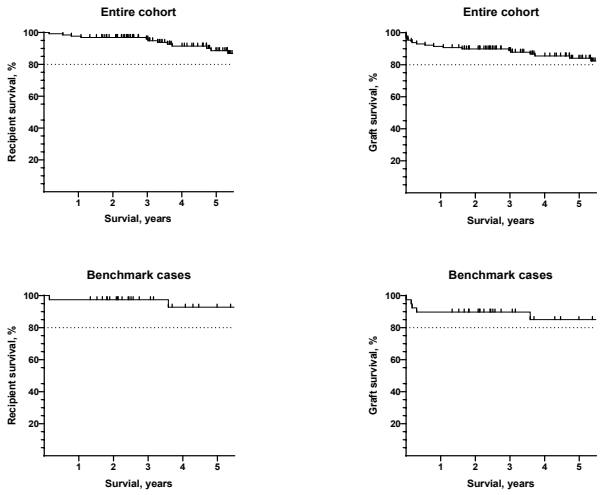
Background: A comprehensive outcome analysis of ex situ right split liver graft transplantation (RSLT) is currently lacking. Benchmarking outcomes of RSLT against best achievable results from whole LT offers a novel comparative approach.
Methods: This retrospective study includes all consecutive ex-situ RSLT for adult recipients performed from 2014-2019 at 4 high volume transplant centers (>70 LT/year) in France. Outcomes including overall morbidity expressed by the comprehensive complication index (CCI) and graft related complications were compared to the published benchmark cutoffs from whole LT.
Results: We included 129 ex-situ RSLT with 76% H45678 (n=98) and 24% (n=31) H5678 grafts. The median follow-up was 4.8 years. Overall and severe 1-year morbidity expressed by the CCI were within established whole LT benchmarks (Table 1). Biliary complication rates were slightly higher than the benchmark due to the occurrence of cut-surface leaks. The arterial thrombosis rate was outside the benchmark cutoff (7% vs ≤4.4%) leading to a higher re-transplantation rate. However, overall 1-year graft and recipient mortality were well within the benchmark cutoffs, resulting in a 5-year overall recipient survival of 88.5% (Figure 1). Selecting benchmark cases for RSLT defined by low-risk recipient-donor criteria including static cold storage time ≤10h and recipient MELD≤20 points, did not significantly reduce overall morbidity nor arterial complication rate. In contrast, the type of split graft (H45678 vs. H5678) did significantly impact on both arterial and biliary complications.

Conclusions: This large multicenter series of ex-situ right split grafts disclosed an overall 1-year morbi-mortality comparable to the best achievable results in whole LT. The results show that the main morbidity burden in adult RSLT is related to technical criteria rather than graft-recipient matching.

Table 1: Post-Transplant Outcomes in Benchmark and Non-Benchmark Cases

	Entire Cohort *n=129*	Benchmark Cohort *N=38*	Non-Benchmark Cohort *n= 91*	*Benchmarks for whole LT*
CCI discharge, points	20,9 (0-36,2)	20.9 (0-39.7)	26.2 (0-33.7)	*≤29.6*
CCI 12 months, points	33,5 (26,2-51,8)	40.8 (20.9-61.3)	33.7 (26.2-50)	*≤42.1*
At least 1 ≥ Grade III, n (%)	71 (55)	21 (55.3)	50 (54.9)	*≤59%*
Overall biliary complications, n (%)	**38 (29.4)**	11 (28.9)	**27 (29.7)**	*≤28%*
Anastomotic biliary stenosis, n (%)	20 (15.5)	7 (18.4)	13 (14.3)	
NAS, n (%)	3 (2.3)	1 (2.6)	2 (2.2)	
Anastomotic leak, n (%)	10 (7.6)	4 (10.5)	6 (6.6)	
Cut surface leak, n(%)	23 (17.8)	5 (13.1)	18 (19.8)	
Overall arterial complication, n (%)	20 (16)	4 (10.5)	16 (17.6)	
Arterial stenosis, n (%)	14 (10.8)	2 (5.3)	12 (13.2)	
Arterial thrombosis, n (%)	**9 (7)**	**3 (7.9)**	**6 (6.6)**	*≤4.4%*
Re-transplantation, n (%)	**9 (7)**	**3 (7.9)**	**6 (6.6)**	*≤4%*
- Arterial thrombosis, n	4	0	4	
- Primary non function, n	3	2	1	
- Non-anastomotic biliary stricture, n	2	1	1	
1-year graft loss , n (%)	8 (6.2)	2 (5.3)	6 (6.6)	*≤11%*
1- year mortality, n (%)	3 (2.3)	1 (2.6)	2(2.2)	*≤9%*

Figure 1: Graft and Recipient Survvial for the entire cohort and benchmark cases



OS14_2 LIVER TRANSPLANTATION IN THE ELDERLY: PROPOSAL FOR AN INNOVATIVE PATIENT SELECTION PROTOCOL

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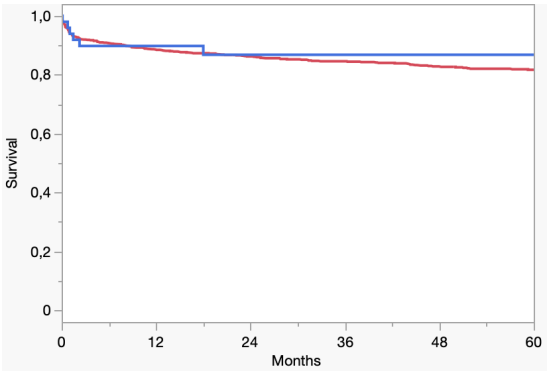
Background: Despite European and international guidelines that don't pose a specific contraindication to liver transplantation (LT) in elderly patients and invite to take into account physiological rather than chronological age, most transplant centers and regulatory institutions have widely adopted an upper age limit (65 or 70 years old). We sought to evaluate the outcome of patients who exceeded 70 years while waiting for LT in our center in the last ten years to develop a prospective pre-listing selection protocol for over-seventy patients.
Methods: We enrolled consecutive patients aged between 71 and 75 years old who received LT from a deceased donor at our center for chronic end-stage liver disease or hepatocellular carcinoma in the previous ten years. The primary endpoint was five years post-LT survival in over seventy compared to younger adult recipients. Moreover, propensity score values and inverse probability weights (IPW) were calculated to correct all biases in the comparison between groups. This retrospective study represents a preliminary analysis to design a prospective protocol for the selection of elderly patients for LT.
Results: We evaluated 1015 patients undergoing LT from deceased donors performed at our center between 01/01/2010 and 31/12/2022. Among them, forty-nine patients aged ≥70 years old received LT. Five-year patient and graft overall survival rates were respectively 92% and 88% for patients 70-75 years old and 88% and 84% for patients aged <70 years old (p > 0.05). Even the survival analysis comparing the two IPW-adjusted populations demonstrated the absence of statistically significant differences between groups. Based on these results, we developed a prospective protocol in the fashion of a decision algorithm; this can be used to super-select a population with a high prevalence of comorbidities to prevent a waste of resources.
Conclusions: The post-transplant outcome in over-seventy patients seems acceptable, provided that extreme care is used in evaluating the recipient's comorbidities and functional status, according to objective and widely accepted protocols focused on sparing donor and healthcare resources.



OS14_3 AGE AND LIVER GRAFT: A SYSTEMATIC REVIEW WITH METAREGRESSION

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Background: The increasing shortage of organs for liver transplantation has led to the greater use of Extended Criteria Donors (ECDs) to meet the growing demand for liver grafts. The demographic changes result in the increased use of elderly donors, historically considered marginal donors, for liver transplantation. Despite this, the exact age cut-off for donor eligibility remains unclear and is a subject of debate in the transplant community. This study was conducted to evaluate the effect of donor age on transplant outcomes, including 1-year graft survival, biliary complications, and hepatic arterial thrombosis.
Methods: The method included a search in PubMed, Scopus and Cochrane Library. The primary outcome was 1-year graft survival; the secondary outcomes were biliary complications and hepatic arterial thrombosis. The pooled effect was calculated using either the fixed effects or the random-effects model. A meta-regression model was used to analyse the temporal trend relation in the survival outcome.
Results: The meta-analysis included 11 studies. The meta-analysis results showed that the 1-year graft survival of liver grafts from elderly donors (with age cut-offs at 50, 60, 70, and 80) was similar to that of standard donors. However, elderly donors were found to have an increased risk of overall biliary complications (OR: 1.89, 95% CI: 1-3.65) and hepatic artery thrombosis (OR: 2.27, 95% CI: 1.27-4.11). A meta-regression analysis also showed a significant correlation between 1-year graft survival and the year of publication (coef. 0.00027, 95% CI: -0.0001 to -0.0003, p=0.0009).
Conclusions: In conclusion, the meta-analysis results show that donor age alone cannot be considered a criterion for extended criteria in liver transplantation. The 1-year graft survival of liver grafts from elderly donors has improved over time, but there is still a risk of biliary and arterial complications. The decision to use elderly donors as liver transplant donors should be based on a comprehensive assessment of risk factors and balanced by reducing other risk factors using new technology such as machine perfusion.

OS14_4 DEVELOPMENT OF A 'LIVER ATLAS' USING OVER 1,000 CONSECUTIVE DECEASED DONOR LIVERS TO IDENTIFY HEPATIC STEATOSIS PRIOR TO RETRIEVAL

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Background: Hepatic steatosis is associated with poor liver transplantation outcomes. This study describes the development of a first large-scale 'Liver Atlas' of deceased donor livers to:(i) investigate the incidence of biopsy-confirmed steatosis;(ii) identify pre-retrieval predictors of steatosis severity, and;(iii) evaluate the impact of steatosis severity on organ retrieval, utilisation and graft/recipient outcome.
Methods: Consecutive biopsies from 1,048 deceased donors collected between 2017-2019 were requested from the national QUOD bioresource. Steatosis severity was quantified using imageDx™ AI-based image analysis of H&E stained slides. 906 out of 1,048 donor livers had sufficient tissue for histological assessment and were included in the final analysis with none (*n*=670), mild (*n*=102), moderate (*n*=81) and severe steatosis (*n*=53).
Results: Pre-retrieval predictors including anthropometric measures (WC and BMI), clinical risk scores (fatty liver index and hepatic steatosis index) and biochemical measures (GGT, triglycerides and insulin) all demonstrated significant differences between imageDx™ scores. Multivariate regression analysis demonstrated that only GGT was useful in differentiating between steatosis severity: mild-moderate (*P*=0.059) and mild-severe steatosis (*P*=0.001). Overall, 685/906 livers (75.6%) were retrieved with intent to transplant with none (*n*=522), mild (*n*=71), moderate (*n*=57) and severe steatosis (*n*=35). A poor concordance was found between retrieval surgeon's macroscopic 'fat' assessment and imageDx™ scores: none (*n*=298, 57%), mild (*n*=31, 44%), moderate (*n*=23, 40%) and severe steatosis (*n*=10, 29%). The proportion of retrieved livers resulting in transplantation significantly decreased with increasing steatosis severity which was associated with a non-significant reduction in 12-month graft and patient survival.
Conclusions: This 'Liver Atlas' supports utilisation of pre-retrieval steatosis predictors and routine retrieval biopsy to avoid unnecessary liver discards. Transcriptomic analysis of this cohort is also being undertaken to map independent signatures associated with increasing steatosis severity. This will enable targeted ex-situ optimisation to improve utilisation of the high-risk steatosis category.

Histological steatosis degree (imageDx™ score, 0-3)				
Pre-retrieval steatosis predictors, Mean [±SD] & Transplant Outcomes, Number [%]	None (0)	Mild (1)	Moderate (2)	Severe (3)	*P* - value
Body Mass Index, BMI (m²)	26.2 [±4.9]	28.5 [±4.5]	29.1 [±4.7]	30.4 [±6.4]	<0.001
Waist Circumference (cm)	94 [±15]	103 [±16]	103 [±12]	107 [±15]	<0.001
Fatty Liver Index (FLI)	28.9 [±27.5]	41.7 [±29.1]	50.2 [±29.2]	57.8 [±31.2]	<0.001
Hepatic Steatosis Index (HSI)	36 [±8.6]	39.2 [±8.9]	37.6 [±7.2]	39.8 [±9.9]	<0.001
GGT (U/L)	96.8 [±135]	95.3 [±128.6]	159.8 [±217]	205.5 [±349.7]	<0.001
Total triglycerides (mmol/L)	1.38 [±0.82]	1.65 [±0.95]	1.86 [±1.75]	1.98 [±2.43]	<0.001
Insulin (pmol/L)	223.7 [±292.1]	281 [±333.1]	254.3 [±248.4]	379.5 [±381.3]	0.003
Liver Retrieved	522 [78]	71 [70]	57 [70]	35 [66]	0.051
Liver Transplanted	472 [90]	57 [80]	35 [61]	15 [43]	<0.001
12-month graft survival	442 [94]	55 [96]	31[89]	13 [87]	0.339
12-month patient survival	433 [91]	50 [88]	30 [86]	13 [87]	0.469

Table 1: Pre-retrieval predictors of steatosis demonstrating significant difference across four groups (none, mild, moderate and severe). A significant reduction in organ utilisation (demonstrated by number of livers transplanted) with increasing steatosis severity.

Histological steatosis degree (imageDx™ score, 0-3)					
Multivariate regression (Bonferroni) *P* – value		None (0)	Mild (1)	Moderate (2)	Severe (3)
Body Mass Index, BMI (m²)	None	-	<0.001	<0.001	<0.001
	Mild	<0.001	-	1.0	0.183
	Moderate	<0.001	1.0	-	0.609
	Severe	<0.001	0.183	0.609	-
Waist Circumference (cm)	None	-	<0.001	<0.001	<0.001
	Mild	<0.001	-	1.0	0.431
	Moderate	<0.001	1.0	-	0.451
	Severe	<0.001	0.431	0.451	-
Fatty Liver Index (FLI)	None	-	<0.001	<0.001	<0.001
	Mild	<0.001	-	0.539	0.013
	Moderate	<0.001	0.539	-	0.803
	Severe	<0.001	0.013	0.803	-
Hepatic Steatosis Index (HSI)	None	-	0.002	0.721	0.013
	Mild	0.002		1.0	1.0
	Moderate	0.721	1.0	-	0.9
	Severe	0.013	1.0	0.9	-
GGT (U/L)	None	-	1.0	0.005	<0.001
	Mild	1.0	-	0.059	0.001
	Moderate	0.005	0.059	-	0.960
	Severe	<0.001	0.001	0.960	-
Total triglycerides (mmol/L)	None	-	0.128	0.001	0.001
	Mild	0.128	-	1.0	0.498
	Moderate	0.001	1.0	-	1.0
	Severe	0.001	0.498	1.0	-
Insulin (pmol/L)	None	-	0.8	1.0	0.003
	Mild	0.8	-	1	0.293
	Moderate	1.0	1.0	-	0.197
	Severe	0.003	0.293	0.197	-

Table 2: Multivariate regression analysis (with post-hoc Bonferroni correction) demonstrating performance of pre-retrieval predictors in differentiating steatosis severity between steatosis grades.

OS14_5 PREDICTING POST-TREATMENT (SURGICAL, ABLATIVE, LIVER TRANSPLANT) RECURRENCE IN EARLY-STAGE HEPATOCELLULAR CARCINOMA USING DEEP MACHINE LEARNING

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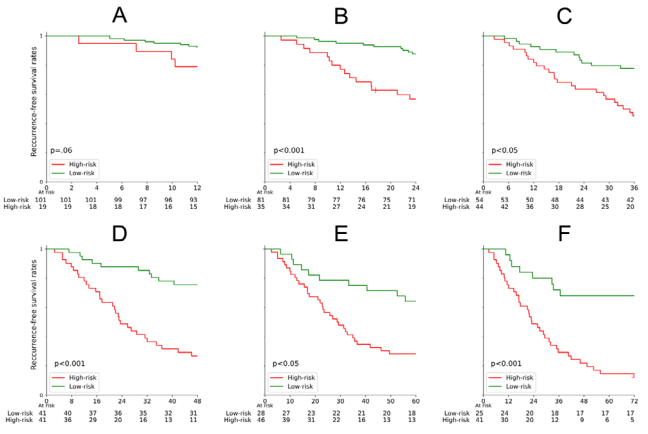
Background: Early-stage HCC patients are treated with curative intention, but the recurrence burden remains high affecting patient outcomes and compromising liver transplant utility
Methods: Our study aims to build, validate, and test a deep learning approach to predict the post-treatment (surgical, ablative, or OLT) recurrence risk in early-stage HCC patients from pre-treatment MR imaging.
Retrospective study with 120 patients who underwent either thermal ablation, surgical resection or OLT as first-line, stand-alone treatment for HCC between 2005 and 2018. Multiparametric contrast-enhanced MRI was analyzed by our machine learning model. The imaging dataset was labelled in six categories, with time-to-recurrence cutoffs at 1 - 6 years. Area under the receiver operating characteristic curves (AUC-ROC) was used to evaluate algorithm performance. Recurrence-free survival (RFS) was evaluated by Kaplan-Meier analysis, and survival curves were compared using the log-rank test
Results: Red line classifies as recurrent (high risk).Green line classifies as non-recurrent (low risk). For 1-6 years, our model was able to predict tumor recurrence with moderate to high accuracy and test-AUCs between 0.71 to 0.85. In Kaplan-Meier analysis, predictions allow patients to be stratified into risk groups with significant differences in expected RFS at six recurrence time frames, with greater levels of certainty for the later time points
Conclusions: Our work serves as proof of principle that deep learning-based algorithms can predict recurrence from pre-treatment MR imaging in patients with early-stage HCC. Deep Learning-based modelling of imaging features could be used to individualize treatment options with improved prognostications.

Performance metrics for each investigated time frame of recurrence							
	Time frame (years)						Total
	1	2	3	4	5	6	
N (recurrence)	120 (12)	116 (26)	98 (36)	82 (40)	74 (43)	66 (44)	120 (44)
Test-AUC mean (SD)	0.71	0.75	0.71	0.81	0.75	0.85	0.76 (0.05)



OS14_6 DOES NATIVE HEPATECTOMY TECHNIQUE HAVE ANY IMPACT ON ONCOLOGIC OUTCOMES OF LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA?

Riccardo Pravisani*[1], Federico Mocchegiani[2], Fabio Melandro[3], Damiano Patrono[4], Andrea Lauterio[5], Fabrizio Di Francesco[6], Matteo Ravaioli[7], Marco Zambelli[8], Claudio Bosio[9], Daniele Dondossola[10], Quirino Lai[11], Andrea Della Penna[12], Jule Dingfelder[13], Luca Toti[14], Alessandro Iacomino[15], Sermed Nicolae[16], Paolo De Simone[3], Renato Romagnoli[4], Luciano De Carlis[5], Matteo Cescon[7], Salvatore Gruttadauria[6], Michele Colledan[8], Amedeo Carraro[9], Lucio Caccamo[10], Marco Vivarelli[2], Massimo Rossi[11], Silvio Nadalin[12], Georg Gyoeri[13], Giuseppe Tisone[14], Giovanni Vennarecci[15], Andreas Rostved[16], Maria De Martino[17], Miriam Isola[17], Umberto Baccarani[1]

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Background: To date, caval sparing(CS) and total caval replacement(TCR) for recipient hepatectomy in liver transplantation(LT) have been compared only in terms of surgical morbidity. Nonetheless, CS technique is inherently associated with an increased manipulation of the native liver and later exclusion of the venous outflow, which may both increase the risk of intraoperative systemic shedding of tumor cells when LT is performed for hepatocellular carcinoma(HCC). The aim of the present multicentre study was to assess the impact of native hepatectomy technique on the risk of post-LT HCC recurrence.
Methods: This was an international, retrospective, multicenter, observational study to assess the impact of recipient hepatectomy (CS versus TCR) on the risk of post-transplant HCC recurrence, among 16 Transplant Centers that used either TCR or CS native hepatectomy, as elective protocol surgical procedure.
Results: In 1851 patients with viable HCC in the explanted native liver, CS and TCR approaches were used in 1030 (55.6%) and 821(44.4%) cases, respectively. The cumulative incidence of post-LT tumor recurrence at 1, 3 and 5 years was 4.4%, 10.1% and 12.1%, respectively. Group adjustment with inverse probability weighting was performed using the following baseline variables: recipient age, MELD score, Child-Pugh class C, viral hepatitis, alcohol abuse, pre-LT alphafetoprotein serum levels, clinical HCC stage according Milan criteria, pre-LT downstaging/bridging, tumor number and size, grading, microvascular invasion and cold ischemia time. In a multivariate competing risk regression model, CS was associated with a higher risk of HCC recurrence (SHR 1.699, p=0.020). However, in patients with histology-proven complete necrosis of all tumor nodules(CS,n=423; TCR,n=149) neither technique was associated with a significantly higher risk of recurrence.
Conclusions: TCR approach should be considered alongside other preventive measures to reduce the risk of post-transplant HCC recurrence.

OS14_7 PREDICTION AND DIAGNOSIS OF REJECTION IN LIVER TRANSPLANTATION USING A BIOMARKER MODEL BASED ON CXCL-10 AND MICRORNAS 155-5P AND 181A-5P

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Background: The diagnosis of rejection in liver transplantation (LT) relies on a liver biopsy (LB) lecture in the setting of abnormalities in the liver function tests (LFT). The use of non-invasive biomarkers may avoid the need for LB and could help in a more efficient immunosupressive therapy adjustment. Plasma microRNA expression and certain chemokines have been proposed as potential biomarkers of rejection.
Methods: Prospective, observational study conducted in a cohort of 79 patients followed during the first year after LT. Plasma samples were collected on predetermined timepoints for the analysis of microRNAs 155-5p, 122-5p and 181a-5p and CXCL-10 chemokine. Patients with LFT abnormalities were submitted to a LB to rule out rejection, assessing previous and concurrent expression of the biomarkers to evaluate their predictive and diagnostic ability. Information from 87 patients included in a previous study was collected and used as a validation cohort.
Results: Twenty-four episodes of T-cell mediated rejection were diagnosed in 22 patients. Plasma CXCL-10 concentration and the three microRNA expression were significantly elevated prior and at the moment of the diagnosis of rejection. These and other significantly altered variables were used to develop a logistic model for rejection prediction and diagnosis. The model included CXCL-10 and microRNAs 155-5p and 181a-5p. Area under the ROC curve (AUROC) for rejection prediction was 0.97 (81.6% sensitivity, 98.7% specificity) and 0.99 for diagnosis (91.3% sensitivity, 99.5% specificity). In the validation cohort, the AUROCs were 0.89 and 0.92 for rejection prediction and diagnosis, respectively. In patients with graft dysfunction (LFT abnormalities at the moment of the LB) of both cohorts, the biomarker model could identify those with rejection with an AUROC of 0.98 (97.3% sensitivity, 94.7% specificity).
Conclusions: The biomarker model based in CXCL-10 and microRNA 155-5p and 181a-5p allows the prediction and diagnosis of rejection and identifies patients with graft dysfunction due to rejection.

OS14_8 WORLDWIDE DATA FROM THE IMPROVEMENT LIVER TRANSPLANT STUDY: AN INTERIM ANALYSIS OF DONOR AND RECIPIENT PROFILES

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Background: The IMPROVEMENT project was designed to optimise predictive models of 90-day and 1-year allograft failure after liver transplantation (LT). This data collection (donor, preoperative recipient, postoperative and outcome data) involves several LT centres with different transplant activity volumes from Europe, North America, South America, and Asia.
Methods: From Jan-2017 to Jan-2023, we enrolled 2,015 adult LTs. Centre- and patient-specific inclusion criteria are fully reported on the IMPROVEMENT website (https://gemelligenerator.it/projects/the-improvement-study-2/) and on ClinicalTrials.gov (Ref. NCT05289609). Enrolment is ongoing, with 4000 LT cases expected at completion. All data from 21 centres are anonymised and stored in an online REDCAP database. Eight centres have already completed data collection and fifty more are in the process of submitting their data. This interim exploratory, descriptive analysis was conducted to identify potential inconsistencies/discrepancies.

Results: Donors had a median age of 58 yrs, BMI of 26 kg/m^2, donor risk index of 1.9, 39% were extended criteria (ECD), 9.1% were DCD, and perfusion machines were used in 6.4% of cases (Table 1). Recipients had a median age of 59 yrs and BMI of 26 kg/m^2. Median MELD and MELDNa at listing were 16 and 15, respectively. The indications for LT were alcohol-related cirrhosis (29.8%), viral infections (HCV in 21.2% and HBV in 12.2%), and NASH (9.8%). 31% cases had hepatocellularcarcinoma as a co-indication. Postoperative complications, according to Clavien-Dindo were 59.5% class 1-3a and 40.5% class 3b-5, with a median comprehensive complication index of 39.5. Median post-LT ICU and hospital stay were 0 and 17 days, respectively.
Conclusions: The definition of an epidemiological and clinical profile of LT is mandatory to provide the basis for more complex prognostic models. The broadening of enrolment and data from other LT centres will allow an accurate worldwide representation of LT and the development/validation of robust prognostic models.

Characteristics	Median	IQR
Donor age, median (IQR)	58	46 - 71
Donor BMI, median (IQR)	25.7	23,4 - 28,1
DCD, %	9,1%	-
DRI, median (IQR)	1.9	1 – 2
ECD, %	39%	-
Machine perfusion, %	6,4%	-
Recipient Age, median (IQR)	59	52 - 65
Recipient BMI, median (IQR)	26	23,1 - 29,3
CONUT score, median (IQR)	4	2 - 6
MELD at listing, median (IQR)	16	10 - 25
MELDNa at listing, median (IQR)	15	10 - 21
MELD at LTx, median (IQR)	15	10 - 21
MELDNa at Ltx, median (IQR)	16	10 - 25
Non-neoplastic main indication to LTx, %		
Alcohol	29.8%	-
HCV disease	21.2%	-
HBV disease	12.2%	-
Metabolic (NAFLD + NASH)	9.8%	-
Cholestatic	3.7%	-
Other indications	23.3%	-
HCC Co-indication	31.7%	
Neoplastic-non neoplastic ratio, %	45,9%	-
Packed RBC during surgery, median (IQR)	2	0 - 4
Lactate 120 min post reperfusion, median (IQR)	2.92	1,9 - 4,5
L-GRAFT 7 score, median (IQR)	-3.07	-3,69 - -2,07
L-GRAFT 10 score, median (IQR)	-3.29	-4,01 - -2,24
EASE score, median (IQR)	-3.7	-4,8 - -2,9
Clavien-Dindo, %		
1 - 3A	59,5%	
3B - 5	40,5%	
Comprehensive Complication Index, median (IQR)	39.5	22,6 - 54,8
Hospital stay, median (IQR)	17	12 - 28

Table 1. Demographic and clinical characteristics of the patients

Organ preservation and ischemia reperfusion

OS15_1 PROLONGED HYPOTHERMIC MACHINE PERFUSION TO ENABLE DAYTIME LIVER TRANSPLANTATION – A RANDOMIZED CLINICAL TRIAL

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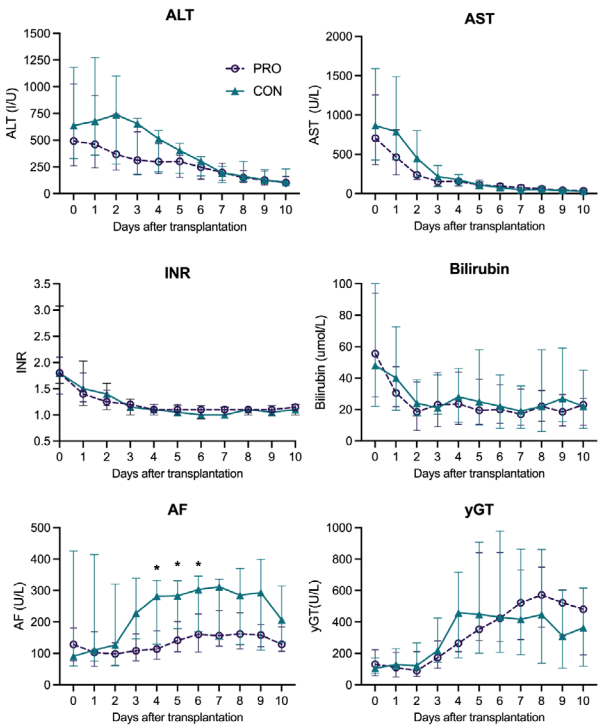
Background: Liver transplantation is emergency surgery because the graft deteriorates with each additional minute of cold ischemia. To ease logistics and allow daytime transplantation, the DHOPE-PRO trial was initiated to assess safety and feasibility of dual hypothermic oxygenated machine perfusion (DHOPE) to prolong liver preservation time.
Methods: Donation after brain death donor livers were randomized to prolonged (PRO) or conventional (CON) DHOPE based on donor hepatectomy time. Livers were assigned to PRO when donor hepatectomy was finished between 16:00–3:59 hours, followed by prolonged DHOPE until implantation the following day. Livers were assigned to the CON when donor hepatectomy was finished between 4:00–15:59 hours, followed by 2 hours DHOPE prior to implantation. The primary endpoint was a composite of all serious adverse (device) events [SA(D)E] up to 30 days after liver transplantation.
Results: From September 2020 to July 2022, 24 patients received a liver randomized to PRO (n=12) or CON (n=12). Median DHOPE duration and total preservation times in the PRO group were 9:18 hours and 14:32 hours, versus 2:10 hours (P<0.001) and 7:54 hours (P<0.001) in the CON group, respectively. In each group, 3/12 patients (25%) developed a SA(D)E (P=1.00). In the CON group, one device error occurred, and 2 patients developed post-reperfusion syndrome. In the PRO group, 3 patients experienced post-reperfusion syndrome. Immediate postoperative liver function and injury markers were similar in both groups **(Figure 1)**. After a minimum follow-up time of 6 months no patients have developed non-anastomotic biliary strictures, with 100% patient and graft survival in both groups. Markers of ischemia-reperfusion injury and oxidative stress were not different between the groups.
Conclusions: DHOPE is a safe and feasible method to prolong the preservation time of donor livers. Implementation of this technique has the potential to transform current clinical practice by changing liver transplantation from emergency surgery into a semi-elective, daytime operation.
Disclosure: This abstract was also submitted to the ILTS 2023 meeting.

Figure 1.



OS15_2 WHAT IS THE OPTIMAL PRESERVATION STRATEGY FOR MARGINAL LIVER GRAFTS USING HYPOTHERMIC OXYGENATED PERFUSION? A PRECLINICAL STUDY

Xavier Muller*[1;2], Antoine Breton[1], Joris Couillerot[1], Kayvan Mohkam[1;2], Jean Yves Mabrut[1;2], Guillaume Rossignol[1;2]

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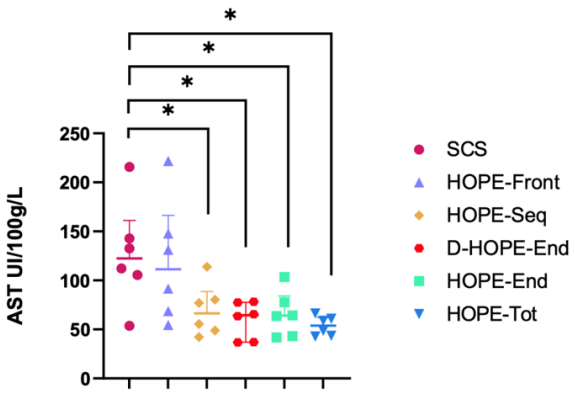
Background: End-ischemic hypothermic oxygenated perfusion (HOPE) has been shown to protect marginal liver grafts. However, the optimal perfusion modality and timing of HOPE remains unknown.
Methods: We evaluated different preservation strategies with HOPE in a porcine model of marginal liver grafts undergoing 30min of asystolic warm ischemia and 6h of static cold storage (SCS). The SCS group was used as control. First, end-ischemic dual portal/arterial perfusion (D-HOPE) was compared to single portal perfusion (HOPE). Second, end-ischemic HOPE was compared to upfront, sequential, and continuous HOPE (**Figure 1**). All grafts then underwent ex-vivo reperfusion with autologous blood at 37°C for 2h to assess graft ischemia-reperfusion injury and function. Six pigs were randomly assigned to each group.
Results: D-HOPE and HOPE displayed comparable mitochondrial injury (FMN release 52 vs 53 ng/ml, p=0.81), peak AST (64.5 vs 64 UI/100g/L, p=0.75) and histological ischemia-reperfusion injury (IRI) score (7 vs 7points, p=0.85). Based on these results portal HOPE was used to compare the 4 different preservation strategies. Total, end-ischemic and sequential HOPE presented with comparable peak AST. Higher transaminase release was observed in Upfront HOPE within the range of the SCS group (p=0.013). Viability criteria were met in a higher rate in end-ischemic and continuous HOPE without statistical differences. Histological IRI scores were not significantly different among groups.
Conclusions: End-ischemic HOPE and D-HOPE showed comparable protective effects on marginal liver grafts. Continuous HOPE perfusion did not show a significant improvement in liver injury and function compared to end-ischemic HOPE. However, adding >2h of SCS after HOPE showed a significant increase in graft injury similar to static cold storage. These results will guide future clinical applications of HOPE for example in the context of liver graft reconditioning centers.

Figure 1: Transaminase release after 2h of ex-vivo reperfusion among the different study groups



OS15_3 HYPOTHERMIC OXYGENATED PERFUSION AFTER NORMOTHERMIC REGIONAL PERFUSION TO EXTEND SELECTION CRITERIA IN CDCD LIVER TRANSPLANTATION

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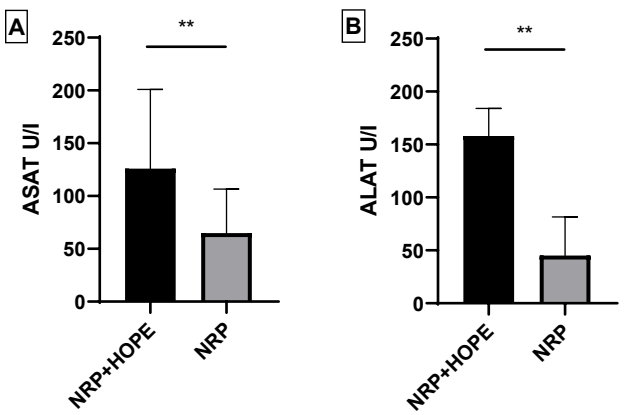
Background: The French controlled donation after circulatory death (cDCD) liver transplant (LT) program with normothermic regional perfusion (NRP) has achieved benchmark outcomes using strict selection criteria. To reduce graft discard rates, selection criteria were extended in September 2021 with mandatory use of hypothermic oxygenated perfusion (HOPE) after NRP.
Methods: All consecutive cDCD LT performed in 4 centres since the extension of selection criteria were included and followed up for 3 months. HOPE was mandatory in liver grafts previously discarded for transaminase levels ranging from 4N-8N during NRP and/or 20%-30% macrosteatosis. Outcomes after NRP+HOPE were compared to NRP alone.
Results: Fifty-nine cDCD grafts were transplanted during the study period of which 13(22%) underwent NRP+HOPE due to high NRP transaminase levels (85%) or liver steatosis (15%). Donor characteristics and warm ischemia times were comparable between both groups except for significantly higher peak transaminases during NRP in the NRP+HOPE group. (**Table 1, Figure 1**). The median HOPE duration was 113 min resulting in a significantly longer ex-vivo preservation (412 vs 347 min, p=0.130) compared to the NRP group. The NRP+HOPE group displayed a lower early allograft dysfunction rate (7.7 vs 21.7%, p=0.251) with comparable L-Graft7 risk scores (-3.21 vs -3.89, p=0.182). Arterial and biliary complications were similar between both groups without occurrence of primary nonfunction or re-LT after NRP+HOPE.
Conclusions: HOPE after NRP resulted in transplantation of >20% additional grafts otherwise discarded with the strict French selection criteria. Additional HOPE significantly prolonged ex-vivo preservation and achieved early outcomes observed in highly selected NRP cDCD grafts.

Table 1: Donor and graft characteristics and early post-transplant outcomes

	NRP n= 46	*NRP+HOPE n= 13*	*P*
Donor age, years	56 (42-62)	53 (51-58)	*ns*
Macrosteatosis > 20%, n(%)	0 (0)	2 (15)	*p=0.007*
TDWI, min	30 (27-40)	36 (30-54)	*ns*
FDWI, min	22 (18-25)	22 (19-25)	*ns*
AWI, min	18 (15-22)	18 (17-20)	*ns*
NRP duration, min	195 (160-229)	205 (176-230)	*ns*
Static cold storage time, min	347 (316-408)	325 (284-356)	*ns*
Biliary complications, n (%)	7 (15.2)	2 (15.4)	*ns*
- NAS, n(%)	1 (2.2)	0 (0)	*ns*
Re-transplantation, n (%)	1(2.2)	0 (0)	*ns*
- Arterial thrombosis, n	1(2.2)	0 (0)	*ns*
3month graft loss , n (%)	1(2.2)	0 (0)	*ns*
3 month mortality, n (%)	1(2.2)	0 (0)	*ns*

TDWI: total donor warm ischemia; FDWI: functional donor warm ischemia; AWI: asystolic warm ischemia; NRP: normothermic regional perfusion; NAS: non anastomotic stenosis

Figure 1: Peak transaminases during normothermic regional perfusion in the NRP+HOPE and NRP groups



A. Peak aspartate aminotransferase B. Peak alanine aminotransferase

OS15_4 DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION IS ASSOCIATED WITH IMPROVED RECOVERY OF ACUTE KIDNEY INJURY AFTER DCD LIVER TRANSPLANTATION

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Background: The use of donation after circulatory death (DCD) donor livers is associated with acute kidney injury (AKI) and chronic kidney disease (CKD) after liver transplantation (LT). End-ischemic dual hypothermic oxygenated machine perfusion (DHOPE) resuscitates donor livers prior to implantation and mitigates ischemia reperfusion injury, compared to static cold storage (SCS) alone. In this study we analyzed the impact of DHOPE on the incidence of AKI and CKD after DCD LT.
Methods: In this post-hoc analysis of a multicenter randomized controlled trial, patients received either a DCD liver after SCS alone (control) or after end-ischemic treatment with DHOPE. The incidence of AKI based on serum creatinine within the first week and CKD at 6 months after LT were scored according to KDIGO. Rapid reversal of severe AKI (stage 2&3) within 48 hours (transient AKI) was assessed.
Results: 99 patients without prior renal dysfunction were included. There were no significant differences in risk factors associated with AKI, including donor and recipient BMI, blood product transfusions and recipient warm ischemia time. Postreperfusion syndrome occurred in 12% of the DHOPE group and in 27% in the control group (risk ratio, 0.43; 95% CI, 0.20 to 0.91).
In controls 23% (12/52) developed severe AKI (KDIGO stage 2&3) vs 28% (13/47) in the DHOPE group (p=0.600). Reversal of severe AKI within 48 hours was 0% (0/12) in controls vs 38% (5/13) in the DHOPE group (p=0.016). At 6 months after DCD LT, the incidence of severe CKD (severe CKD & end-stage renal disease) was 6.3% (3/48) in controls vs 0% (0/42) in DHOPE (p=0.099).
Conclusions: DHOPE did not reduce the incidence of AKI, however DHOPE was associated with improved early recovery of AKI after DCD LT. This translated into a trend towards less severe chronic kidney injury at 6 months after DCD LT.

OS15_5 LACTATE DYNAMICS DURING THE FIRST 6 HOURS OF LIVER NORMOTHERMIC MACHINE PERFUSION PREDICTS CLINICAL OUTCOME – A MULTICENTER STUDY

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Background: A growing number of livers undergo normothermic machine perfusion (NMP) prior to transplantation. However, robust and validated biomarkers to predict the clinical outcome are still lacking. To aid the decision making for transplantation, we investigated the dynamics of lactate clearance as a basic function of liver viability during the first 6 h of NMP in a multicenter study.
Methods: 504 livers underwent ≥ 6 h of NMP before transplantation in 6 centres in the UK, Germany, and Austria. The donor age was 49.74 ± 16.30 y (mean ± SD), the donor liver risk index was 1.97 ± 0.68. 29 % of livers were donated after cardiocirculatory death; static cold storage time was 412 ± 124 min. All centers applied a back-to-base approach and used the OrganOx Metra® system for NMP. The perfusate lactate levels at start (5-15 min), 1 h, 2 h, 4 h and 6 h of NMP were assessed and area under the curve (AUC) was calculated. Primary endpoints were MEAF (Model for Early Allograft Function) and L-GrAFT (Liver Graft Assessment Following Transplantation). Linear regression and correlation studies were performed using R and GraphPad Prism.
Results: The total NMP time was 723 ± 334 min. EAD occurred in 26 %, MEAF was 4.86 ± 1.86 and L-GrAFT at day 7 and 10 was 0.53 ± 1.25 and -0.21 ± 1.25, respectively. The respective 1-year patient and graft survival was 86 % and 80 %. Lactate levels at 1 h, 2 h and 6 h correlated significantly with MEAF and the correlation increased in robustness over time. Rather than a binary assessment with a cut-off value of < 2.5 mmol/L at 2 h, the actual 2 h lactate level correlated with the MEAF (Pearson r = 0.1043 *vs.* r = 0.1734, p = 0.0306 *vs.* p = 0.0003). Further to the absolute lactate concentration at 6 h, the AUCs of 0-6 h and 1-6 h lactate concentrations (p < 0.0001, r = 0.3176) have strong predictive value towards MEAF. No correlation between perfusate lactate and L-GrAFT was found.
Conclusions: Lactate AUC up to 6 h and lactate levels at 6 h of NMP correlate strongly with the risk of liver allograft dysfunction upon transplantation. The predictive value of lactate is increasing with the duration of NMP. The time frame of monitoring lactate levels should be extended to at least 6 h of NMP to retrieve robust data.

OS15_6 BLOCKADE OF REGULATED CELL DEATH ABROGATES EFFECTOR T-CELL INFILTRATION AND MINIMIZES HEPATIC ISCHEMIA REPERFUSION DAMAGE

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Background: Ischemia-reperfusion injury (IRI) remains an important problem in clinical organ transplantation. We demonstrated that unconventional effector T cells, specifically γδ T cells, play a key role in mediating early hepatic IRI. Regulated cell death (RCD) such as ferroptosis is also involved. Here, we aim to show whether and, if so, how inhibition of ferroptosis in hepatic ischemia affects γδ effector T cells.
Methods: In this study, we examined early immunological events in several models of hepatic IRI. First, in genetically selected mice, (ferroptosis-resistant knockout mice, as well as permanently ferroptosis-activated mice) subjected to 90 minutes of partial warm ischemia followed by 24 hours of reperfusion. We also used a more clinically relevant mouse model in which we blocked the pathway of RCD (inhibition of ferroptosis) with drugs. Since the mouse experiments focussed strictly on ischemia reperfusion, we finally investigated ferroptosis inhibition in a large animal model of porcine liver transplantation. In all cases, hepatocellular injury was assessed by HE histology and serum transaminase measurement. Murine hepatic leukocyte subsets, such as innate effector cell populations and cytokine secretion, were characterized by immunohistochemistry, ELISA, RT-PCR, and polychromatic FACS. For porcine livers, γδ -T-cell analysis was performed by RT-PCR and immunohistochemistry.
Results: Mice whose ferroptose regulators were genetically knocked out were protected from hepatic IRI (serum transaminase levels 920U/l vs. 2540U/l in control mice; p=0.02). We found that γδ T cells were significantly decreased in these livers. Similarly, there was a significant reduction in γδ-cells in the livers of mice in which ferroptosis was blocked with drugs. We also show that regulation of γδ-T cells occurs after ferroptosis inhibition in a true porcine transplantation model.
Conclusions: Ferroptosis events appear to be the initial activator for hepatic IRI and lead to further progression through activation of γδ T cells. This can be abrogated by the use of ferroptosis inhibition, which opens new clinically relevant therapeutic options to improve liver transplantation outcomes.

OS15_7 THE USE OF A CYTOKINES ADSORPTION CARTRIDGE DURING EX-SITU HYPO AND NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION: A PILOT RANDOMIZED STUDY

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Background: Few studies correlate cytokines (IL) release during ex-situ machine perfusion (MP) to postoperative liver transplantation (LT) outcomes. We assessed safety and efficacy of an IL hemadsorption device (HA) integrated in a MP device during hypo- (D-HOPE) and normothermic MP (NMP)
Methods: We compared perfusate IL-6, IL-10 and TNF-alpha concentrations and postoperative outcomes in 4 groups of patients receiving old grafts (i.e. >80 years): those receiving a graft after D-HOPE with or without a HA device (D-HOPE-HA and D-HOPE groups respectively, n=3 each) and after NMP with or without a HA device (NMP-HA and NMP groups respectively, n=3 each). IL perfusate concentrations were evaluated at commencing perfusion and hourly thereafter together with perfusion parameters and post-operative outcomes. Liver biopsies for H&E and electron microscopy evaluation were obtained at the end of back table, MP and LT
Results: Twelve liver grafts were perfused and transplanted. Median donor ages were 85, 81, 82 and 82 and grafts perfused for 228, 231, 229, 266 minutes in D-HOPE, D-HOPE-HA, NMP and NMP-HA groups respectively. Median IL-6, IL-10 and TNF-alpha concentration at 1 and 2 hours are reported in table1. The amount of IL-6, IL-10 and TNF-alpha adsorbed between the minute 60 to 120 (60 minutes period) in the D-HOPE-HA and NMP-HA was 12960, 3960, -2160, and 372.600, 172.800 and 203.400pg respectively. There was one case of primary non-function and re-LT in the NMP group. In that case the TNF-alpha perfusate concentration at 2-hours was 1733pg/ml (the other 2 cases mean value was 23 pg/ml). No biliary or vascular complications were reported after a median follow up of 15 months
Conclusions: The use of an IL HA device during ex-situ MP is safe and feasible. It significantly and unspecifically reduces interleukines perfusate concentration, in particular during NMP. Its capacity to improve clinical outcomes should be verified in large multicentric trials

Table 1: Median interleukines levels in the groups during the first 2 hours of MP.

Perfusion	Start	1 hour	2 hours
Interleukine-6			
D-HOPE	0	7.3	9
D-HOPE-HA	0	2.2	1.1
NMP	3	62	269
NMP-HA	0.1	9.7	126
Interleukine-10			
D-HOPE	2.8	3.4	3.4
D-HOPE-HA	1.6	1.7	1.7
NMP	0.1	123	139
NMP-HA	0.1	16.7	39
TNF-alpha			
D-HOPE	0.1	0.1	0.1
D-HOPE-HA	1.5	2.9	0.9
NMP	0.1	36	124
NMP-HA	0.1	0.5	22
Data are expressed in pg/ml			

OS15_8 HYPOXIA INDUCIBLE FACTOR MODULATION DURING NORMOTHERMIC MACHINE PERFUSION (NMP) ACCELERATES REDUCTION IN HEPATIC STEATOSIS

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Background: The hypoxia-inducible factor (HIF) pathway has been implicated in hepatic steatosis with the HIF-1a isoform providing a hepatoprotective effect through enhancement of liver fat metabolism and the HIF-2a isoform conversely promoting intrahepatic lipid accumulation. The objective of this study was to selectively modulate HIF-1a during oxygenated normothermic machine perfusion (NMP) of four discarded human steatotic livers using deferoxamine (DFO, a potent activator of both HIF-1a & HIF-2a) with selective HIF-2a inhibition using PT2385 (a HIF-2a dimerisation inhibitor). The specific aims were to: (i) improve ex-situ liver function and fat metabolism and; (ii) to test this with an established NMP defatting protocol (DeFat: insulin/glucose reduction, L-carnitine, forskolin and lipid filter).
Methods: Livers were perfused using the OrganOx *metra* NMP device over 24 hours and received the following perfusion protocols: Liver 1(control): NMP alone protocol; Liver 2: NMP with DFO; Liver 3: NMP with DFO and PT2385, and; Liver 4: NMP defatting protocol (DeFat), DFO and PT2385 (Table 1). Perfusion metrics including pH, lactate and glucose metabolism were recorded during perfusion. Macrosteatosis (MaS) was quantified using Visiopharm® digital image analysis software. HIF expression was confirmed with immunoblots and downstream target activation was determined through serial perfusate EPO measurements.
Results: All livers demonstrated evidence of function during perfusion (Figure 1). However, only those subjected to HIF modulation demonstrated a DFO/PT2385 dependant response to EPO production (with HIF1a and HIF2a expression confirmed on immunoblot) (Figure1) and a reduction in MaS over 24 hours. The greatest reduction in MaS was observed in Liver 4: pre-NMP 33% and end-NMP MaS: 8% (75.8% decrease).
Conclusions: This study is the first to report pharmacological HIF modulation during oxygenated liver NMP and demonstrates accelerated defatting through using pharmacological HIF modulators (DFO and PT2385) when tested in combination with the established NMP defatting protocol (DeFat). The effect of these interventions on ischaemia-reperfusion injury remains to be elucidated.

Liver	Age	Sex	Donor Type	Surgeon's assessment	Cold ischaemia time (CIT)	NMP duration	Intervention during NMP	%MaS Start	%MaS End
1	67	M	DCD	Normal Capsular damage	20h 24 mins	24h	NMP alone (control)	7%	8%
2	58	F	DCD	Moderate steatosis	10h 56 mins	24h	DFO (delivered at 4h perfusion)	23%	11%
3	57	M	DCD	Mild steatosis Capsular damage	14h 2mins	24h	DFO (delivered at 4h perfusion) & PT2385 (delivered at 16h perfusion)	6%	3%
4	56	F	DBD	Moderate steatosis	20h 15 mins	24h	DFO, PT2385 & NMP defatting protocol, DeFat (delivered at start of perfusion, 0h): • Insulin/glucose reduction • L-carnitine • Forskolin (NKH477) • Lipid filter	33%	8%

Table 1: Donor demographics, graft characteristics (including pre-NMP %MaS and end-NMP %MaS) and perfusion protocol.

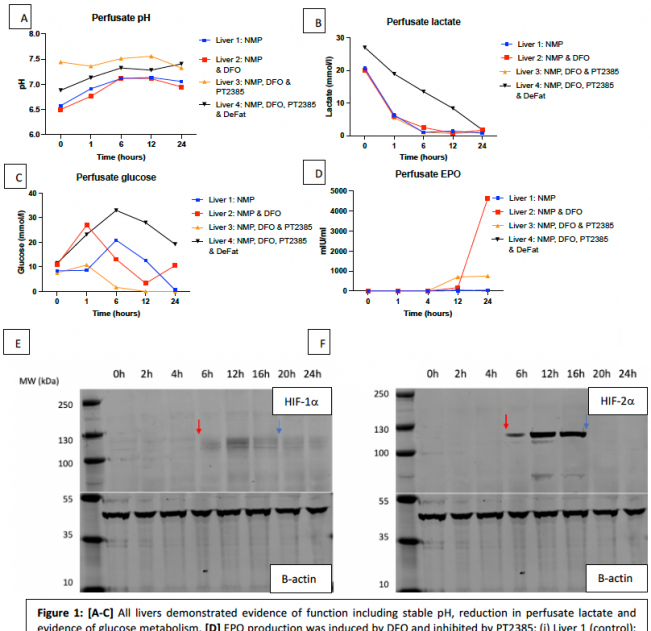

Figure 1: [A-C] All livers demonstrated evidence of function including stable pH, reduction in perfusate lactate and evidence of glucose metabolism. **[D]** EPO production was induced by DFO and inhibited by PT2385: (i) Liver 1 (control): NMP alone protocol; (ii) Liver 2: NMP with DFO (delivered at 4h); (iii) Liver 3: NMP with DFO (delivered at 4h) and PT2385 (PT2385 delivered at 16h), and; (iv) Liver 4: NMP defatting protocol (DeFat), DFO and PT2385 (all delivered at the start of perfusion, 0h). **[E, HIF-1α]** Liver 3 with delivery of DFO & PT2385 over 24h. 0h signifies end of static cold storage (before liver is placed on machine). Between 0h-4h the liver is perfused with pRBC in normothermic oxygenated conditions. After 4h biopsy (red arrow), DFO is administered. After administration of DFO, HIF-1α signal (100-130kDa) becomes apparent for remaining duration of perfusion (up to 24h) despite PT2385 being administered after 16h biopsy (blue arrow). **[F, HIF-2α]** Following delivery of PT2385 after the 16h biopsy (blue arrow), the HIF-2α signal disappears for the remaining duration of perfusion. This is also correlates with a reduction in perfusate EPO [Liver 3, 1D].

Organ preservation and ischemia reperfusion

OS15_9 PRIMARY CILIA AS A TARGETABLE NODE BETWEEN BILIARY INJURY, SENESCENCE AND REGENERATION

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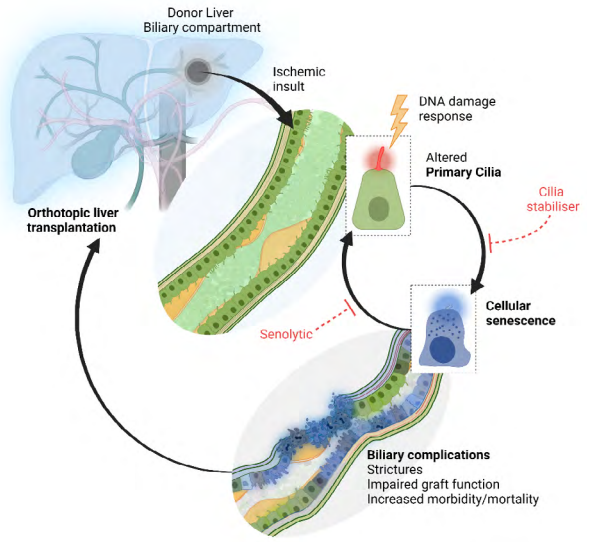
Background: Biliary complications are a major cause of morbidity and mortality in liver transplantation, developing in up to 25% of liver transplant recipients, frequently requiring additional surgical procedures, re-transplantation or, in the absence of a suitable regraft, death. Here, we investigate the role of the primary cilium, a highly specialised sensory organelle, in biliary injury leading to post-transplant biliary complications.
Methods: Human biopsies were used to study the structure and function of primary cilia in liver transplant recipients that develop biliary complications (*N*=7) in comparison with recipients without biliary complications (*N*=12). To study the biological effects of primary cilia during transplantation, we generated murine models that recapitulate liver procurement and cold storage, as well as the *K19CreER^{T} Kif3a$^{flox/flox}$* mouse model to conditionally eliminate primary cilia in biliary epithelial cells. To explore the molecular mechanisms responsible for the observed phenotypes we used *in vitro* models of ischemia, cellular senescence and primary cilia ablation. Finally, we used pharmacological and genetic approaches to target cellular senescence and primary cilia, both in mouse models and discarded human donor livers.
Results: Prolonged ischemic periods before transplantation result in ciliary shortening and cellular senescence, an irreversible cell cycle arrest that blocks regeneration. Our results indicate that primary cilia damage results in biliary injury and a loss of regenerative potential. We found that the initiation of senescence negatively impacts primary cilia structure, establishing a negative feedback loop that further impairs regeneration. Finally, we explore how targeted interventions for cellular senescence and/or the stabilisation of the primary cilia, improve biliary regeneration following ischemic injury.
Conclusions: Primary cilia play an essential role in biliary regeneration and we demonstrate that senolytics and cilia-stabilising treatments provide a potential therapeutic opportunity to reduce the rate of biliary complications and improve clinical outcomes in liver transplantation.



Organ donation: clinical perspectives

OS16_1 PREDICTIVE RADIOLOGIC SIGNS TO EVOLVE TO BRAIN DEATH OR CIRCULATORY DEATH

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Background: Donors after brain death (DBD) are the main source of organ transplantation. Recently there has been an increase of donors after circulatory death (DCD). It is known that most patients who develop brain death (BD) do so during the first 72 hours, but to identify these patients on admission is difficult, due to the lack of predictive elements. The objective of this study is to identify those radiologic signs associated with BD and to find a cut-off value for the brain midline deviation (MLD) as a predictive factor to evolve to BD.
Methods: Retrospective and observational study of patients admitted to a polyvalent intensive care unit (ICU) of a tertiary hospital, between the years 2015-2022, assessed as possible donors (PD), due to severe neurological damage. All of them underwent a head CT at the time of admission, registering 13 radiologic signs and collecting the main causes of BD and CD.
Results: A total of 523 patients were assessed as PD, 67.12% were men, with a mean age of 61.2 +/- 18.8 years. 314 were real donors, 203 DBD (64.65%) and 111 DCD (35.35%). The causes of BD and CD (*Figure 1*) and 13 radiologic signs were recorded, as well as the statistical relationship between the findings and the type of donor (*Table 1*). The MLD cut-off point was 9.5mm, with a sensitivity of 78.57%, a specificity of 51.51%, a positive predictive value of 82.8%, and a negative predictive value of 44.73%.
Conclusions: According to our study, the radiologic signs that can anticipate a BD evolution are: presence of cerebral herniation, MLD, ABC and the presence of SAH or edema. Other associated signs are the presence of UH, rebleeding, SDH and contusions. A MLD > 9.5mm is highly suggestive of a PD developing to BD.

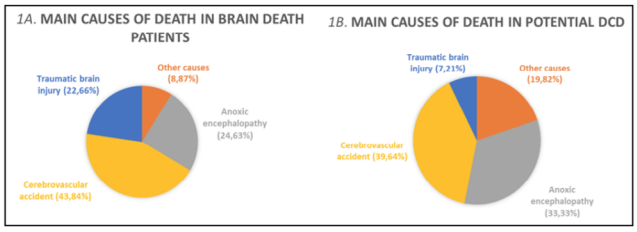

***Figure 1*. (A).** Main causes of death in BD. **(B).** Main causes of death in potencial DCD..

N = 314	DBD	DCD	OR (CI 95%)	p value
HYDROCEPHALUS	42	18	1,34 (0,73-2,47)	> 0,05
BLEEDING	14	18	0,38 (0,18-0,80)	< 0,05
SPOT SIGN	3	2	0,81 (0,13-4,96)	> 0,05
HERNIATION	107	25	3,83 (2,27-6,47)	**< 0,001**
UNCAL HERNIATION (UH)	58	16	2,37 (1,28-4,37)	**< 0,01**
INTRAPARENCHYMAL HEMATOMA (IPH)	71	33	1,27 (0,77-2,09)	> 0,05
MIDLINE DEVIATION (MLD)	98	33	2,20 (1,34-3,6)	**< 0,001**
ABSENT OF BASAL CISTERNI (ABC)	109	37	2,32 (1,43-3,75)	**< 0,001**
SUBDURAL HEMATOMA (SDH)	44	11	2,41 (1,24-5,09)	**< 0,01**
SUBARACHNOID HEMORRHAGE (SAH)	82	18	3,5 (1,96-6,23)	**< 0,001**
CONTUSIONS	26	3	5,2 (1,56-5,28)	**< 0,01**
ISCHEMIA	42	40	0,4 (0,27-0,77)	**< 0,01**
EDEMA	118	41	2,37 (1,47-3,81)	**< 0,001**

***Table 1*.** Number of patients, in BD and CD, who presented each of the 13 reported findings.

OS16_2 FACTORS DETERMINING CONSENT FOR ORGAN DONATION AFTER BRAIN DEATH IN FRANCE

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Background: Opposition to organ donation remains the principal factor in the lack of organ procurement from potential brain-dead donors (DBD) in France. The underlying causes and organizational determiners of this opposition are not well understood due to a lack of research. In order to improve donation rates, this study seeks to address it by examining factors that contribute to organ donation opposition. Our aim was to understand clinical and organizational factors associated with opposition to organ donation in France.
Methods: All potential DBD entered into the French national registry CRISTAL between 2018 and 2019 were included. Connections between donor sociodemographic and clinical data, hospital care quality and procurement center characteristics and refusal to donate were assessed using multivariable multilevel logistic regression models with procurement hospitals as random effects.
Results: We analyzed 6734 DBD. Opposition occurred in 30% of cases. Independent risk factors associated with a higher rate of opposition were age (reference > 65, 50-64 (OR=1.37; 1.19-1.58), 18-49 (OR=1.57; 1.35-1.83), 0-17 (OR=2.03; 1.45-2.84) and blood type B (OR=1.35 ; 1.11-1.64) probably linked with lower socioeconomic level and origins as well as a longer hospital stay prior to brain death (OR=1.14 per 10 days; 1.01-1.28). Factors associated with lower rate of opposition were a suicide context (OR=0.71; 0.55-0.91), being in an hospital with higher satisfaction regarding medical and surgical care as reported by systematic certification visits of all hospitals in France (OR 0.95; 0.91-1.00), being in an hospital in which the process of organ donation was audited (2-3 days audits performed by professionals from the national agency) (OR=0.77; 0.59-1.00), being in an hospital with a higher ratio of paramedical donor coordinators (cut-off > 8 donor coordinators per 100 potential donors; OR=0.72; 0.58-0.90).
Conclusions: On a recent set of all DBD in France, we found several factors correlated with higher or lower levels of opposition to organ donation. Some factors are well known including lower age, socio-economic level and suicide but other offer scientific evidence of the advantages of auditing the hospital organ donation process and increased staffing of donor coordination teams.

OS16_3 MODULATORY EFFECT OF ALTEPLASE AND METHYLPREDNISOLONE ASSOCIATION ON BRAIN DEATH DONOR

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Background: Brain-death (BD) patients are a common source of transplant organs. Studies describe microcirculatory compromise and systemic inflammatory processes related to BD, which are related to micro-aggregates formation and platelet aggregation reducing blood flow. In this sense, this study aimed to investigate the effect of thrombolytic (alteplase- rTPA) and corticoid therapy (methylprednisolone) after BD in male rats.
Methods: Wistar rats were submitted to BD by the rapid inflation of an intracranial catheter, and maintained for 6 h. After 3 h, rats were treated with rTPA (rTPA - 3 mg/kg, i.v for 30 minutes) associated or not with methylprednisolone (rTPA+P - 20 mg/kg, i.v for 30 minutes) Sham-operated (Sham) rats were used as controls. After the experimental period blood samples were collected for platelet aggregation analysis and serum quantification of inflammatory mediators (ELISA).
Results: In BD group we observed increased platelet aggregation when compared to Sham, and both treatments protocols reduced the aggregation (Sham: 17.7±4.3; ME: 49.7±11.9; rTPA: 20.2±3.6; rTPA+P: 27.6±2.5; result presented in percentage; P= 0.0156). Platelet count did not differ among the groups (P= 0.3521). Besides, BD increased inflammatory mediators, such as IL-6 and TNF-α concentrations compared to Sham, only rTPA+P group decreased the IL-6 (Sham: 2688±957; ME: 5334±253; rTPA: 4085±773; rTPA+P: 1400±588; pg/mL P= 0.0018) and TNF-α (Sham: 0.592±0.571; ME: 1.583±0.588; rTPA: 1.243±0.524; rTPA+P: 0.091±0.060; pg/mL P= 0.0682) concentration compared to BD. CINC-1 (Sham: 42.1±9.6; ME: 36.5±7.6; rTPA: 174±36.7; rTPA+P: 165.7±46.7; pg/mL P= 0.0023) and NOx (Sham: 60.8±25.5; ME: 34.1±8.7; rTPA: 222.3±115.8; rTPA+P: 54.4±14.2; pg/mL P= 0.3985) concentrations were increased in the rTPA group compared to BD. The rTPA+P group did not modify CINC-1 release, however NOx concentration presented lower values.
Conclusions: This study demonstrated the effectiveness of a thrombolytic treatment to decrease platelet aggregation in rats submitted to BD. At the same time, rTPA increased the inflammatory response in which the association with corticoid therapy decrease these parameters. Thus, the association between thrombotic and corticoid therapy can be a good therapeutic option for BD donor organs.

OS16_4 ACTIVATION OF THE COMPLEMENT SYSTEM EARLY ON DURING BRAIN DEATH MANAGEMENT

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Background: Brain death (BD) results in an inflammatory environment, including activation of the complement system. Currently, the clinical impact of prolonged duration of BD on the donor organ is still unknown. Here, we investigated how different BD durations impact complement activation levels both systemically and locally within renal tissue.
Methods: The QUOD biobank was used to obtain EDTA-plasma samples and kidney biopsies from BD donors. Samples were routinely taken at several time points during BD management. Samples were grouped based on short (<15h), average (18-22h) or long (>25h) BD duration. Furthermore, groups were divided based on the presence of delayed graft function (DGF) (6 groups, n=20 per group for plasma, n=10 per group for biopsies).
Results: ELISAs were used for specific quantification of C4d, C3c and C5b-9 in plasma samples. All three complement activation factors showed high levels at the start of donor management (DB2). C4d levels decreased over time, and were significantly lower in samples taken just before organ retrieval (DB4) compared with DB2 (mean 6122 ng/mL vs. 3601 ng/mL, p=<0.001). C3c and C5b-9 also showed a similar trend towards lower complement activation levels at the end of donor management (DB3) and at DB4 compared with DB2. Preliminary analysis between different BD duration groups did not show a difference in C4d, C3c and C5b-9 levels. C4d, C3c and C5b-9 levels, at any point during BD management, did not appear to influence the development of DGF. Biopsies (collected at the time of organ retrieval) have been stained for C4d, C3d and C5b-9 and showed clear signs of local complement activation at different compartments, including glomerular, tubular and peritubular regions. The quantification of different staining patterns is currently under investigation.
Conclusions: In conclusion, the complement system is activated in BD donors already early on during the management period, and is decreasing over time. Prolonged duration of BD does not appear to be associated with increased levels of C4d, C3c and C5b-9. Future studies on administering complement inhibitors to BD donors could benefit from starting therapy early on during management period.

OS16_5 ANALYSIS OF RISK FACTORS FOR KIDNEY TRANSPLANTATION AFTER CONTROLLED CIRCULATORY DEATH AND SYSTEMATIC USE OF NORMOTHERMIC REGIONAL PERFUSION

Emilie Savoye[1], Laurent Martin-Lefèvre[2], Jacques Dantal[3], Didier Dorez[4], Francois Gaudez[5], Bruno Riou[6], Sarah Drouin[6], Guillaume Strecker[7], Antoine Thierry[8], Camille Legeai[1], Régis Bronchard[1], François Kerbaul[1], Corinne Antoine*[1]

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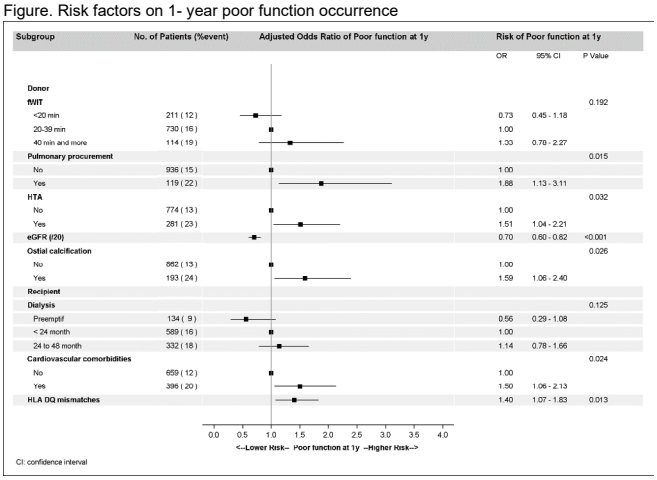
Background: The French controlled circulatory death (cDCD) program is characterized by normothermic regional perfusion (NRP), constrained asystole times according to donor age, hypothermic machine perfusion, and short cold ischemia time (CIT). Compared to the outcome of matched DBD kidney transplants, the outcome of cDCD ones was found to be better, especially due to NRP use.
Methods: This analysis of 1071 adult primary kidney transplants (2015-2020) aims to support these findings and identify risk factors for graft failure. The average of donor age was 51 years, of functional warm ischemia time (fWIT) 27 min, of asystolic phase was 21 min and of CIT 10 hours. Risk factor analysis of primary non-function (PNF, n=32), of delayed graft function (DGF, n=136 after exclusion of 166 preemptive and PNF) and of graft failure (estimated glomerular filtration rate (eGFR) < 30ml/min or graft loss at 1 year, n=163 after exclusion of 16 missing) were performed by multivariable logistic regression.
Results: Donor HTA (OR=2.37, p=0.032), admission for ischemic vascular stroke (OR=4.95, p=0.014) and HLA DR mismatches (OR=2.24, p=0.004) are independent risk factors for PNF. fWIT>40 min (OR=3.11, p<0.001), dialysis >2 years (OR=1.83, p=0.003), recipient BMI >30 (OR=2.23, p<0.001), recipient diabetes (OR=2.25, p=0.001) and CIT>10h (OR=1.59, p=0.02) were independent risk factors for DGF. Donor HTA (OR=1.51, p=0.032), pulmonary procurement (OR=1.88, p=0.015), ostial calcification (OR=1.59, p=0.026), recipient comorbidities (OR=1.50, p=0.024) and HLA DR mismatches (OR=1.40, p=0.013) were independent risk factors of graft failure at 1 year. Donor eGFR (continuous form / 20) was a protected factor for DGF and graft failure at 1 year (respectively OR=0.75 and 0.70 p=0.001 and <0.001). After adjustment restricted to recipient and graft factors, the risk of PNF, DGF and graft failure increases with donor age up to 65 years and then remains stable.
Conclusions: Overall, results of renal transplants from cDCD are excellent but impacted by lung procurement (being analysed), poor HLA DR matching and warm ischemia time according to the donor age validating a posteriori the shorter delays required after 65 years.

Figure. Risk factors on 1- year poor function occurrence



OS16_6 'SPREADING' AGING WITH THE TRANSPLANTATION OF OLD ORGANS: AN EXPERIMENTAL REALITY

Maximilian Roesel*[1], Andreas Schroeter[1], Jasper Iske[1], Tomohisa Matsunaga[1], Tamara Tchokina[2], Yao Xiao[1], Friederike Martin[1], Utkarshi Tripathi[3], James Kirkland[2;3], Hao Zhou[1], Stefan G. Tullius[1]

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Background: Old donor organs represent an underutilized potential to meet the demand for transplantation (Tx). During aging, senescent cells that secrete inflammatory products termed the senescence-associated secretory phenotype (SASP) accumulate in older organs. We hypothesized that the engraftment of old organs induces senescence in younger recipients, promoting age-related pathologies.
Methods: Heart transplants from either young (3 months/mths) or old (18-21 mths) C57Bl/6 donor mice or p16Ink4a-GFP reporter mice were transplanted into young or middle-aged C57Bl/6 recipients (3 & 12 mths, resp.). Recipient tissues were collected by 30 days after Tx; the accumulation of senescent cells and SASP derived molecules (mt-DNA) was assessed by IHC, RNA in situ hybridization and qPCR. Physical and neurobehavioral testing was performed sequentially up to 5 mths after Tx. Assessing mechanisms, senolytics (Dasitinib & Quercetin) were applied to old donor animals prior to organ procurement.
Results: Recipients that had received old hearts showed augmented frequencies of senescent cells in draining lymph nodes, livers, and muscles (3.1-fold, 20.3-fold, 1.8-fold increase, day 30 after Tx; p≤0.01, p≤0.0001, & p≤0.05) in addition to augmented systemic mt-DNA levels 24 hours after Tx (p≤0.05) when compared to recipients that had received young grafts. Strikingly, transplanting old organs led to compromised physical capacities (RotaRod & minimum grip strength; p≤0.01 & p≤0.0001 by 30 days) and significant impairments in neurobehavioral tests (locomotor test, Novelty Y-maze by 1 & 4 mths after Tx, p≤0.05 for each test). Treating old donors with senolytics prior to organ procurement resulted into significantly reduced mt-DNA levels (p≤0.05) and improved physical fitness (RotaRod by 4 & 6 weeks after Tx, p≤0.01 & p≤0.05) in young recipients. Thus, depleting senescent cells in donor organs prevented the 'transfer/spread' of senescence through a diminished accumulation of mt-DNA and SASP factors.
Conclusions: We show that transplanting old organs induces not only molecular and cellular changes characteristic of accelerated aging, but also leads to both physical and cognitive impairment. Treating organs prior to transplantation with senolytics was effective in preventing the transfer of senescence.

OS16_7 LONG-TERM MORTALITY OF LIVING KIDNEY DONORS: A NATION-BASED COHORT STUDY

Jongman Kim*[1], Jae Heon Kim[2], Jin Yong Choi[1;3], Hyun Jung Kim[4], Jae-Won Joh[1]

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Background: Morbidity and mortality issues in living kidney donors (LKDs) after donor nephrectomy are still debated. The purpose of the present study is to evaluate the long-term risks to LKDs compared with multiple control cohorts undergoing overall health assessment.
Methods: The cohort study included 14,484 LKDs in South Korea, who donated a kidney between 2002 and 2018 in the Korean Network for Organ Sharing. Three control groups comprising a total of 144,840 subjects were selected from Korean National Health Insurance Services.
Results: In the LKD cohort, 187 deaths (135 males and 52 females) occurred during the study period. When compared with Control I, the mortality rate in LKDs was 1.60 (95% CI: 1.39-1.85). The MRR and adjusted HR in the LKD group were 2.01 (95% CI: 1.71-2.36) and 1.98 (95% CI: 1.64-2.38), respectively. With respect to Control II and III, there were no statistical difference in mortality rate, MRR, and adjusted HR. The crude HR demonstrated an elevated risk for HD (2.64; 95% CI: 1.45-4.80; p < 0.001), ESRD (2.53; 95% CI: 1.39-4.60; p < 0.001), and CKD (4.99; 95% CI: 1.54-16.17; p = 0.01), compared with Control I. Among cause of death, event of undetermined intent, self-harm, all external cause of death, circulatory disease, abnormal clinical finding, and all internal cause of death showed higher risk in LKDs compared with health control group (HR=5.22 (95%CI: 1.03 – 26.34), 2.66 (95%CI: 1.66 – 4.18), 2.61 (95%CI: 1.86 – 3.67), 2.53 (95%CI: 1.16 – 4.1), 2.35 (95%CI: 1.1 – 5.66), and 1.69 (95%CI: 1.35 – 2.11), respectively).
Conclusions: Long-term mortality of LKDs is notably increased when compared with healthy control subjects. LKDs had a higher risk of psychosocial mortality and classical chronic disease including circulatory disease than healthy control.

FULL ORALS

Organ donation: clinical perspectives

OS16_8 EXCELLENCE IN ORGAN UTILISATION – A QUANTITATIVE AND QUALITATIVE EVIDENCE BASE FOR A NEW APPROACHES IN THE UK

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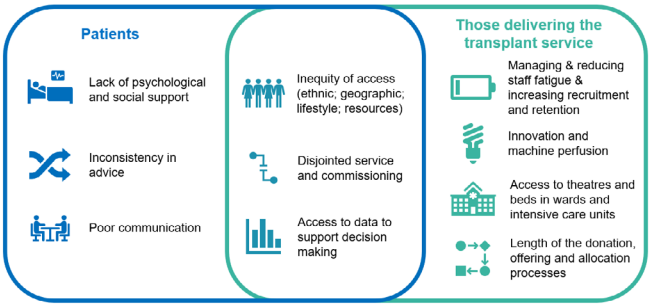
Background: Organ utilisation has not kept pace with the rate of improvements in donation in the UK. The UK compares poorly against international heart, lung and liver transplant activity. An Organ Utilisation Group (OUG) was established by the Department of Health and Social Care in England, to develop new approaches to maximise the potential for the number of organs transplanted for adult and paediatric patients, from living and deceased donors.
Methods: The OUG membership included: patients; lay members; multi-disciplinary transplant team representatives; hospital management; commissioning. Subgroups were convened for: commissioning; data; workforce; standards.
The OUG consulted widely with UK and international stakeholders to identify barriers along the care pathway and opportunities for improvement, with: 345 responses to online surveys; 27 patients participated in focus groups; 58 delegates attended workshops; 10 site visits to transplant and referring centres; 6 international meetings; a literature review. Data analyses identified fresh areas for consideration – e.g. Table 1 demonstrates the impact of a lack of resources on utilisation.
Results: The evidence collated by the OUG identified key themes as demonstrated in Figure 1.The OUG report builds on the comprehensive evidence base and includes 12 recommendations for service improvement, with supporting actions, against 6 themes: **1.** Placing the patient at the heart of service. **2.** An operational infrastructure that maximises transplant potential. **3.** Creating a sustainable workforce that is fit for the future. **4.** Data provision that informs decisions and drives improvements. **5.** Driving and supporting innovation. **6.** Delivering improvements through new strategic and commissioning frameworks
Conclusions: The OUG recommendations aim to reduce inequity of access, make the best use of available resources and drive innovation. Implementation will increase transplant activity, through increased organ utilisation, improve patient experience, outcomes and empowerment and support the transplant community.

Table 1: Number of deceased donor organ offer declines for lack of resource within the transplant centre, 1 April 2018 – 31 March 2019. Source: NHS Blood and Transplant

Organ type	Total declines	Declines due to lack of resource (% of all declines)
Kidney	7,241	72 (1)
Pancreas	4,497	260 (6)
Liver	9,006	192 (2)
Intestinal	262	4 (2)
Heart	3,051	40 (1)
Lung	2,967	61 (2)
Totals	**27,024**	**629 (2)**

Figure 1: Summary of key challenges to be addressed, raised by stakeholders



AI & Digital Health: from donation to the outcome

OS17_1 INCREASING ORGAN DONORS AND TRANSPLANTS VIA INTEROPERABILITY

John Piano[*1]

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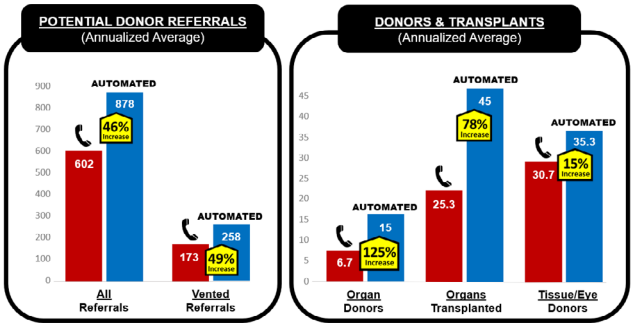
Background: In the United States, national regulatory organizations require that hospitals refer all potential organ and tissue donors to an Organ Procurement Organization (OPO). To replace the current time-consuming and error-prone telephonic referral process, secure, direct, electronic donor referral interfaces are being launched across the country.
Methods: The secure technical interface ("iReferral") directly connects the OPO and Hospital systems and is accompanied by seamless donor referral triggers within the Hospital Electronic Medical Record (EMR). These carefully tuned triggers automatically prompt delivery of electronic donor referrals from the Hospital to the OPO, greatly reducing the need for decision-making and donation knowledge by the hospital staff. An additional trigger option allows staff to "one click" electronically refer for cases such as end-of-life discussions or cardiac death. Immediately the OPO receives a new referral auto populated with actionable patient information and real-time notifications alert OPO staff. The interface automatically returns the associated OPO referral ID number to the patient's EMR to provide confirmation to the referring clinician.
Results: This interface is currently implemented at 56 hospitals across the country. At a pilot hospital, annualized data after the first year of implementation demonstrated a 49% increase in vented referrals and 78% increase in organs transplanted. At a large hospital network, nearly 9,000 referrals have been sent electronically since launch in February 2021, saving an estimated 3,000 nursing hours.
Conclusions: This interface has increased the number and timeliness of referrals (and thus transplantable organs) and reduced Hospital and OPO resource costs. There is unlimited potential for streamlining the referral process through donor referral interoperability solutions, ultimately leading to more donors and transplantations.

Image 1: Pilot hospital results with annualized data from January 2019-April 202 compared to the time period prior to interface launch.



OS17_2 THERMODYNAMIC CHARACTERIZATION OF ORGANS PRESERVED ON ICE – INVESTIGATING THE ASSUMPTION THAT ICE IS 4°C

Pratik Patel[*1], **Daniel Klauer[2], Ben Bulka[2], Lucas Churchill[2]**

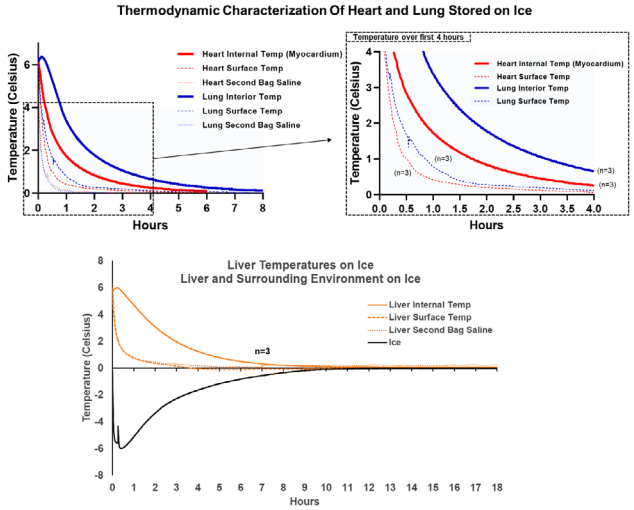
[1]Paragonix Technologies, Cambridge, United States, [1]Paragonix Technologies, Cambridge, United States

Background: Clinical literature and conventional knowledge assumes organs stored on ice are held at 4°C. However, this is not supported with empirical data as the typical environment of organ storage is not measured or controlled, increasing risk of freezing injury. As a community, it is critical we better understand the conditions organs are being preserved and transported under as programs are evaluating the clinical and logistical trade-offs of various perfusion strategies.
Methods: Porcine hearts (n=3), lungs (n=3) and livers (n=3) were packaged within 3 bags (3M) with and placed on ice in a cooler (Coleman). Hearts were packaged with 1L HTK in the inner bag, 1L saline in the second bag. Lungs were packaged with 2L Perfadex in the inner bag, 1L saline in the second bag. Livers were packaged in 2L HTK, 2L saline in the second bag. The third bag did not have any solution. Temperature probes were inserted into the left ventricle myocardium, into the left inferior lung lobe, into one of the liver lobes, as well in the preservation solution in contact with the organ, and in the saline solution. Measurements (Onset) were recorded every 30 seconds up to 6 hours (hrs) for hearts, 12 hrs for lungs and 15 hrs for livers.
Results: A total of 24,858 temperature measurements were recorded and analysed (6,489 heart, 12,969 lung, 5,400 liver). Average cardiac myocardium temperatures evolved from an initial 6.2°C to 1.7°C (1 hr) and 0.3°C (4 hrs), while average external epicardium temperatures evolved from 6.1°C to 0.4°C

(1 hr) and 0.1°C (4 hrs). Average interior lung lobe temperature evolved from 6.1°C to 3.4°C (1 hr) and 0.7°C (4 hrs), while average lung surface temperature evolved from 6.7°C to 0.8°C (1 hr) and 0.1°C (4 hrs). Average interior liver temperature evolved from 5.7°C to 1.2°C (4 hrs) and 0.2°C (8 hrs), while average liver surface temperatures evolved from 5.9°C to 0.8°C (1 hr) to -0.1°C (4 hrs). See Figure.

Conclusions: Donor organs packaged on ice undergo rapid drops in temperature, approaching freezing in an uncontrolled manner. Preservation solutions provide insufficient levels of protection against freezing temperatures. As this decline in organ temperature occurs within clinically routine cold ischemic times, risk of freezing injury should be considered when procuring and transporting organs for transplant.

Figure:



OS17_3 NEXT GENERATION SEQUENCING: FROM BANFF SCORE MOLECULAR SIGNATURES AND CLASSIFIERS TO HISTOLOGICAL ARCHETYPES OF KIDNEY BIOPSIES

Esteban Cortes Garcia[*1], **Olivier Aubert[1], Maud Racape[1;2], Pierre de la Grange[3], Clément Coudereau[1], Jessy Dagobert[1], Franck Letourneur[1;2], Carmen Lefaucheur[1;2], Alexandre Loupy[1;2]**

[1]Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, [2]EU-TRAIN consortium, Paris, France, [3]GenoSplice, Paris, France

Background: To improve risk stratification in kidney transplantation, molecular diagnostic tools are increasingly investigated. Nonetheless, previously published studies focused on sequencing technologies and gene panels with suboptimal consideration of the transcriptome. The EU-TRAIN consortium was built to discover new predictive intra-graft biomarkers for histology parameters.
Methods: EU-TRAIN (NCT03652402) is a prospective multicentric study including unselected kidney transplant cohorts from 11 centres from 4 countries (France, Spain, Germany, Switzerland). We performed a bulk RNA sequencing on 770 kidney biopsies (n=540 kidney recipients) collected between 2018 and 2021. For all Banff scores, differentially-expressed genes (DEGs) were derived, then reduced using an ElasticNet feature selection and we trained four machine learning classifiers (Naïve Bayes, Extreme Gradient Boosting, Linear Support Vector Machine (LSVM) and K-Nearest Neighbours) using cross-validation. Models' performances were compared on a test set (30% of the total samples). Finally, we trained an archetypal analysis based on the samples' predicted Banff score probabilities from the best classifier.
Results: The ElasticNet feature selection lowered the number of DEGs to be included from a range of [859;10,839] to [52;867]. The best discriminations were obtained with the LSVM with a precision-recall area under the curve in the interval [0.708;0.980] (t/ptc). Excluding cv and ah, all models calibrated properly (Hosmer and Lemeshow goodness of fit p-value > 0.05). The gene expression-based predicted Banff score probabilities were used for an archetypal analysis which resulted in 8 profiles: acute and chronic antibody-mediated rejection (DSA, C4d, g, ptc and cg lesions), acute T-cell mediated rejection (i, t and ti lesions), chronic TCMR (i, t, ti, ci, ct and i-IFTA lesions), mixed rejection (g, ptc, i, t and ti lesions), vascular injuries (cv and ah), fibrosis (ci and ct lesions, older donors with history of hypertension), minimal fibrotic change (ci and ct) and minor changes (no lesions).
Conclusions: From new transcripts, we managed to develop gene expression-based models that predict accurately the Banff score lesions and 8 clinically-meaningful histological profiles were identified among these predictions.

OS17_4 DEVELOPMENT, APPLICATION, AND VALIDATION OF A HISTOLOGICAL CLASSIFICATION AUTOMATION SYSTEM FOR KIDNEY ALLOGRAFT PRECISION DIAGNOSTICS

Valentin Goutaudier[*1], **Daniel Yoo[1], Gillian Divard[1], Juliette Gueguen[1], Olivier Aubert[1], Marc Raynaud[1], Zeynep Demir[1], Julien Hogan[1], Ktd-Innov Investigators[2], Eu-Train Investigators[3], Mark Haas[4], Carmen Lefaucheur[1], Marion Rabant[1], Alexandre Loupy[1]**

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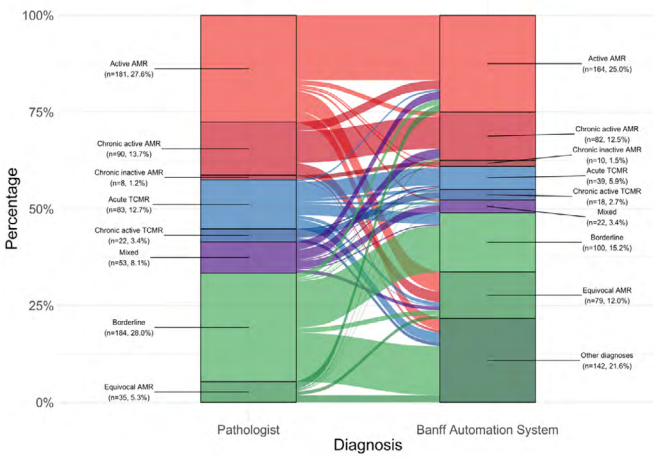
Background: For three decades, the Banff International classification has been the gold standard for kidney allograft rejection diagnosis but has become complex over time, leading to misclassifications with therapeutic consequences. We aimed to develop an automated rejection classification system, and demonstrate its clinical impact by validating its ability to improve rejection diagnoses and risk stratification of allograft outcomes.
Methods: We built an interdisciplinary consortium to translate all Banff rules until the latest published in 2019 into an algorithm covering every possible kidney allograft diagnostic scenario, embedded in an online application which automatically assign diagnoses. We tested the Banff Automation System's ability to reclassify and stratify the risk of rejection diagnoses on 4,409 kidney transplant biopsies from 3,054 adult and pediatric patients, from multicenter and large clinical trials, totaling 20 centers in Europe and North America. ClinicalTrials.gov, NCT05306795.
Results: We devised a system that generates automatic diagnostic reports with a decision tree. In the adult kidney transplant biopsies, the system reclassified 83 of 279 (29.75%) antibody-mediated rejection (AMR) cases and 57 of 105 (54.29%) T-cell mediated rejection (TCMR) cases, while 237 of 3,239 (7.32%) biopsies with non-rejection-related diagnoses were reclassified as rejection (Figure 1). In the pediatric kidney transplant biopsies, the rejection reclassifications rates were 8 of 26 (30.77%) and 12 of 39 (30.77%) for AMR and TCMR, respectively. Finally, we found that the non-rejection diagnoses according to the pathologists which were reclassified as rejections by the Banff Automation System had similar outcomes as those of confirmed rejection cases.
Conclusions: We built the first comprehensive and fully integrated histological Banff Automation System and confirmed its ability to reclassify and stratify the risk of kidney transplant rejection. This decision support system might improve reproducibility, thereby reducing misclassifications; standardizing histology-based endpoints in clinical trials and posttransplant diagnostics; and optimizing therapeutic management.

Figure 1. Banff Automation System's reclassification of rejection-related diagnoses.



OS17_5 DEVELOPMENT, VALIDATION, AND AUTOMATED REPORTING OF GENE EXPRESSION-BASED DIAGNOSIS OF RENAL ALLOGRAFT REJECTION BASED ON THE B-HOT GENE PANEL

Dina Zielinski[1], Valentin Goutaudier[1], Marta Sablik[1], Gillian Divard[1], Juliette Gueguen[1], Jessy Dagobert[1], Fariza Mezine[1], Anais Certain[1], Blaise Robin[1], Marion Rabant[1], Jean-Paul Duong van Huyen[1], Aurélie Sannier[1], Mehdi Maanaoui[2], Oriol Bestard[3], Kevin Louis[1], Ivy Rosales[4], Neal Smith[4], Candice Roufosse[5], Edmund Huang[6], Benjamin Adam[7], Michael Mengel[7], Robert Colvin[4], Carmen Lefaucheur[1], Olivier Aubert*[1], Alexandre Loupy[1]

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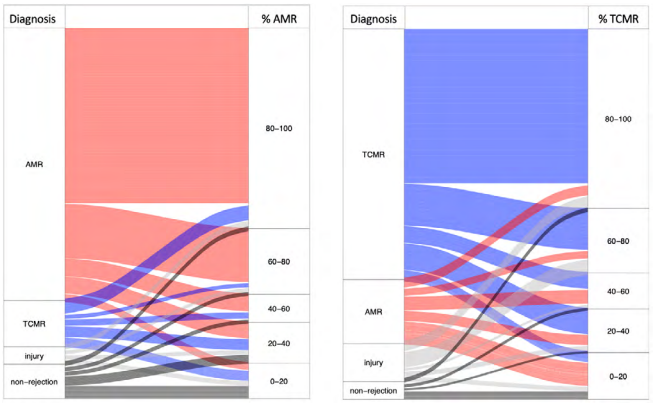
Purpose: Gene expression profiling of allograft biopsies is an unmet need in kidney transplant patient care with demonstrated potential to improve rejection diagnosis and guide therapeutic decision making. Despite several gene sets being described and validated over the past few decades, molecular assessment of biopsies has yet to be integrated into clinical practice.
Methods: The Banff Human Organ Transplant (B-HOT) gene panel has the advantage of being performed on the same tissue sample as used for histology, allowing histo-molecular data integration. We sequenced 664 biopsies from a well-phenotyped multicenter renal transplant cohort consisting of more than 180 variables, including recipient and donor baseline characteristics, histology, clinical data, infection status, treatments, and graft characteristics. Predictive models were developed based on B-HOT expression data for AMR (antibody-mediated rejection) and TCMR (T-cell mediated rejection). Gene selection was performed for each outcome using regularized logistic regression. Models were developed using an ensemble approach, with the median probability of the base models assigned to each biopsy.
Results: Model performance was assessed in one internal and two external validation cohorts (respective PR-AUC for AMR=0.82, 0.86, 0.9 and TCMR=0.7, 0.82, 0.78). Discrepancies between histology and expression-based probabilities were primarily challenging cases for which molecular analysis could be useful, including histology below diagnostic thresholds, non-specific lesions, BKV nephropathy, AMR without C4d or DSA, and post-treatment control biopsies. To facilitate clinical validation, we developed *HistoMx*, a fully automated report of gene expression based precision diagnosis.
Conclusions: Gene expression profiling can address the complexity and uncertainty in histology-based assessment of allograft injury and rejection. Providing probabilistic scores can increase diagnostic accuracy by more precisely capturing disease activity, stage, and degree of injury, detect disease before it is visible from histology, and help guide therapeutic intervention for challenging cases.



Flow diagrams of histology based diagnosis and gene expression based predicted probability for AMR and TCMR for each biopsy in all validation cohorts (n=397).

OS17_6 EXTENDED VALIDATION OF THE IBOX IN REAL LIFE SETTING, DIFFERENT TRANSPLANT SYSTEMS AND CLINICAL TRIALS: THE IBOX EXTENDED TRIAL

Sofia Naser[1], Gillian Divard[1], Marc Raynaud[1], Maarten Naesens[2], Dorry Segev[3], Mark Stegall[4], Carmen Lefaucheur[1], Olivier Aubert*[1], Alexandre Loupy[1]

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Background: The iBox is a validated prognostication system predicting long-term kidney allograft failure. It received regulatory endorsement by EMA for surrogate endpoint for clinical trials. As it was primarily built using a deep phenotyped cohort, there is a need for proof of validity in geographically distinct and diverse medico-economic cohorts and transplant allocation systems.
Methods: 10,851 transplant recipients were included from 17 academic medical centers. We applied the iBox algorithm that integrates eight independent prognostic factors: time from transplantation to risk evaluation, functional parameters (eGFR, proteinuria), allograft histological lesions (IFTA, g+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. We stratified the recipients according to several real-life scenarios: 1) iBox + different eGFR formulas ($MDRD_{186}$, $MDRD_{175}$, CKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional without immunological data); 4) iBox functional without histological data; 5) iBox in response to treatment in T-cell mediated rejection (TCMR); 6) iBox for in response to treatment antibody mediated rejection (ABMR) clinical trials. The performances of the iBox were assessed with the discrimination and the calibration.
Results: The derivation cohort included 4,000 recipients from France and the external validation cohort included 6,851 recipients from Europe (n=4,643), the United States (n=1,537) and South America (n=671). The mean recipient age was 50.3 years, with a median follow-up after evaluations of 5.4 years [IQR: 3.3 to 7]. 12.3% of patients lost their graft during the study follow-up. The performances were confirmed as follows: 1) iBox + different eGFR formulas 0.81; 2) iBox + urinary dipstick 0.80; 3) iBox Functional without immunological data 0.80 (derivation) and 0.84 (validation); 4) iBox functional without histological data 0.80 (derivation) and 0.83 (validation); 5) iBox in response to treatment in TCMR 0.81; 6) iBox for in response to treatment ABMR trials 0.81. The score showed an accurate calibration in every scenario.
Conclusions: The $iBox^{EXTENDED}$ trial confirms in various medico-economic settings the performances transportability and surrogacy of the iBox system, further reinforcing its use as a surrogate end point for clinical trials including TCMR and ABMR.

OS17_7 A RANDOMIZED CONTROLLED TRIAL OF EHEALTH PROGRAM FOLLOW-UP BASED ON A 1-YEAR PREDICTION OF LONG-TERM GRAFT FAILURE (KTFS) IN KIDNEY TRANSPLANTATION

Aurelie Houzet[1], Philippe Tessier[2], Florent Leborgne[3], Jean-Benoît Hardouin[2], Sandra Gaboriau[4], Solene Schirr Bonnans[5], Youssouf Compaore[5], Maryvonne Hourmant[1], Jacques Dantal[1], Diego Cantarovich[1], Gilles Blancho[1], Claire Garandeau[1], Emmanuelle Papuchon[1], Yohann Foucher[6], Magali Giral*[4]

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Background: The primary aim of the study was to evaluate the efficiency of video conferencing at home (eHealth) compared with a standard of care at hospital (SOC), the follow-up frequency being adapted according to the risk of long-term graft failure estimated by the 1-year Kidney Transplant Failure Score.[1]
Methods: This was an open label, 1:1 randomized study in which 155 patients at 1 year of transplantation were allocated either in the eHealth program or in the SOC during 2 years. The primary outcome was defined by the absence of major complications (death, graft failure, acute rejection, decrease in the graft filtration rate (eGFR) >25% or cancer). We aimed to show the non-inferiority of the eHealth program based on a lower limit of the 90%CI of the difference in the primary outcome higher than 3%. The secondary outcomes were the incremental cost-effectiveness ratio (ICER) expressed as the cost per Quality-Adjusted Life-Year (QALY) gained, and the evolution of the several patient-reported outcomes. Despite the randomization, we considered possible confounders by weighting on propensity scores.
Results: 135 patients respecting the intention-to-treat principle and without missing data were analyzed in whom 31 patients presented at least one major complication (2 deaths, 3 graft failures, 5 rejection episodes, 9 decreases in eGFR and 21 cancers). The confounder-adjusted difference of proportions of

recipients with major complications between the SOC and eHealth was 1.9% (90%CI from -11.7% to 15.6%). The ehealth program is associated with a higher mean number of QALYs and sensibly higher mean costs (mostly due to higher hospitalization costs) which produces an ICER of 243,510€ per additional QALY. At a 100,000€ per QALY threshold there is less than 30% chance that it is a cost-effective alternative to SOC. The only significant difference was observed in favor of the eHealth program for the depression scale at 2 years post-randomization (-1.42, 95%CI from -2.83 to -0.01).
Conclusions: We observed comparable outcomes in terms of efficacy, safety, and cost-effectiveness. Regarding the sample size, further studies are still needed to conclude to the non-inferiority of the eHealth program.

Foucher Y et al. *Kidney Int.* 2010;**78**:1288
* authors contributed equally

OS17_8 RISK CLASSIFICATION MODELS FOR KIDNEY GRAFT FAILURE FROM A LARGE GERMAN KIDNEY TRANSPLANT CENTRE

Marcel Naik*[1], Aadil Rasheed[2], Mozhgan Bayat[2], Matthieu Schapranow[2], Janis Bakker[1], Tim Gielsdorf[1], Calvin Hanisch[1], Danilo Schmidt[3], Verena Graf[1], Klemens Budde[1]

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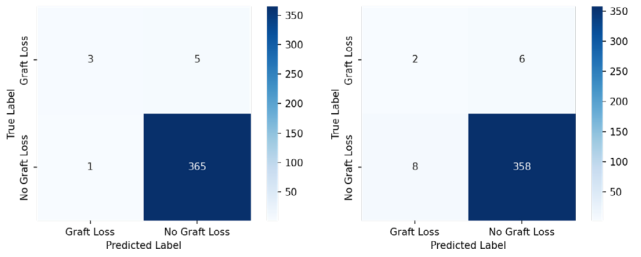
Background: Longterm graft survival after kidney transplantation (TX) is stagnant over the last decades. In our project NephroCAGE, we are developing an end-to-end data analysis pipeline to predict graft loss individually between 1 to 5 years after TX. In this work we present the results of two machine learning models.
Methods: All kidney TX patients at our centre between 2000 and 2020 were included. After preprocessing raw data (demographics of donor, recipient and transplant) from our database and exploratory data analysis we created a first gradient boosting model using the following features only: gender and age of recipient and donor at TX, cold ischemia time, HLA mismatches, type of donation. In a second model we used more features in a Kbest approach with extreme gradient boosting (XGBoost). Data was split into 72% training 18% validation and 10% test set. Hyperparameter were optimized using Optuna framework optimizing F1-score.
Results: After applying data preprocessing to the selected cohort (table1, N=3455, 62% male recipients, 32% living donation, mean age 51.3±13.97years, 17.7% graft loss), gradient boosting achieved an AUC 0.6, with a sensitivity, specificity, accuracy and F1-score of 0.25, 0.978, 0.963, and 0.22, respectively. XGBoost showed an AUC of 0.84 with a sensitivity, specificity, accuracy, and F1-Score are 0.375, 0.99, 0.98, and 0.5, respectively. Shown in figure 1 are the models' results.
Conclusions: XGBoost outperformed gradient boosting using only minimal data that is available at time of transplantation. Longitudinal data will be introduced next to improve these local models. Finally, local models at each site will be refined using a federated learning approach incorporating into one model. Finally, factors to lower the risk for graft loss will be investigated in future studies to improve long-term outcomes.

Parameter	Cohort (n=3455)
Recipient	
Center CVK (%)	53.5
Gender Female (%)	37.5
Age at transplantation (years)	51.3 ± 13.97
Living donation (%)	29.9
Time on dialysis (years)	6.1 ± 1.45
Preemptive (%)	8.1
Follow-up time (years)	7.8 ± 6.3
Donor	
Age (years)	50.4 ± 14.8
Female (%)	49.8
Transplant	
Delayed graft function (%)	33.2
Cold ischemia time (hours)	8.6 ± 5.85
Mismatches (mean+/-SD)	2.8 ± 1.65
Outcomes	
Death or graft loss (%)	40.2
Graft loss (%)	16.7
death (%)	30.8



OS18_1 BELATACEPT OUTCOMES IN PEDIATRIC KIDNEY TRANSPLANTATION: AN INTERNATIONAL MULTI-CENTER STUDY

Julien Hogan*[1;2;3], Charlotte Duneton[2], Roshan George[4], Rachel Liverman[4], Anne-Laure Sellier-Leclerc[5], Olivier Dunand[6], Houaida Dahdouh[2], Véronique Baudouin[2], Elodie Cheyssac[2], Rouba Garro[4]

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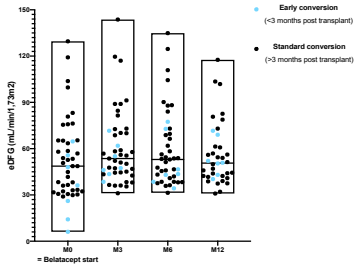
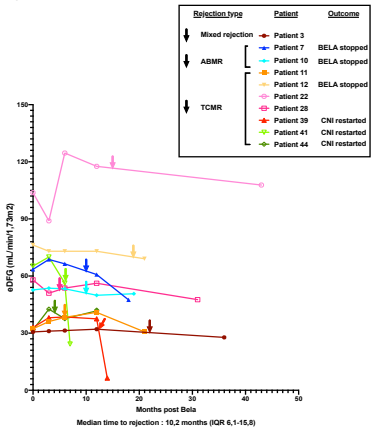
Background: Belatacept is associated with better long-term outcomes in adult patients compared to CNI based regimens. Data on its use in older children and young adults are lacking. We are the 1st to report outcomes for 45 pediatric kidney transplant recipients converted to belatacept.
Methods: Patients were included from 4 centers (USA and France) from 2018 to 2021. Patients received an induction with basiliximab (n=39) or ATG (n=6). Maintenance immunosuppression included CNI, MMF +/- steroids. Patients' viral status (EBV, CMV) were monitored monthly and allograft biopsies were performed prior and ~6 months after starting belatacept. The first 5 belatacept injections were administered at 5mg/kg/dose (10mg/kg/dose if early conversion) every 2 weeks, then monthly. CNI were progressively reduced and stopped. MMF doses were also increased at CNI withdrawal.
Results: Median age at conversion was 17.7y (range 10.3-20.6). 7/45 patients received an early conversion (median: 1 month post-transplant, IQR 0.5-1.2): 6 patients for delayed graft function and 1 for post-transplant diabetes. 38/45 patients were converted after a median of 4.1 years post-transplant (IQR 1.7-6.0). Conversion indication was CNI avoidance: either because of toxicity (histology, post-transplant diabetes, tremors; n=13) or sub-optimal creatinine (n=12) or to improve adherence (n=13). CNI were withdrawn in 42/45 patients by a median of 2.4 months (IQR 1.4-6.0). GFR was stable or improved over a median follow-up time of 1.6 years (IQR 1.1-2.4), Fig A. Ten rejections (22%) after a median of 10.2 months (IQR 6.1-15.8) and included 7 TCMR, 2 ABMR and 1 mixed rejection. None of these patients were converted early (<3m), 5 had been converted for non-adherence, 4 had pre-existing DSA and 4 had prior history of rejection. Evolution of GFR in rejectors is shown in Fig B. CNI were reintroduced for 6/10 and belatacept stopped for 3/10. Regarding viral complications, 1 severe BKv nephropathy required the discontinuation of belatacept. All patients were EBV+ at conversion (4 were EBV- at the time of transplant). No EBV replication was observed.
Conclusions: Selected pediatric kidney recipients benefit from long-term CNI toxicity avoidance, but selection criteria need to be refined to avoid rejection under costimulation blockade.

A **Evolution of graft function (eGFR Schwartz formula) after initiation of belatacept**
N = 45 patients



B **Evolution of graft function (eGFR Schwartz formula) and outcomes in patients who developed rejection on belatacept**
N = 10 patients



OS18_2 LONGITUDINAL DYNAMICS OF SOLUBLE IMMUNE MEDIATORS IN PAEDIATRIC LIVER TRANSPLANTATION IDENTIFIED SIGNATURES ASSOCIATED WITH A FREEDOM OF REJECTION

Evgeny Chichelnitskiy*[1], Imeke Goldschmidt[2], Louisa Ruhl[1], Nicole Rübsamen[3], Veronika Jäger[3], Andre Karch[3], Lorenzo D'antiga[4], Dominique Debray[5], Loreto Hierro[6], Deirdre Kelly[7], Valérie MC Lin[8], Emanuele Nicastro[4], Joanna Pawłowska[9], Piotr Czubkowski[9], Ulrich Baumann[2], Christine Falk[1]

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Background: In the European multicentre "ChilSFree" study, we aimed to characterize longitudinal dynamics of soluble and cellular immune mediators during the first year after pLT and identify early biomarkers associated with outcome.
Methods: Using Luminex-based multiplex technique, we measured 50 cytokines/chemokines, growth and adhesion factors in recipient plasma at eight visits: before (V0), day 7/14/21/28 (D7/14/21/28), 3/6/12 months (3/6/12Mo) after pLT (n=244). Absolute cell counts and relative proportions of immune populations in patient blood (n=180) were quantified by flow cytometry.
Results: The longitudinal dynamics of soluble immune mediators (SIM) after pLT revealed major changes in plasma secretome from V0-D14. While timing was dominant first, at later visits, the patterns identified patients with specific recovery patterns. One pattern was characterized by the absence of pro-inflammatory markers CXCL8/9/10/12, CCL7, reduced liver enzymes (AST, GGT), rejection score and, hence, might be predictive for improved outcome after pLT. In addition, we found higher frequencies of CD56^{bright} NK cells in the blood of the same patients, a cellular hallmark described in operationally tolerant patients. Of note, this special SIM pattern was observed few weeks after pLT and could predict superior outcome of the underlying patients over entire year. The longitudinal dynamics of immune cells revealed that absolute cell counts and proportions of myeloid cells peaked at D7, followed by gradual decrease at later visits. Simultaneously, CD4$^+$ and CD8$^+$ T and CD56$^+$ NK cell counts were reduced at D7 but recovered at D21 with a further increase at 12Mo. The dynamics of T and NK cells but not B cells, granulocytes and monocytes after pLT was affected substantially by the age of patients.
Conclusions: SIM blood signatures may act as biomarkers for improved outcome after pLT, hence, paving the way to early adjustment of immunosuppression and improved therapeutic options.

OS18_3 MOLECULAR HLA MISMATCHING FOR PREDICTION OF PRIMARY HUMORAL ALLOIMMUNITY AND GRAFT FUNCTION DETERIORATION IN PAEDIATRIC KIDNEY TRANSPLANTATION

Jon Jin Kim*[1], Alexander Fichtner[2], Hannah Charlotte Copley[1], Loren Gragert[3], Caner Susal[4], Isabella Guzzo[5], Raphael-Sebastian Schild[6], Lars Pape[7], Lutz Weber[8], Marcus Weitz[9], Jens Koenig[10], Kai Krupka[2], Burkhard Toenshoff[2;11], Vasilis Kosmoliaptsis[1]

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Background: Rejection remains the main cause of allograft failure in paediatric kidney transplantation and is driven by donor-recipient HLA mismatching. Modern computational algorithms enable assessment of HLA mismatch immunogenicity at the molecular level (molecular-mismatch, molMM). Whilst molMM has been shown to correlate with alloimmune outcomes, evidence demonstrating improved prediction performance against traditional antigen mismatching (antMM) is lacking.
Methods: We analysed 177 patients from the CERTAIN registry (median follow-up 4.5 years). molMM scores included Amino-Acid-Mismatch-Score (AAMS), Electrostatic-Mismatch-Score (EMS3D) and netMHCIIpan (netMHC1k: peptide binding affinity ≤1000 nM; netMHC: binding affinity ≤500 nM plus rank <2%). We stratified patients into high/low-risk groups based on risk models of DSA development.
Results: Donor-specific HLA antibodies (DSA) predominantly targeted the highest scoring molMM donor antigen within each HLA locus. MolMM scores offered superior discrimination versus antMM in predicting de novo DSA for all HLA loci; the EMS3D algorithm had particularly consistent performance (area under the receiver operating characteristic curve (AUC) >0.7 for all HLA loci vs. 0.52-0.70 for antMM). ABMR (but not TCMR) was associated with HLA-DQ molMM scores (AAMS, EMS3D and netMHC). Patients with high-risk HLA-DQ molMM had increased risk of graft function deterioration (50% reduction in baseline eGFR (eGFR50), adjusted HR: 3.5, 95% CI 1.6-8.2 high vs. low EMS3D). Multivariable modelling of the eGFR50 outcome using EMS3D HLA-DQ stratification showed better discrimination (AUC EMS3D vs. antMM at 2 years: 0.81 vs. 0.77, at 4.5 years: 0.72 vs. 0.64) and stratified more patients into the low-risk group, compared to traditional antMM.
Conclusions: Molecular mismatching was superior to antigen mismatching in predicting humoral alloimmunity. Molecular HLA-DQ mismatching appears to be a significant prognostic factor for graft function deterioration in paediatric kidney transplantation.

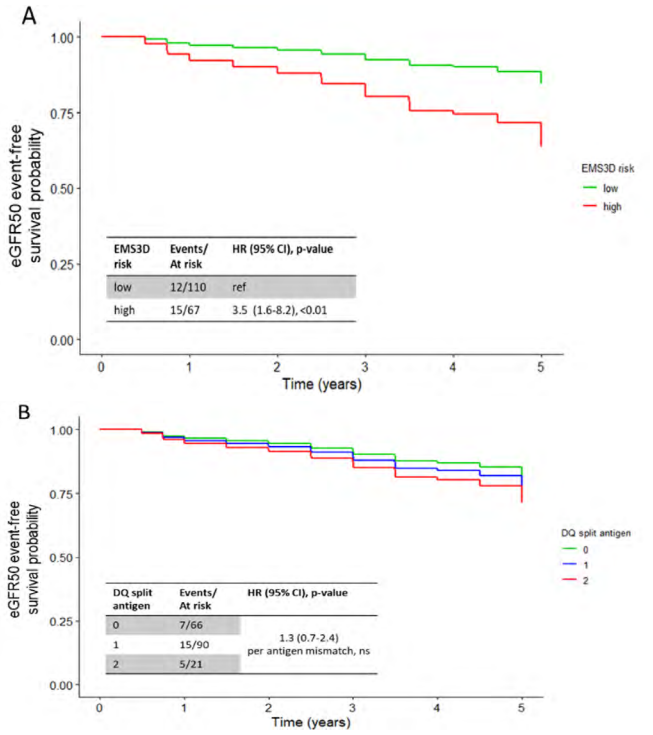

Figure: Survival analysis for eGFR50 outcome, adjusted for baseline eGFR, recipient age, donor age and transplant number based on HLA-DQ mismatching: A) molMM stratification using EMS3D, B) antigen mismatching.

OS18_4 CAN HOPE MITIGATE ISCHEMIA-REPERFUSION INJURY IN EX-SITU SPLIT GRAFTS? A COMPARATIVE STUDY WITH LIVING DONATION IN PEDIATRIC LIVER TRANSPLANTATION

Guillaume Rossignol*[1;2;3], Xavier Muller[2;3], Mathias Ruiz[4], Sophie Collardeau-Frachon[5], Remi Dubois[1], Celia Depaulis[6], Teresa Antonini[7], Kayvan Mohkam[1;2;3], Jean Yves Mabrut[2;3]

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Background: The gold standard in pediatric split liver transplantation (SLT) is living donation (LD) providing high-quality grafts with short static cold storage (SCS). This study investigates the protective effect of hypothermic oxygenated perfusion (HOPE) on ex-situ partial grafts from deceased donors in comparison to standard ex-situ Static-Split and LD SLT.
Methods: We included all consecutive HOPE-Split, Static-Split and LD SLT performed from 2018-2022. The primary endpoint was early ischemia-reperfusion injury (IRI) based on reperfusion biopsy (graded from none/0 to severe/4), the occurrence of post reperfusion syndrome (PRS, drop≥30% of systolic arterial pressure) and post-LT transaminase release.

Results: A total of 46 SLT (14 HOPE-Split, 17 Static-Split, and 15 LD) were included. With a median perfusion duration of 100min, HOPE-Split had a significant decrease of SCS compared to Static-Split (473 min vs 538 min; p=0.02) with similar total preservation time (p=0.13). This translated into lower rates of mild to severe IRI (grade≥2; p=0.03) and significantly reduced neutrophilic infiltrate than Static-Split (p=0.04; Fig.1). The PRS was also reduced in HOPE-Split (0% vs 35%, p=0.02) with less transaminase release. Despite prolonged SCS (473 vs 117min, p<0.001), HOPE-Split was comparable to LD regarding grade≥2 IRI (64 vs 40%; p=0.17) and PRS (0 vs 6.7% p=0.34), with however higher transaminase release (571 vs 244 UI/L/100g; p=0.004). Overall, 3-months surgical complications, graft and recipient survival did not differ among groups.
Conclusions: HOPE allowed improved preservation of split grafts compared to Static-Split, resulting in similar early IRI profiles to LD.

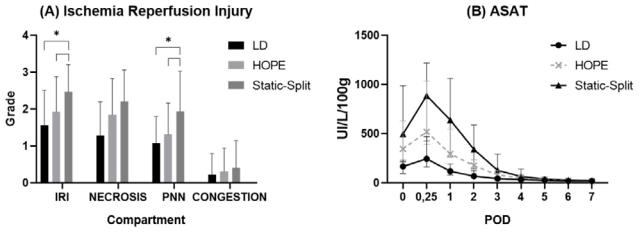

Figure 1: Panel A Histological analysis of ischemia reperfusion injury on reperfusion biopsy. Panel B Serum ASAT during the first post-operative days.
(A) IRI: overall IRI grade (none=0; minimal=1; mild=2; moderate=3; severe=4).
Data are expressed as mean with range. *p <0.05. (B) Data are expressed as median and IQR

Table 1: Demographic and post-operative data
Data are expressed as n (%) or median (interquartile range).

	HOPE-Split n=14	Static-Split n=17	LD n=15	p value
Recipient characteristics				
Recipient Age, months	43 [19.5-51]	21 [13-38]	17 [9.5-56.5]	0.37
Weight, kg	15 [10-17]	10 [8.5-14]	10.5 [7.5-16]	0.32
Retransplantation, n (%)	4 (28.5)	0 (0)	1 (6.7)	0.03
PELD, points	19 [16-21]	23 [15-29]	16 [9-21]	0.09
Outcomes				
AST peak, UI/L/100g	571 [466-1066]	983 [442-1320]	244 [174-469]	0.001
90days arterial complications Grade ≥3 Clavien-Dindo	1 (7%)	1 (6%)	0(0%)	0.59
90days Biliary complications Grade ≥3 Clavien-Dindo	5 (37.5%)	4 (23.5%)	4 (26.5%)	0.94
3 months graft survival	12 (85.7)	15 (88.2)	15 (100)	0.34
3 month recipient survival	12 (85.7)	16 (94.1)	15 (100)	0.29

OS18_5 'UNIQUE' STUDY - A 20 YEAR UK NATIONAL STUDY ON CLINICAL OUTCOMES AND QUALITY OF LIFE IN CHILDREN WITH MULTI-ORGAN TRANSPLANTS

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Background: Due to advances in modern medicine, children with previously fatal conditions are now surviving much longer and presenting as transplant candidates. Generation Alfa of paediatric transplant candidates brings an increasing number of children requiring multiple different solid-organ transplants (MSOT). However, there is limited data on long-term clinical outcomes and no data on their quality of life (QoL). The UNIQUE study aims to gain a better understanding of the long-term clinical outcomes and QoL in these patients.
Methods: Clinical outcomes were analysed for all children who received a kidney and one other solid-organ transplant as a child in 2000-2021 in the UK. These were extracted from the national NHS Blood and Transplant (NHS BT) registry and included patient and graft survival at 1, 5 and 10 years post-transplant, graft function and post-operative complications. QoL was measured using the PedsQL 3.0 Transplant Module questionnaire following informed consent and ethics approval.
Results: 92 children were on the NHS BT Registry as having MSOTs in the UK during the study period. The types of transplant were heart/heart-lung and kidney n=15, liver and kidney n=72, pancreas and kidney n=4 and multivisceral n=1. All patients had their clinical outcomes analysed; thus far 22% of families participated in the QoL arm of the study. Patient survival was 98%, 93% and 89% at 1, 5 and 10 years post-transplant. Kidney allograft survival was 91%, 83% and 77% at 1,5 and 10 years post-transplant. Kidney allograft function was comparable to single-organ transplant recipients in the literature and comparatively, patients with MSOT had fewer episodes of acute rejection. Clinical outcomes were significantly better in patients with combined liver and kidney transplants compared to patients with sequential liver and kidney transplants. QoL was reported to be very good with a mean score of 73%. Areas of QoL to improve on were that patients have difficulties with fitting in with their peers and also reported health-related anxiety. Patients' worries and concerns increased as they got older, which may require further support through a personalized multi-disciplinary approach.
Conclusions: This is the first study to look at QoL in paediatric MSOT recipients and results show excellent long-term clinical and QoL outcomes.

OS18_6 MONITORING OF TORQUE-TENO VIRUS LOADS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS MAY PREDICT OPPORTUNISTIC VIRAL INFECTIONS DURING FOLLOW-UP

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Background: The risk for infectious complications and graft rejection by alloimmunity, still remaining as the major cause of late graft failure after kidney transplantation (KTX), is subject of careful balance of immunosuppression during post transplant follow-up. Torque Teno virus (TTV) plasma load was identified as a biomarker reflecting patients individual immune status after solid-organ transplantation (i.e., was also shown to correlate with immunosuppressant dosage in pediatric KTX patients). The aim of this study was to investigate associations and the predictive capability of TTV loads with major opportunistic viral infections (e.g., cytomegaly virus [CMV]) during follow-up of pediatric KTX patients.
Methods: All pediatric patients at the Medical University of Vienna with a post KTX time of >3 months were included. Viral loads (TTV, CMV, Epstein-Barr virus [EBV], BK polyomavirus [BKV]) were routinely measured every four to eight weeks by quantitative PCR. Generalized poisson mixed models and mixed effects logistic regression for log10 TTV loads with log10 EBV, CMV, and BKV loads were calculated with fixed effects accounting for potential confounders (age, time after KTX), alongside Receiver Operating Characteristics (ROC).
Results: In total 72 pediatric KTX recipients were included. Baseline characteristics and primary kidney disorders are displayed in Table 1. TTV loads were able to predict significant CMVemia above predefined plasma loads of 10^3 c/mL 4 to 8 weeks before occurrence (OR 2.56, p=0.002) after adjustment for potential confounders. Prediction of the first significantly positive CMVemia with plasma TTV achieved a sensitivity of 88% and a specificity of 79%. Furthermore, TTV loads were able to significantly predict significant BKVuria (p=0.02) above predefined urine loads of 1.7 x 10^9 c/mL for the next visit and BKVemia above predefined plasma loads of 10^4 c/mL on the same visit (p=0.005). Associations with EBV were not significant.
Conclusions: This is the first study to demonstrate significant predictive capability of TTV plasma loads for the occurrence of clinically relevant viral infections (CMV, BKV) above relevant cut-offs on the same or for the next visit, 4 to 8 weeks later, in pediatric KTX patients during follow-up.

Table 1.

Primary kidney disorders	**N**	**%**
CAKUT	35	49
Glomerular disorders	15	21
Polycystic kidney disease	9	13
Congenital nephrotic syndrome	9	13
Metabolic disorders	2	3
Other	2	3
Baseline KTX characteristics	**N**	**%**
Male	47	65
Living Donors	45	63
Basiliximab induction	72	100
Tacrolimus	64	89
Cyclosporin A	4	6
Sirolimus	3	4
w/o calcineurin- or mTOR-inhibitor	1	1
Mycophenolate mofetil	61	85
Azathioprine	5	7
w/o antiproliferative substance	6	8
Steroids	71	99
	Median	**IQR**
Age (years)	12.2	8.0-15.8
Age at KTX (years)	8.1	3.4-13.0
Time post KTX (months)	19	3.3-63
HLA mismatch (n)	3	2-3
Creatinine (mg/dl)	0.89	0.54-1.31
eGFR (ml/min/1.73m²)	96.1	75.9-134.3
Study period (years)	3.5	0.7-6.1
Follow-up time (years)	6.6	0.9-19

CAKUT = congenital anomalies of the kidney and urinary tract, eGFR = estimated glomerular filtration rate

OS18_7 NATIONAL LIVER ALLOCATION POLICIES FOR PEDIATRIC LIVER TRANSPLANTATION ACHIEVE OPTIMAL OUTCOMES: INTENTION-TO-TREAT ANALYSIS OF ITALIAN WAITING LIST

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Background: Despite pediatric liver transplantation (pLT) achieved excellent outcomes, the waiting list (WL) mortality is still an issue. We analyzed the Italian pLT WL to evaluate the intention-to-treat (ITT) success rate and identifying factors influencing success.
Methods: All children (<18 years) listed for pLT in Italy during 2002-2018 were included [Era 1(2002-2007): center-based pediatric organ allocation; Era 2(2008-2014): start of pediatric national allocation; Era 3(2015-2018): start of national mandatory-split policy].
Results: 1,424 patients [age:2.0 years (IQR=1.0-9.0); weight:12.0kg (IQR=7-27)] were listed for pLT. Indications included chronic (70.1%) and acute liver failure (13.3%), metabolic disease (7.4%), tumor (7.2%) and undetermined (2%). Median WL time was 2 days (IQR=1-5) for Status 1, while 44 days (IQR=15-120) for non-Status 1. 1,302 (91.4%) were transplanted (64.4% with split liver grafts), while 50 children (3.5%) dropped from WL due to death (n=36,2.5%) or clinical deterioration (n=14,1.0%). Predictive factors for receiving LT included recipients' weight <25 kg, Status 1 (HR=1.66;95%CI=1.25-2.20;p=0.000), Status 1B (HR=1.96;95%CI=1.13-3.38;p=0.016), Status 2A (HR=2.15;95%CI=1.11-4.19;p=0.024) and each additional point of PELD/MELD score. Children with blood group 0 or awaiting pLT combined with other organs had less change to receive a graft. ITT patient survival rates were 90.5% at 1 year and 87.5% at 5 years and didn't change across Eras. Risk factors for ITT survival were re-transplantation (HR=5.83;95%CI=3.02-11.25;p<0.000), Status 1 (HR=2.28;95%CI=1.27-4.07;p=0.006), Status 1B (HR=2.90;95%CI=1.24-6.78;p=0.014), Status 2A (HR=9.12;95%CI=3.81-21.83;p<0.000), recipient weight <6kg (HR=4.53;95%CI=2.15-9.52;p<0.000) and low volume listing activity (HR=4.38;95%CI=1.80-10.69;p=0.001).
Conclusions: In Italy, the continuous adaption of the pediatric organ allocation policies permitted to constitute a unique national allocation model. The presence of a national organ exchange organization, pediatric prioritization rules, and mandatory-split liver policy are key factors to maximize the use of donors for pediatric candidates and to minimize the WL mortality without compromising outcomes.

OS18_8 PEDIATRIC KIDNEY TRANSPLANT PROGRAM IN WAR CONDITIONS

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Background: Pediatric patients with end-stage kidney disease (ESKD) require transplant to achieve the appropriate quality of life. Kidney transplant (KT) program was launched in the main pediatric clinic of Ukraine, both living donor (LDKT) and deceased donor (DDKT). Since February 2022 the program development slowed.
Methods: analyze 28 kidney transplants (KTs) performed in "Okhmatdyt" between March 2021 and January 2023
Results: a total of 28 children (12 males and 16 females, diagnosed kidney disease at the mean age of 6.67±0.91 years) underwent KT in our clinic at the mean age of 12.0±0.89 years. ESKD in recipients resulted from kidney dysplasia (n=14; 50%), congenital anomalies (n=9; 32.1%), glomerulonephritis (n=2; 7.2%), acute kidney injury (n=2; 7.2%), nephrolithiasis (n=1; 3.5%). Median pretransplant peritoneal or hemodialysis duration was 7(95%CI 5-22) months. LDKT was performed half of all cases; LDKT to DDKT ratio was 8/10 in a pre-war period, and 6/4 after February 2022. Median posttransplant hospital stay was 8(95%CI 5-7) days. Delayed renal graft function was observed in 3(10,7%) recipients. Graft survival is 92,8%, (n=26), one renal graft was removed for acute rejection and graft rupture, one for pyelonephritis in chronic rejection. Recipients survival is 92,8%, (n=26), sepsis and COVID-19 complications caused mortality. Kaplan-Meyer test showed no difference in LDKT survival 0.923 (95%CI 0.59-0.989) in comparison to DDKT survival 0.928 (95%CI 0.566-0.988). The mean follow-up period is 11.8±1.2 months. Rejection episodes were registered in 3 (20%) children, one of them resulted from medication intake defection for social reasons. 8 children are in the waiting list for DDKT with no related donors available. Mean time in the waiting list before was 4.8±0.5 months, which increased up to 9.5±0.7 up to now (p<0.001), with no sign of fast improvement soon.
Conclusions: The variety of ESKD causes in children results into the need of KT for pediatric population on regular basis. Pediatric transplant development was fast and effective, with results corresponding to those in world centers. The program in Ukraine is now basically focused on LDKT; War conditions limited DDKT, it significantly increased the time in the waiting list for children without related donors.

FOCUS GROUPS

Access to transplantation & donation: is luck involved?

FG1_1 THE KIDNEY DISTRIBUTION SYSTEM FOR TRANSPLANTATION IN CHILE EXPLAINED ACCORDING TO GAME THEORY: HOW THEORETICAL GENEROSITY TRANSFORMS INTO SELFISHNESS

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Background: There is a huge mismatch between demand and supply of kidneys for transplantation. While allocation systems try to assign this scarce resource equitably to the best recipient, using different graft survival maximization; allocation systems can also incentivize the procurement activity. The Chilean allocation system delivers one kidney to the procurer institution and the second nationally; policy designed seeking to stimulate procurement in transplant institutions, which should receive a kidney every time they procure a donor. Has this policy been effective in achieving its intent?
Methods: We obtained all records of organ donors by private and public institutions, and matched those organs with the centers that implanted them between 2010-2020. We used descriptive statistics and game theory modeling to analyze healthcare institution's behavior. We obtained public and private prices of kidney procurement and compared them to the price an institution must transfer to the system in exchange for a pool kidney.
Results: We found no significant increase in the number of donors in the country during that period. We observed that private institutions are increasing their participation in the transplant market (p = 0.003), and they do so at the expense of public institutions (p = 0.702) and without increasing their contribution of organs (8.2 ± 1.7 vs 5.8 ± 1.6 donors pmp for public vs private, p = 0.002). Private centers have higher transplant / procurement ratios (4.40 ± 1.59 vs 2.56 ± 0.54; p = 0.0017), which means that these institutions benefit over public ones from the organ allocation system that delivers one of the two kidneys to a national waiting list over a local one. In terms of price, we found it is 2,7% more expensive to procure a kidney in private centers, and both costs are 5 times higher than the transfer price set by law.
Conclusions: This behavior can be framed within Game Theory, specifically the Tragedy of the Commons, describing that the players maximize their benefit at the expense of the rest, leading to an imbalance between demand and supply of organs that worsens over time and lengthens waiting lists, especially those listed in a public institution. Chile must change its allocation model to achieve equity and increase transplants. We propose shifting to a local model as most countries in the world.

FG1_2 IMPROVING THE ACCESS TO HEART TRANSPLANTATION FOR FOREIGN PATIENTS OVER 10 YEAR PERIOD

Giada Giovannelli[*1], **Annamaria Minervini**[1], **Laura Borgese**[1], **Marco Valente**[1], **Letizia Marcantoni**[1], **Francesca Aversano**[1], **Laura Giovannini**[1], **Sofia Martin-Suarez**[1], **Antonio Russo**[1], **Marco Masetti**[1], **Paola Prestinenzi**[1], **Mario Sabatino**[1], **Lucia Golfieri**[1], **Luciano Potena**[1]

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Background: While disparities in access to transplantation related to ethnicity and socioeconomic status have often been reported in private-based healthcare systems, reports in the setting of public healthcare system are sparse. We reviewed waitlist and heart transplant outcomes of adult foreign residents (FR) referred in the 2012-22 period aiming to assess potential disparities related to descent nationality, and the impact of the change of the procedures for referral and psychosocial management developed in our center in 2019
Methods: We reviewed waitlist registry and clinical charts for demography, clinical features, and outcomes of patients listed in the period 2012-22. We compared outcomes of FR to patients of Italian descent (ID), over the entire study time frame and between 2012-18 vs. 2019-22
Results: 337 patients were listed (82(24%) females, 50±12y; 37(10%) FR), and 200(59%) were transplanted in the 2012-22 period. Most of FR were from Eastern Europe (56%) or Africa (24%), with overall 18 countries represented. The proportion of FR listed significantly raised in the 2019-22 period vs. 2012-18 (6.5 vs 15.3%; P<0.01), achieving a rate similar to that of age matched FR living in Northern Italy. Rate of waitlist death/deterioration was similar between FR and ID (12 vs. 17%; P=0.5), while FR were transplanted significantly earlier than ID [2.1(0.5-5.4) vs. 5.7(1.6-17.8) months; P<0.01]. However, time to transplant was shorter in FR only in the 2012-18 period, but not in 2019-22. In the 2012-18 period ICD/CRT implants were less common in FR than ID (46% vs. 85%; P<0.01), but not in those listed in the 2019-22 period (70% vs. 82%; P=0.4). The differences between time periods suggest that before 2019 FR referred for transplant were undertreated or referred late with a more severe phenotype needing a short waitlist period. Post-transplant estimated 10-y survival was similar between FR and ID (70±9 % vs. 65±10% P=0.5)
Conclusions: Despite universal healthcare coverage, disparities in access to transplantation are possible between FR and ID. This analysis suggests that the current referral and psychosocial framework implemented at our Center eased access to care for FR by improving the number of patients with timely access to our transplant waitlist. Of note, descent nationality did not impact post-transplant survival

FG1_3 APOL1 GENETIC RISK FACTORS ELIMINATES POTENTIAL LIVING KIDNEY DONORS

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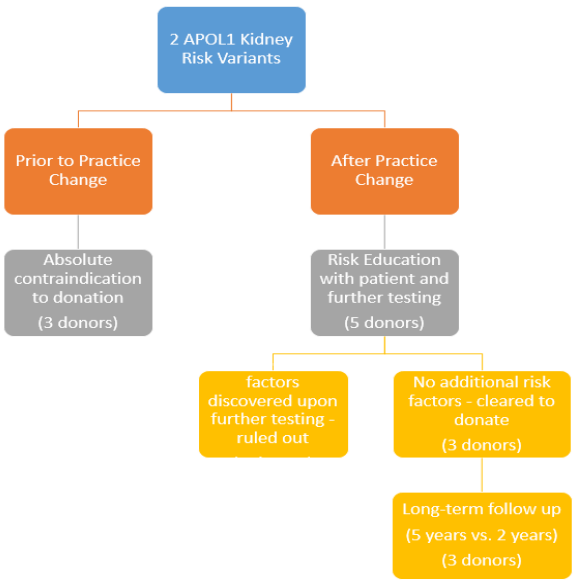
Background: Apolipoprotein L1 (APOL1) genetic testing is used in living kidney donor (LD) evaluation to assess risk of CKD in those with African heritage. The presence of 2 kidney risk variants (KRVs) is an absolute contraindication. To increase equity in transplant access for patients with African heritage, we changed our practice allowing for more thorough assessment and shared decision making.
Methods: We received requests from potential donors who were declined by other centers due to the presence of two APOL1 KRVs. Some were healthy with no additional CKD risk factors. Patients wished to be included in decision making when informed about their testing. To examine options to reduce barriers to living donation in disadvantaged groups, our team established a workgroup to reassess the application of APOL1 genetic testing in LD evaluation.
Results: A workgroup of nephrologists, surgeons, nurses, a research associate, and medical ethicists discussed the practice of APOL1 screening and its impact on LD. Extensive literature review was conducted. A team survey reflected willingness to change historical practice which prohibited any donor with 2 KRVs from donation. We established a new guideline focused on patient education regarding APOL1 KRV and risk factor assessment for kidney disease which supported shared decision making. A donor with 2 KRVs also completes a 24-ABPM and echocardiogram. A transplant nephrologist reviews the results with donor, discusses available data on LD with APOL1 KRVs and the impact of social determinants of health in long-term outcomes. Donors with a normal 24-hour ABPM, ECHO, excellent creatinine clearance, no proteinuria or other metabolic risk factors can be considered for donation.
5 donors completed further testing since Fall 2021. 1 declined due to abnormal ABPM results and 1 due to unrelated findings. 3 donors successfully donated and have will have longer follow up than lower-risk donors (5 years vs. 2 years).
Conclusions: Transplant centers should consider examining historical practices that may potentiate the disparities that exist in access to transplanttion and LD. By implementing a practice of careful testing and supporting engagement in shared decision making, we are able to eliminate one of the potential barriers to donation in patients who identify with African ancestry.



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FG1_4 GENDER DISPARITY TO ACCESS TO KIDNEY TRANSPLANTATION IN TURKEY: 10-YEARS EVALUATION

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Background: Kidney transplantations in Turkey have increased since the first transplantation in 1975. Most of them are from live donors. It is known that there is gender disparity to access to transplantation, especially those from live donors. This study aimed to examine the effect of gender on access to kidney transplantation in Turkey in the past ten years.
Methods: In this descriptive, retrospective study, data were obtained from the reports issued by The Turkish Society of Nephrology Registry of The Nephrology, Dialysis and Transplantation in Turkey.
Results: Official electronic records of data about all transplantations in Turkey started in 2013. Data about transplantations in 2022 have not been revealed yet. Therefore, data issued between 2013 and 2021 were evaluated. The males and the age group of 45-64 years had the highest rates of hemodialysis and peritoneal dialysis. The males and the age group of 20-44 years had the highest rate of kidney transplantations and the females and the age group of >75 years had the lowest rate of transplantations. The highest rate of kidney transplantations was from live donors and in the age group of 20-44 years. The highest rate of the live donors was first-degree relatives. The rate of hemodialysis was high initially (66.58%), but it decreased later and preemptive transplantations increased and reached the highest rate over the years (55%).
Conclusions: A higher rate of the males has accessed hemodialysis, peritoneal dialysis and transplantation for end-stage renal disease in Turkey recently. It is seen that being a woman is a disadvantage in accessing renal replacement therapy in Turkey, and this inequality is more common in older women. This suggests gender disparity in access to kidney transplantation, which can be attributed to cultural features, gender inequalities and economic factors.

FG1_6 EXCELLENCE IN ORGAN TRANSPLANTATION – A QUALITATIVE STUDY OF GENDER SPECIFIC CARE NEEDS IN TRANSPLANTATION

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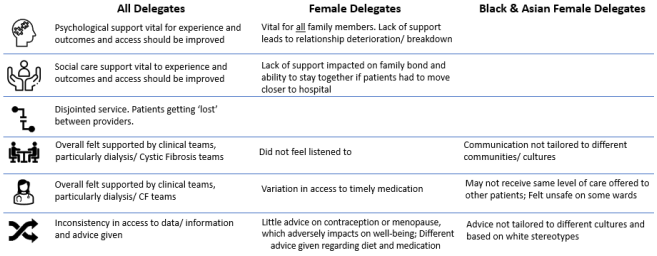
Background: Current National Health Service care models are often based on male prototypes. An Organ Utilisation Group (OUG) was established in the UK, to identify ways to improve transplant patient experience and outcomes, including a focus on the 'less heard' female patient voice.
Methods: Four online focus groups were held in 2021, Chaired by patient representatives. Delegates were invited via patient representative groups and were self-selected. Delegates were not identifiable by the focus group organisers and responses were completely anonymised.Table 1 summarises the diversity of delegates.
Results: Figure 1 demonstrates the key points raised by patients. Effective psychological and social support pre- and post-transplantation was important for all patients. Female patients highlighted the impact and importance on the wider family (children; partners/ spouses; parents; siblings). A lack of social care adversely impacted on families being able to stay together and therefore the family bond. A lack of effective psychological support led to a deterioration in relationships and in some cases a complete breakdown. Some female patients also expressed concerns: that they did not feel listened to; poor pain management; limited information about the impact of/ care through the menopause; a lack of advice regarding contraception, which adversely impacted on their experiences with partners and on psychological well-being.
Conclusions: Whilst there are similarities between male and female needs, female transplant patients have specific needs that may be unmet. The focus group participants explained how a lack of tailored care and support is adversely impacting on outcomes and experiences. The focus groups had limitations: small sample size; self-selected participants. Further qualitative and quantitative research is needed, with increased segmentation (ethnicity; geography; socio-demographic) to identify how needs vary between female patients.

Not misogynistic but myopic: the new women's health strategy in England - The Lancet
Table 1: Diversity of Focus Group Delegate

	Focus Group 1: Kidney	Focus Group 2: Lung	Focus Group 3: Kidney	Focus Group 3: Liver
Ethnicity of delegates	1 Asian; 5 Black; 2 White	5 White	6 Black	8 White
Gender	2 male; 6 female	1 male; 4 female	2 male; 4 female	4 male; 4 female
Age	1 parent of paediatric patient	1 patient who had been a child at the time of listing	6 adult patients	8 adult patients
Pre- or Post-transplant	8 post-transplant	2 pre-transplant; 3 post-transplant	2 pre-transplant; 4 post-transplant	2 pre-transplant; 6 post-transplant
Patient/ carer	6 patients; 1 parent of paediatric patient with special needs; 1 representative of adult special needs patient	5 patients	6 patients	8 patients

Figure 1: Summary of feedback from Focus Group delegates, segmented by gender and ethnicity



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FG1_8 THE GRAPHIC NOVEL "THE NEW US" TO SUPPORT DOCTOR-PATIENTS RELATIONSHIP IN TRANSPLANT PATIENT CARE-PATHWAY

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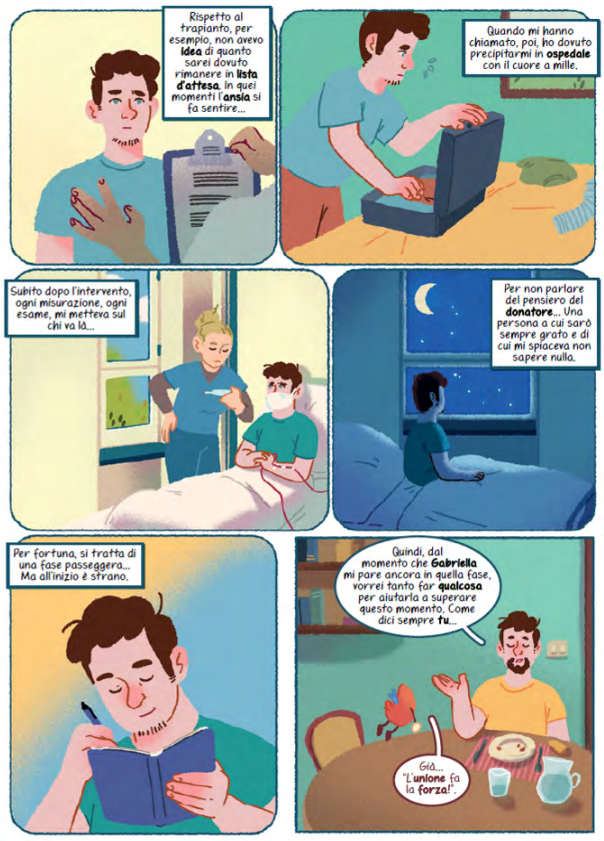
Background: Transplant recipients will need to learn to live with a new condition that has implications for day-to-day life. Many communication tools for improving lifestyle and adherence to immunosuppressive therapy are often developed based on the assumptions of health care providers (HCPs) on the needs of the patients without prior consultation of them. This project aims to creatively bridge this gap-including transplant patients and HCPs in the development of a graphic novel to improve the doctor-patient relationship and dialogue and to become leader of their long-term health.

Methods: Insight from previous ethnographic research on twelve transplant patients were the input guided the style and substance of the graphic novel. The interviews focused on what were the most bothersome aspects of life post-transplant: adherence to lifestyle and immunosuppression therapy, what patients may be worried about in the future, and difficulties in communication with HCPs. A team composed by HCPs, a Patient Expert, illustrator, communication expert and writer has developed a graphic novel that has the potential for empowering patients through customized patient relevant information, thus equipping them with the skills to make fully informed decisions.

Results: Two main characters were identified: Luca, a kidney transplant recipient with a story of illness that shaped his identity and Gabriella, transplant liver recipient who finds herself unprepared for the new life. The story has two parallel tracks: the evolution of their relationship, and the evolution of their role as patients that become in charge of their care-pathway. In between a funny animated kidney, Renny, that helps Luca to manage the 'rules' of his daily life. The story script, as well as the models for characters during the drawing process, were defined, reviewed, and revised with input and clarifications from the whole team to enhance trustworthiness of ethnographic research analysis/transposition into narrative and graphic form, and to ensure that the content was appropriate and accurate. "The new us" was distributed to Transplant Centers.

Conclusions: "The new us", realized through patients and HCPs co-creation, can offer multi-faceted communication opportunities and support doctor-patients relationship in the transplant patient care-pathway.



FOCUS GROUPS

Insights on IRI and PGD in cardiothoracic transplantation

FG2_1 POSITIVE LONG-TERM EFFECTS OF 17ß-ESTRADIOL AND METHYLPREDNISOLONE ASSOCIATION ON LUNG INFLAMMATION TRIGGERED BY BRAIN DEATH IN FEMALE RATS

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Background: After brain death (BD), females tend to present higher lung inflammation in comparison to males. It is believed that the acute reduction of estradiol (E2) after BD compromises the female immune response and evidence points to a connected action of E2 and corticoids in this sex. Impairment of the donor response to BD could compromise the recipient prognostic in the long-term. Thus, we aimed to investigate the prolonged effects of E2 and methylprednisolone (MP) treatment on lung inflammation in female BD rats using tissue culture method.
Methods: Female Wistar rats were submitted to BD by rapid insufflation of a balloon catheter in the intracranial space and maintained for 6h. Rats received MP (4 mg/ml i.v–2 ml/h) or MP and E2 (MP/E2, 50 ug/ml i.v–2 ml/h) after 3h of BD until the end of experiment. Sham-operated (S) were used as control. Bronchoalveolar lavage (BAL) and lung tissue were collected. Lung fragments were kept in culture for 24h (explant) and inflammatory mediators were measured.
Results: Compared to sham, BD animals present higher total leukocyte infiltration in BAL, which was prevented by both treatments (S: 10.75±1.3; BD: 23.63±3.6; MP/E2:11.50±2.97; MP: 15.5±2.75 cells (x10^5)/ml- p=0.0028). In the differential count, granulocytes were only reduced in the MP/E2 group (S:0.612±0.05; BD:1.08±0.65; MP/E2:0.52±0.04; MP:0.88±0.17 cells (x10^5)/ml - p=0.047). Explant measurements of inflammatory mediators are presented below.
Conclusions: These results point to lasting positive effects of the association between MP and E2 in lung inflammation triggered by BD in females rats. This is highlighted by the decrease of infiltrate cells, followed by the reduction of cytokines and chemokine release after 24h in the MP/E2 group, as well an overall lower level of VEGF in the same group, suggesting modulation of vascular permeability.

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	Sham	BD	MP/E2	MP	p
IL-1ß$^\alpha$	2357±1845	21403±6597	385.7±195.2*	497.5±311.2	0.0295
IL-6$^\alpha$	93274±20474	88887±24106	43352±19033*	46532±2514*	0.0027
CINC-1$^\alpha$	23148±8456	21403±6597	8613±4987*	9188±4855	0.0075
NOX-$^\gamma$	234.9±262	754.2±684.5	95.7±170.2*	280±245.1	0.0845
VEGF$^\alpha$	3863±3604	2764±3065	281.6±194.6	2009±3106	0.0616

α pg/ml/mg, dry weight; γ nM/ml/mg, dry weight; *p≤ 0.05

FG2_2 MITOCHONDRIAL DAMAGE COMPARISON BETWEEN BRAIN DEATH DONORS AND DONORS AFTER CIRCULATORY DEATH IN LUNG TRANSPLANTATION: PROSPECTIVE MULTICENTER STUDY

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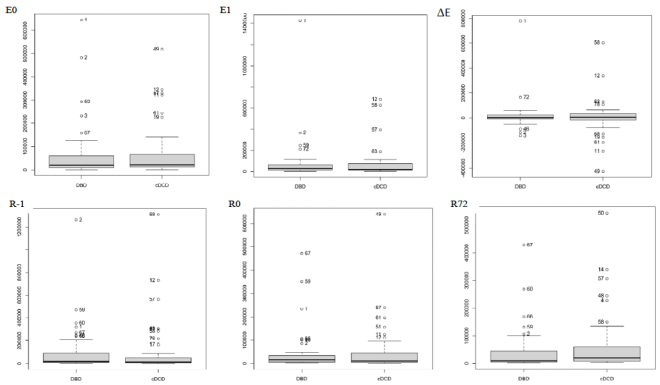
Background: The warm ischemia time associated to donation after controlled circulatory death (cDCD) may enhance the apoptosis process in lung tissue leading to post-mortem degradation of mitochondrial-DNA (mtDNA) into damage associated molecular patterns (DAMPs). Multiple observations suggest that the DAMPs could serve as sentinel marker to primary graft dysfunction (PGD). Our objective is to compare the DAMPs observed in lung recipients from donors after brain death (DBD) and cDCD.
Methods: Eighty adult lung recipients, 40 from DBD and 40 from cDCD donors (paired by lung transplantation indication and age) were prospectively enrolled in 4 Spanish transplant centres from Jul-18 to Jul-19. Blood samples were collected from the donor before (E0) and during the retrieval process (E1), and from the recipient before implant (R-1), after graft reperfusion (R0) and 72(R72) hours after lung transplantation. Mitochondrial damage (DAMPs) was analysed and compared between groups.
Results: Demographics of donors and recipients as well as transplant surgical procedure characteristics were similar between groups except for a higher rate of corticoid treatment and vaso-active support in DBD group and higher blood transfusion requirements in cDCD group. No differences were found in mitochondrial damage between groups in E0, E1, ΔE, R-1,R0 and R72 (Figure 1). Primary graft dysfunction (PGD) incidence and mortality did not have statistically differences between both groups.(Table 1).
Conclusions: Controlled DCD did not have higher mitochondrial damage and PGD incidence than DBD despite warm ischemic time in our cohort. Lung transplantation from cDCD is a safe alternative to increase the lung donor pool.

Table 1. Outcomes

		DBD (n=40)	DCD (n=40)	P -value
Outcomes	Primary graft dysfunction, n (%)			
	Of any grade	27 (67.5)	26 (65)	0.100
	Grade III	14 (35)	11 (27.5)	0.469
	Post-operative mortality	0 (0)	2 (5)	0.494
	Three-month mortality	0 (0)	2 (5)	0.494

Fig.1. mtDNA number of copies/µLplasma



FOCUS GROUPS

Insights on IRI and PGD in cardiothoracic transplantation

FG2_3 A NOVEL WHOLE-BODY COOLING SYSTEM PROTECTS DONOR LUNGS FROM ISCHEMIA REPERFUSION INJURY:TARGETING UNCONTROLLED DONATION AFTER CIRCULATORY DEATH DONORS

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Background: Lung transplantation using lungs from uncontrolled donation after circulatory death (uDCD) may increase lung donor pool. We developed a novel chest cooling system for uDCD donors without surgical intervention. We hypothesized that the system described as involving whole-body cooling using a proprietary material could improve pulmonary function of uDCD donors. The aim of this study was to verify whether the cooling system ameliorates the physiological parameters, compared to control using ex vivo lung perfusion (EVLP).
Methods: Ten pigs were divided into 2 groups (DCD or cooling group). In the DCD group, lungs were subjected to 90 min of warm ischemia time (WIT) at room temperature, whereas lungs were cooled with the cooling system during WIT in the cooling group. Tracheal temperature was continuously measured during WIT. Subsequently, lungs were procured in a standard fashion and then perfused in 2 hours of Lund-type EVLP following 5 hours of cold preservation. Transplant suitability was decided based on physiological parameters and visual findings. Lung tissue samples were collected for measurement of wet to dry ratio.
Results: The tracheal temperature in the cooling group gradually decreased during WIT and finally reached 28.5°C, while there was no decrease in the temperature of the DCD group (Figure A). In EVLP evaluation, the cooling group was significantly associated with higher PaO2/FiO2 ratio (412 ± 82 vs. 261 ± 71 mmHg, $p < 0.05$, Figure B), lower peak inspiratory pressure (13 ± 2 vs. 19 ± 4 cmH2O, $p < 0.05$), lower lung weight ratio (lung weight at 2 hour/lung weight at 0 hour, 109 ± 15 vs. 166 ± 35%, $p < 0.05$), lower wet to dry ratio (5.35 ± 0.32 vs. 6.35 ± 0.24, $p < 0.05$), and higher rate of transplant suitability (100 vs. 0%, $p < 0.05$) than control.
Conclusions: These results demonstrated that the novel chest cooling system resulted in better pulmonary function in a pig lung uDCD model, suggesting that the new cooling system without surgical intervention may protect uDCD donor lungs from ischemia reperfusion injury and expand the lung donor pool.

Figure A

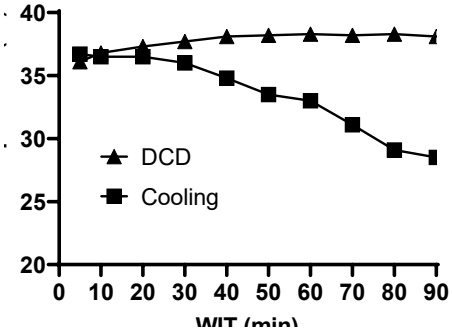
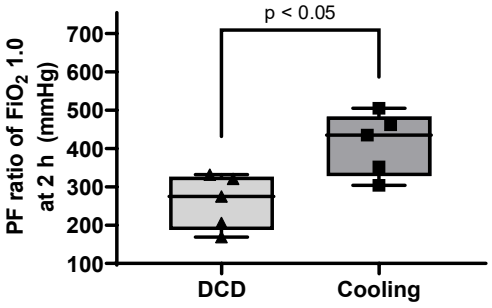


Figure B



FG2_4 NOT TOO WARM, NOT TOO COLD: REAL-WORLD MULTI-CENTER OUTCOMES WITH ELEVATED HYPOTHERMIC PRESERVATION OF DONOR LUNGS

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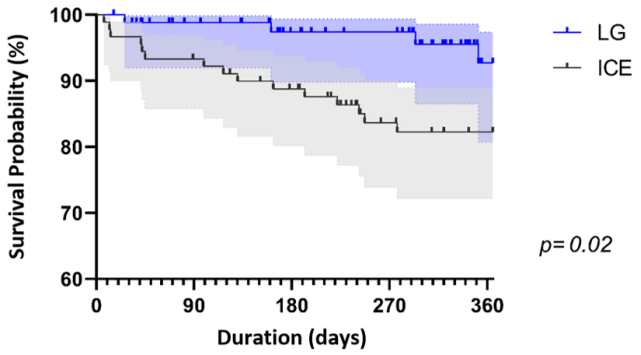
Background: Recent reports highlight the potential clinical improvements from hypothermic preservation at elevated temperatures of donor lungs, avoiding risk of mitochondrial injury with standard ice storage (ICE) where lungs reach temperatures near or below 0°C. The LUNGguard Donor Lung Preservation System (LG) is the only FDA and CE cleared preservation technology which maintains donor lungs at controlled elevated hypothermic temperatures, potentially mitigating temperature-related tissue injury. Real-world experience of this preservation strategy on recipient outcomes as studied in the GUARDIAN-Lung Registry is presented.
Methods: The GUARDIAN Lung Registry is a multicenter registry assessing outcomes following lung transplants comparing LG and ICE. Retrospective review of clinical outcomes was examined using summary statistics and Kaplan-Meyer survival analysis. Continued enrolment will allow updated data to be presented.
Results: Transplants in patients using LG (n=86) vs ICE (n=90) had similar baseline characteristics, except significantly more LG-preserved lungs were retrieved from donors after circulatory death (DCD) donors, 17.6% LG vs 6.7% ICE, $p = 0.025$, see Table). The LG cohort had a clinically meaningful 54% reduction in primary graft dysfunction at 72 hours ($p=0.058$). LG was also associated with significantly improved one year Kaplan-Meier estimated survival, 95.0% vs 90.0%, $p = 0.02$, LG vs ICE, respectively (see Figure).
Conclusions: Use of LUNGguard is associated with a reduction in PGD3 and enhanced 1-year survival compared to ICE. These data support growing evidence that avoiding donor lung near-freezing injury through controlled, elevated hypothermic preservation has a meaningful impact on post-transplant outcomes.

Table: Demographic Characteristics and Post-Transplant Outcomes in GUARDIAN-Lung

	ICE N=90	LG N=86	*p-value*
Donor Age (years)	34.9 ± 11.9	35.7 ± 13.4	0.71
Donor Sex (% Male)	51 / 90 (56.7%)	48 / 86 (55.8%)	0.91
Donor Height (cm)	170.8 ± 10.7	171.0 ± 9.7	0.93
Donor Weight (kg)	80.6 ± 24.2	77.9 ± 18.1	0.39
Donor BMI (kg/m²)	27.5 ± 7.4	26.6 ± 6.0	0.42
Donor PCO2 (mm Hg)	39.3 ± 6.5	37.6 ± 6.2	0.074
Donor PO2 (mm Hg)	374.1 ± 154.4	397.1 ± 124.8	0.28
Pack Years	4.1 ± 7.5	2.9 ± 7.0	0.25
DCD	6 / 90 (6.7%)	15 / 85 (17.6%)	0.025
Recipient Age (years)	60.9 ± 9.6	57.7 ± 12.6	0.062
Recipient Sex (% Male)	46 / 90 (51.1%)	51 / 86 (59.3%)	0.27
Recipient Height (cm)	170.3 ± 9.3	170.5 ± 10.7	0.88
Recipient Weight (kg)	76.5 ± 16.3	75.4 ± 16.5	0.67
Recipient BMI (kg/m²)	26.2 ± 4.1	25.8 ± 4.7	0.60
Waitlist Duration (days)	51.8 ± 76.1	39.3 ± 54.4	0.21
Median Waitlist	22.0	18.0	
LAS Score	51.3 ± 18.5	52.9 ± 18.8	0.56
Median LAS	44.0	46.0	
LUNGguard Temperature (°C)		4.7 ± 1.7	
Median Temperature (°C)		4.9	
TIT (minutes)	437.4 ± 142.2	446.3 ± 111.5	0.64
Distance to Organ (nautical miles)	327.5 ± 364.6	281.4 ± 385.1	0.42
FEV1/FVC Baseline	68.8 ± 22.5	70.9 ± 25.0	0.58
Creatinine (mg/dL)	0.8 ± 0.3	0.8 ± 0.2	0.15
GFR (mL/min)	86.6 ± 22.8	95.2 ± 22.1	0.012
Supplemental O2 (liters)	6.5 ± 7.1	6.3 ± 7.8	0.88
Post-Transplant Outcomes			
PGD Grade 0 at 24h	17 / 90 (18.9%)	23 / 86 (26.7%)	0.21
PGD Grade 0 within 72h	19 / 90 (21.1%)	25 / 86 (29.1%)	0.22
PGD Grade 3 at 24h	23 / 90 (25.6%)	20 / 86 (23.3%)	0.72
PGD Grade 3 at 48h	17 / 90 (18.9%)	16 / 86 (18.6%)	0.96
PGD Grade 3 at 72h	16 / 90 (17.8%)	7 / 86 (8.1%)	0.058
PGD 2 or 3 at 72h	26 / 90 (28.9%)	18 / 86 (20.9%)	0.22
PGD 3 at 48 or 72	21 / 90 (23.3%)	16 / 86 (18.6%)	0.44
Time Intubated (hours)	141.3 ± 524.2	50.4 ± 45.6	0.10
Creatinine 48HRS (mg/dL)	1.2 ± 0.6	0.9 ± 0.3	0.003
Dialysis	11/90 (12.2%)	6/86 (7.0%)	0.24
PO2 (mm Hg)	146.7 ± 69.9	153.2 ± 72.2	0.55
Post MCS	56 / 90 (62.2%)	48 / 86 (55.8%)	0.39
Post Extubation Positive Pressure Ventilation	13 / 90 (14.4%)	9 / 86 (10.5%)	0.42
Reintubation Required	37 / 90 (41.1%)	30 / 86 (34.9%)	0.40
Tracheostomy	19 / 90 (21.1%)	17 / 86 (19.8%)	0.83
ECMO	17 / 90 (18.9%)	15 / 86 (17.4%)	0.80
			0.55
In Hospital Survival	81 / 90 (90.0%)	83 / 86 (96.5%)	0.09
90-day Survival	83 / 89 (93.3%)	75 / 76 (98.7%)	0.08
6-month Survival	76 / 86 (88.4%)	63 / 65 (96.9%)	0.054

Abbreviations: BMI = body mass index; cm = centimeters; CTS = (Paragonix) cardiac transport system; DCD = donation after circulatory death; ECMO = extracorporeal membrane oxygenation; FEV1/FVC = forced expiratory volume/forced vital capacity (Tiffeneau-Pinelli index); kg = kilograms = LAS = lung allocation score; MCS = mechanical circulatory support; mm Hg = millimeters of mercury; Min = minutes; PCO2 = partial pressure of carbon dioxide; PGD = primary graft dysfunction; PHM = predicted heart mass; PO2 = partial pressure of oxygen; TIT = total ischemic time.

Figure: Kaplan-Meier One-Year Survival Analysis in GUARDIAN-Lung



FG2_5 SINGLE-CENTER SHORT TO INTERMEDIATE TERM OUTCOMES AFTER 100 DONOR HEART PROCUREMENTS WITH A NON-PERFUSING HYPOTHERMIC STORAGE SYSTEM

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Background: The Paragonix SherpaPak Cardiac Transport System is a single-use non-perfusing storage device designed for hypothermic donor heart preservation at a constant temperature between 4 and 8° C. We aimed to analyze our single center short to intermediate-term outcomes after heart transplantation following donor heart transportation with the SherpaPack.
Methods: Between November 2018 and December 2022, 100 consecutive patients with terminal heart failure undergoing heart transplantation at our institution after donor heart procurement with the SherpaPack were included in a prospective and ongoing database. Donor and recipient demographics, operative parameters, survival, primary graft dysfunction and hemodynamics were assessed; international validated risk scores for mortality prediction were calculated.
Results: The container temperature remained stable during transportation (5.7±1.4 [3-11]°C) along various distances from the donor hospital (0 to 1140 km). The mean cold ischemic time was 188±63 min. Mean age in the adult cohort (n=87) was 57±12 years, the median age in the pediatric population (n=13) was 2 (0 to 15 years). The Eurotransplant mean heart donor score was 18±4 points, with 66% of the overall donor cohort being at high risk (≥17 points). The mean recipient IMPACT Score was 8±5 points with 67% of whole recipient population at high or very high risk (≥6 points). The 30-day and in-hospital mortality were 9% and 12% and overall survival at one and three years was 85% and 78%, which reflects the higher risk donors and recipients in our cohort. However, no significant difference in survival was observed between risk groups in this small patient population. Severe primary graft dysfunction with need for temporary circulatory support (ECMO) was observed in 10 patients, 8 patients recovered and underwent ECMO explantation.
Conclusions: SherpaPack is a safe method for donor heart at a constant temperature. However further patients and longer follow-up are necessary to confirm the beneficial effect on the postoperative outcomes.

FG2_6 CUSTODIOL-N VERSUS CUSTODIOL: RESULTS FROM A PROSPECTIVE RANDOMISED SINGLE BLIND MULTICETNER PHASE III TRIAL IN PATIENTS UNDERGOING HEART TRANSPLANTATION

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Background: HTK is a well-established preservation solution in organ transplantation. HTK-N, is a novel HTK-based solution, which includes iron chelators to reduce oxidative injury, as well as L-arginine, to improve endothelial cell function. Earlier results in coronary artery bypass surgery, showed good cardiac protection without any safety concerns. The aim of this study was to evaluate the safety and ability of Custodiol-N to preserve cardiac grafts for heart transplantation
Methods: This prospective randomised, single blind multicenter non-inferiority trial was performed at three centers in Austria and Germany. 105 patients were randomized to HTK N (n=53) or HTK (n=52) as preservation solution for their donor hearts. The primary endpoint was creatine kinase (CK-MB) peak value from 4-168 hours after opening of the aortic cross clamp, with a 30% non-inferiority margin. Secondary efficacy endpoints were patient and graft survival, incidence of primary graft failure, length of intensive care unit stay. The primary endpoint was analysed in per-protocol (PP) population, whereas other endpoints were analysed in both as treated and PP populations.
Results: Average donor age (39.42±12.73 vs. 45.05±11.62; p=n.s.) and ischemic times (206.33±49.42 vs. 220.6±65.63; p=n.s.) were comparable between HTK-N and HTK groups. For the PP data set, 19 patients (HTK-N n=12, HTK n=7) were excluded due to missing CK-MB values. Average CK-MB peak values 178.17±202.41 U/L in the HTK group compared to 136.29±70,72 U/L in the HTK-N Group (p-value for non-inferiority of HTK-N by 30% <.0001). Patient and graft survival were comparable between groups at 30 days and 1-year post transplantation (HTK-N: 100%, 88,7%; HTK: 98.1%, 90,4%, p=0.83). The incidence of primary graft failure was 21.5% in the HTK and 11.3% in HTK-N group (p=0.19). Median length of intensive care unit stay was 8 days (25%-75%: 5-11 days) in the HTK-N group compared to 11 days in the HTK group (25%-75%: 6-19 days; p=0.13). Safety assessment showed even distributed adverse events with only 7 (HTK:n=4, HTK-N:n=3) possibly related to the preservation solutions.
Conclusions: This study shows that HTK-N is safe and provides similar cardiac protection as the established HTK solution. Both solutions were safe to use in clinical heart transplantation.

FG2_7 EFFECTS OF TRIIODOTHYRONINE AND PRECONDITIONING ON EX VIVO RAT HEARTS SUBJECTED TO NORMOTHERMIC PERFUSION. IMPLICATIONS FOR DONOR HEART PRESERVATION

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Background: Machine perfusion may become a platform for cardioprotective approaches, enabling repair and reconditioning of donor hearts. Ischemic preconditioning (PC) is a powerful means of cardioprotection. Triiodothyronine (T3) is repairs the injured myocardium and recently this cardioprotective action was shown in an ex vivo rat heart normothermic perfusion model (Transplant Int, in press). This study investigated potential effects of low-flow PC with and without T3 administration in an ex vivo rat heart model.
Methods: Rat hearts were perfused in Langendorff apparatus with constant flow. Control hearts were subjected to normothermic perfusion (NP) with Krebs-Henseleit for 6h (NP, n=9). Another group of hearts, after stabilization for 30min, was perfused with normal flow for 30 min followed by 5 cycles of PC (40 min of low flow perfusion and 20 min normal flow perfusion) with either vehicle (PC, n=11) or 60nM T3 (PC+T3, n=10) in the perfusate. T3 or vehicle administration started at the end of stabilization period (30min). Left ventricular end diastolic pressure (LVEDP), left ventricular developed pressure (LVDP), perfusion pressure (PP), as an indirect index of microvascular function and percentage of change of these parameters from the baseline values were measured.
Results: Results are shown in table. Baseline parameters were similar between groups. LVEDP at the end of perfusion was significantly increased from the baseline in both NP and PC groups. The magnitude of this change was significantly less in PC hearts versus NP. In PC+T3 hearts, LVEDP at the end of perfusion was similar to baseline. PP at the end of perfusion was significantly increased from the baseline in all groups, however this increase was significantly less in both PC and PC+T3 hearts versus NP. LVDP at the end of perfusion was significantly reduced from baseline in all groups and no difference between the groups was observed.
Conclusions: PC limits cardiac and microvascular dysfunction and T3 added to PC prevents the increase in LVEDP after prolonged perfusion. These data may have important therapeutic implications. A clinical study is under design to assess effects of T3 and PC in normothermic perfusion of marginal human donor hearts.

	LVEDP (mmHg)			PP (mmHg)		
	End of stabilization (30 min)	End of perfusion (360min)	% Change	End of stabilization (30 min)	End of perfusion (360min)	% Change
NP (n=9)	7.6 (0.3)	21.8 (7.0)*	188 (94)%	69 (5)	153 (47)	120 (63)%
PC (n=11)	7.7 (0.4)	13.4 (7.8)* #	73 (98)% #	68 (6)	105 (22)* #	58 (35)% #
PC+T3 (n=10)	7.6 (0.3)	8.3 (4.6) #	8 (58)% #	66 (4)	90 (19)* #	39 (27)% #

Data are presented as Mean (SD)
* p<0.05 vs baseline (30min), paired samples t-test
# p<0.05 vs NP, OneWay ANOVA

FOCUS GROUPS

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FG2_8 EARLY ECMO OVERCOMES PRIMARY GRAFT DYSFUNCTION AFTER HEART TRANSPLANT

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Background: Primary graft dysfunction (PGD) is the main cause of early mortality after heart transplantation. Despite affecting approximately 7-8% of all recipients, the etiology and optimal treatment of this condition remains unknown. Extracorporeal membrane oxygenation (ECMO) is a key treatment modality, however optimal timing of initiation has not been established.
Methods :A single-institution retrospective study was conducted. Between January 2003 and December 2022 a total of 25 recipients experienced PGD treated with ECMO. At the beginning of 2016, our institution adopted an early ECMO policy, with PGD patients placed on ECMO prior to leaving the OR at the time of transplant. Patients were stratified into pre-2016 (n=5) and post-2016 (n=20) cohorts. Outcomes including duration of support, ICU and total hospital stay, Ejection Fraction (EF), need for vasoactive or inotropic medication, in-hospital survival, 1-year survival, and complications were analyzed.
Results: Among the pre-2016 and post-2016 cohorts there was no difference in duration of ECMO, ICU stay, and total hospital stay . The average time from release of cross-clamp to initiation of ECMO was 8.04 vs 3.05 hrs in each cohort, respectively (p=0.02). In all patients, ECMO resulted in a reduction in the need for vasopressors and inotropes as assessed by the vasoactive inotrope score . LVEF normalized within the first 5 days of therapy for all patients and was sustained after decannulation. Complication rates among cohorts were similar with respect to bleeding, stroke, infection, and need for temporary dialysis. When compared to the post-2016 cohort, the pre-2016 cohort demonstrated significantly worse in-hospital (75% vs 100%, p=0.04) and 1-year(69% vs 100%, p=0.02) survival.
Conclusions: Early initiation of ECMO results in decreased mortality for PGD after heart transplant without an increased risk of complications.

Biomarkers and monitoring kidney health

FG3_1 EVOLUTION OF DDCFDNA DURING THE FIRST WEEK AFTER SURGERY PREDICTS MEDIUM TO LONG-TERM RENAL OUTCOMES

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Background: Donor-derived cell-free DNA (ddcfDNA) is usually employed starting from the second week after kidney transplantation (KT), as its earlier increase can be due to the ischemia-reperfusion injury (IRI) and would not reflect the presence of rejection. We hypothesized that ddcfDNA released soon after IRI during the first week after surgery is associated with renal function recovery after KT and can have prognostic significance.
Methods: Sixty-one (61) recipients of a first kidney graft enrolled in the Prospective Assessment of Kidney Graft Events after Transplantation by Monitoring of ddcfDNA (PRAS-KAT) study were studied at 24 hours and 7 days after reperfusion by means of ddcfDNA assessed by the Alloseq (CareDx, Brisbane, CA, U.S.) kit. Results were studied in accordance with ddcfDNA relationship with Delayed-Graft Function (DGF) duration, 6-month eGFR and 7-year iBox-estimated graft survival.
Results: Mean age of the included patients was 60.3±12.3 years. Six were recipients of a living donor, 25 of a DBD donor, 25 of a DCD III donor and 5 of a DCD type 2 donor. Levels of ddcfDNA at 24 hours after reperfusion were associated with functional DGF (7,20 [2,35-15,50] versus 2,70[1,55-4,05]%, P=0,023) and eGFR at 6 months after transplantation (r = -0,341, P = 0,015). At day 7, ddcfDNA levels were associated with dialysis duration in patients with DGF ((r = 0,631, P = 0,004) and worse iBox-estimated renal graft survival at 7 year after transplantation at multivariable analysis (β-0,42, P = 0,001). Patients with early normalization of ddcfDNA (<0.5%) at 1 week had better iBox estimated graft survival at 7 years (79,5±16,8 %) in comparison with patients whose ddcfDNA at 1 week was ≥0,5 % (67,7±24,1 %) (p=0,047).
Conclusions: early kinetic of ddcfDNA after transplantation is associated with renal graft recovery and medium to long-term graft. It can also provide an objective estimate of the severity of the IRI

FG3_2 MAGNETIC RESONANCE IMAGING TEXTURE ANALYSIS TO ASSESS GRAFT INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY IN PATIENTS WITH TRANSPLANTED KIDNEYS

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Background: Interstitial fibrosis / tubular atrophy (IFTA) is a common, irreversible, and progressive form of chronic kidney allograft injury, and it is considered a critical predictor of kidney allograft outcomes. In clinical practice, the extent of IFTA in renal cortical tissue is estimated through analysis of graft biopsy, which is an invasive procedure. A non-invasive test accurately reproducing the degree of IFTA would be beneficial for patients. We aimed at evaluating the accuracy of an MRI radiomic-based machine learning (ML) algorithm in estimating the degree of IFTA in a cohort of patients who received graft biopsy and MRI for clinical practice.
Methods: Patients who underwent MRI and renal biopsy within a 6-month interval from 1/1/2012 to 1/3/2021 were included. Stable MRI sequences were selected, and renal parenchyma, renal cortex and medulla were segmented using the 3DSlicer software. After image pre-processing and wavelet filtering, images were elaborated through an in-house version of py-radiomics extracting radiomic features. These were subsequently selected through a LASSO algorithm for their highest correlation with the reference standard and lowest intercorrelation. Selected features and relevant patients' clinical data were used to produce ML-algorithms using 70% of the study cases for training and validation, with a 10-fold cross-validation, and 30% for model testing. Diagnostic performances were evaluated using AUC with a 95% confidence interval (CI).
Results: 70 coupled tests (63 patients, 35.4% females, mean age 52.2 years) have been included and subdivided into a wider cohort of 50 for training and a smaller cohort of 20 for testing (table 1). For IFTA ≥ 25%, AUCs in test cohort were 0.60, 0.59, and 0.54 for radiomic features only, clinical variables only, and combined radiomic-clinical model, respectively. For IFTA ≥ 50%, AUCs in training cohort were 0.89, 0.84, 0.96, and in test cohort were 0.82, 0.83, and 0.86, for radiomic features only, clinical variables only, and combined radiomic-clinical model, respectively.
Conclusions: An ML-based MRI radiomic algorithm showed promising discrimination capacity for patients with IFTA>50%, especially when included clinical variables.

Table 1 Clinical Variables		**Total (n=70)**	**Training set (n=50)**	**Test set (n=20)**
Sex (M : F)		45 : 25	33 : 17	12 : 8
Ethnicity (Caucasian : Sub-Saharan)		62 : 8	45 : 5	17 : 3
Age (years) (mean ±SD)		52.19 ±12.76	54.10 ±12.36	47.41 ±12.78
RM/Biopsy interval (days) (median, IQR)		16, 4-48.75	16, 4-48.75	15, 4.75-49
RM/Biopsy interval >90 days (n, %)		13 (18.57%)	10 (20%)	3 (15%)
BMI (median, IQR)		24.59, 22.47-27.30	25.39, 22.68-27.90	23.50, 22.46-25.39
eGRF at biopsy (median, IQR)		25.68, 11.88-35.51	26.90, 13.08-34.95	20.17, 11.10-38.08
Proteinuria/creatininuria, g/g (median, IQR)		0.79, 0.30-2.10	0.74, 0.21-2.09	0.79, 0.35-2.00
Transplant type (n, %)	**DBD**	59 (84,29%)	42 (84,00%)	17 (85,00%)
	DCD	2 (2,86%)	2 (4,00%)	0 (0,00%)
	LD	9 (12,86%)	6 (12,00%)	3 (15,00%)
Transplant age (years) (median, IQR)		0.78, 0.31-6.36	1.03, 0.36-0.77	0.62, 0.24-1.78
IFTA % (median, IQR)		20, 10-30	20, 10-37.5	20, 10-30
IFTA ≥ 25% (n, %)		29 (41.42%)	21 (42.00%)	8 (40.00%)
IFTA ≥ 50% (n, %)		14 (19.72%)	11 (22.00%)	3 (15.00%)

Table 1: clinical characteristics of the included patients / paired tests. DBD donation after brain death; DCD donation after cardiac death; LD living donor

FG3_3 VALIDATION OF THE INTERNATIONAL IGA NEPHROPATHY PREDICTION TOOL IN KIDNEY TRANSPLANT RECIPIENTS WITH IGA NEPHROPATHY RECURRENCE

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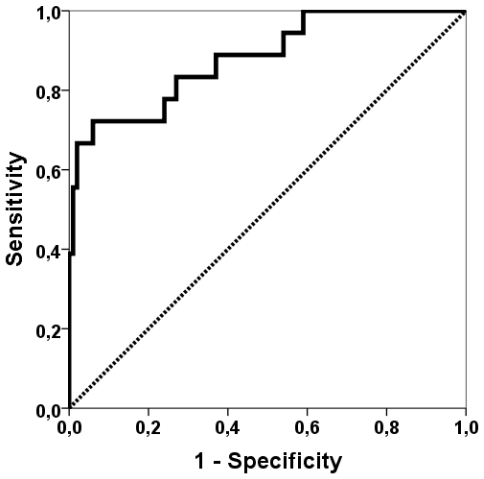
Background: The recurrence of IgA nephropathy (rIgAN) worsens the prognosis of renal transplantation, representing the third cause of graft loss in these patients. Several variables at the time of recurrence, such as renal function, proteinuria, steroid withdrawal, and MEST-C findings relate to a higher risk of graft loss after recurrence. The International IgAN Prediction Tool (IIgAN-PT) uses clinical and histological predictor variables at the time of native kidney biopsy to predict the risk of end-stage kidney disease (ESKD) or a 50% decline in estimated glomerular filtration rate, allowing a proper patient-specific risk stratification. Our aim was to analyze the performance of this tool in a population of kidney transplant recipients with rIgAN.
Methods: A multicenter retrospective study was carried out including renal transplant recipients with biopsy-proven IgA nephropathy as the underlying disease in which the recurrence of the primary disease had been verified by means of graft biopsy. IIgAN-PT was used to calculate the risk of ESKD or a 50% decline in eGFR at 3-years in an app calculator (qxmd.com/calculate-by-qxmd).
Results: 118 kidney transplant recipients were included with an age of 46 ± 14 years at recurrence, 79% male, with a mean time to biopsy of 63 ± 67 months and a post-transplant follow-up of 120 ± 72 months. After recurrence, 32 (27%) transplants were lost after 37 ± 27 months, excluding death. Mean IIgAN-PT was 16 ± 13%. By Cox regression analysis, IIgAN-PT related to death censored graft loss (DCGL) (HR 1.115, 95%CI 1.080-1.151, p < 0.001). By logistic regression analysis IIgAN-PT related to DCGL at 3 years (OR 1.279, 95%CI 1.145-1.428, p < 0.001) with good discrimination (AUC-ROC 0.881, 95%CI 0.78-.0.973, p < 0.001, figure 1) and good calibration (Hosmer-Lemeshow test p = 0.152). Kidney transplant recipients with a calculated risk above 14% had a higher risk of 3-year DCGL (HR 8.112, 95%CI 3.994-16.476, p < 0.001) with a sensitivity of 72%, a specificity of 94%.
Conclusions: IIgAN-PT performed well in a kidney transplant population with rIgAN with good discrimination ability and good calibration to predict DCGL. Using a app calculator, we can stratify patients with the highest risk of graft loss due to IgAN recurrence and carry out the most appropriate therapy to improve their prognosis.



FG3_4 CORTICAL IRON DEPOSITION ASSESSED BY MAGNETIC RESONANCE IMAGE IS ASSOCIATED WITH FIBROSIS

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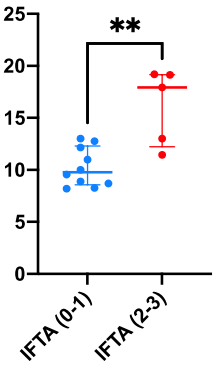
Background: Fibrosis is responsible for the loss of kidney function as a result of several insults, such as ischemia-reperfusion injury (IRI) or hyperfiltration. This process can continue even after cessation of the primary insult, as documented in acute kidney injury to chronic kidney disease. Recently, we discovered that iron accumulation is a hallmark of fibrotic diseases. We found that in mouse models, iron deposition in the kidney accompanies the progression of the disease. Based on these results, we propose that chronic-low grade hemolysis produced in situation like IRI may be one of the drivers of fibrosis through the damage that the filtrated hemolytic iron cause to the kidneys. Early detection of this iron could help the detection of ongoing fibrogenesis and improve the outcomes by prompt intervention. The challenge of this approach is the lack of non-invasive markers of fibrosis. We evaluated if magnetic resonance image (MRI)-based detection of iron levels in the kidney are correlated to fibrosis in biopsies from kidney transplant (KT) recipients.
Methods: After approval from the Institutional Revision Board, we carried out a transversal study in our center between 2020 and 2021. We evaluated iron deposits through MRI in patients who underwent a kidney biopsy (per protocol or by clinical indication) and its association with histological parameters. MRI was performed at the same period the biopsy was done. Iron deposits were estimated by using the R2* sequence considering the *Grassedonio* protocol.
Results: We collected data from 15 kidney transplant recipients. Mean age, time from KT to biopsy and eGFR were respectively 58.3 years old, 4.3 years and 44.4 ml/min/1.73m^2. We analyzed by MRI the R2* signal in the kidney cortex, and their level of fibrosis measured on the biopsies (IFTA score, interstitial fibrosis and tubular atrophy). We found that patients with high IFTA score (2 and 3) presented with significantly higher R2* signal (p=0.005), than patients with low IFTA score (0 and 1). We also found positive and significant correlation between IFTA (0-3) and iron deposits (Spearman correlation index: r=0.7537, p=0.0012).
Conclusions: Iron deposits in the kidney are higher in patients with more fibrosis, and its detection through MRI could be considered a non-invasive marker.



FG3_5 INTRA-GRAFT TEMRA CD8+ T CELLS: AN INDEPENDENT PREDICTOR OF KIDNEY ALLOGRAFT FAILURE INDEPENDENT OF REJECTION CATEGORIES

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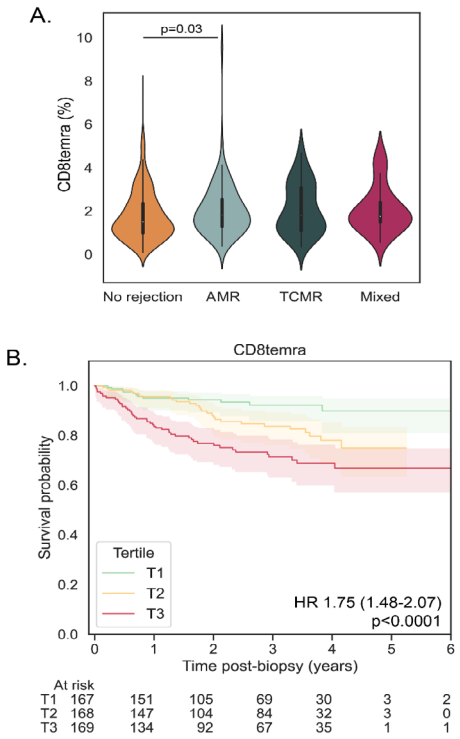
Background: The terminally differentiated effector memory CD8+ (TEMRA CD8+) T cells, which re-express the native CD45RA in absence of CCR7, have been hypothesized to be a potential key player in humoral allograft rejection. This study aims to better characterize the association of intra-graft TEMRA CD8+ T cells with both the main Banff rejection categories and graft outcome.
Methods: The proportion of TEMRA CD8+ T cells was estimated via the deconvolution of three transcriptomic datasets (N=224, N=403 and N=282) of kidney transplant biopsies using a novel signature matrix derived from single cell transcriptomics. Difference in TEMRA CD8+ T cell proportion was assessed with Student t-test for each pair of Banff diagnoses (No rejection, AMR, TCMR and Mixed rejection). The discrimination performance was assessed with pairwise AUC and the polytomous discriminant index (PDI) for multi-class discrimination. Association with graft failure was performed with a Cox model, adjusted for time post-transplantation and reported as hazard ratio (HR). The survival of the TEMRA CD8+ T cell tertiles was visualized with Kaplan Meier estimators.
Results: No significant differences in TEMRA CD8+ T cell proportion were observed between the Banff categories (**Fig. 1A**), excepted for AMR vs No rejection (Student t-test p=0.033, although the magnitude of the difference was low (0.29% [0.03% - 0.58%]). TEMRA CD8+ T cells demonstrated limited discrimination performance between the major Banff rejection categories: AUC rejection vs no rejection: 0.59 [0.54-0.64]; the best AUC for No rejection vs Mixed rejection: 0.60 [0.51-0.69]); PDI: 0.29 [0.22-0.36] (a random classifier has a PDI of 0.25). Despite the lack of relation to specific inflammatory patterns/rejection subtypes, TEMRA CD8+ cells demonstrated a strong association with graft failure (HR 1.75 [1.48-2.01], p<0.0001) (**Fig. 1B**) which remained consistent across the independent subsets with survival data available (HR 2.00 [1.45-2.77], p<0.0001 and HR 1.75 [1.45 -2.11], p<0.0001).
Conclusions: We demonstrated a strong association between the intra-graft proportion of TEMRA CD8+ T cell and graft failure, independent of the Banff rejection subtypes. TEMRA CD8+ T cell cells constitute a promising and specific therapeutic target for improvement of transplant outcome.



FG3_6 LONGITUDINAL MONITORING OF TORQUE TENO VIRUS DNAEMIA IN RENAL TRANSPLANT RECIPIENTS PREDICTS LONG-TERM COMPLICATIONS OF INADEQUATE IMMUNOSUPPRESSION

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Background: Recent studies have suggested that Torque Teno Virus (TTV) load reflects the "depth" of therapeutic immunosuppression during the first 12 months post-transplantation but whether this non-invasive biomarker can predict long-term complications of inadequate immunosuppression is not yet established.
Methods: A discovery cohort of 124 healthy controls and 34 stable kidney transplant recipients enrolled 23±17 months after transplantation was used to defined thresholds of TTV DNAemia. These results were validated in an independent validation cohort of 92 kidney tranplant recipients, enrolled 1-year post transplantation and prospectively followed for 3 years.
Results: with the discovery cohort, we defined the lower (3.75 log_{10} cp/mL) and upper (5.1 log_{10} cp/mL) threshold of TTV DNAemia associated respectively with : i) an increased T cell residual activatability *in vitro* as well as the magnitude of antibody response against a model protein antigen (flu vaccine), ii) and a higher risk for serious infection or cancer during the next 50 months in stable kidney transplant recipients. In the validation cohort, patients in whom the yearly TTV DNAemia was within target at ≥ 2/3 time points were less prone to experience long-term complications due to inadequate immunosuppression (defined as *de novo* DSA, biopsy proven rejection, serious infection or cancer). Multivariate analysis confirmed that in contrast with all other variables (including T0 of CNI), in target TTV DNAemia was the only variable independently associated with a reduced risk for long-term complications due to inadequate immunosuppression [HR:0.29 (0.09-0.82); p=0.025].
Conclusions: Longitudinal monitoring of TTV DNAemia in kidney transplant recipients predicts long-term complications due to inadequate immunosuppression and might serve for individual optimization of therapeutic immunosuppression.

FG3_7 TORQUE TENO VIRUS PLASMA CONCENTRATION TRENDS IN KIDNEY TRANSPLANT RECIPIENTS BEFORE PATHOGENIC INFECTIONS AND ALLOGRAFT REJECTION

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Background: In kidney transplant recipients (KTRs) under or over immunosuppression may lead to allograft rejection and opportunistic infections, respectively. The presence and/or concentration of Torque Teno Virus (TTV), a ubiquitous viral species, may act indicate the net state of immunosuppression, thus informing infection and rejection probabilities.
Methods: 1980 plasma samples from 255 CTOT–08 subjects were analysed by gene expression profiles (GEP) for rejection (AJT 19:98-109,2019) and by NGS for dd cfDNA (CJASN 16: 1539–1551, 2021), as previously described. The NGS data was further analysed to detect DNA viruses, with presence was ascertained by a combination of Reference Assisted Assembly and Kmer-frequency based methods. Viral concentration was calculated as the number of associated NGS reads normalized to viral genome length.
Results: To assess correlation between TTV and infection, TTV concentration was assessed from 150 days before to 49 days after reported clinical infections of BKV, CMV, EBV, hepatitis B or influenza (Fig. 1). Concentrations of TTV increased from 150 to 0 days before the onset of infection, with a Pearson correlation of 0.99 between median values and days pre-infection (p=0.0242). Before and after clinically reported rejection events, TTV concentration values were not significantly different based on the Fisher-test before and after rejection (Fig. 1). The TTV positivity rates did not vary significantly for either infection or rejection events. The probability of allograft rejection (subclinical acute rejection (subAR) or acute rejection (AR)) given a positive GEP was 0.491. For subAR or AR, the rejection probability increased when either TTV or TTV and viral pathogens were absent. Conversely, subAR and AR rejection probabilities decreased when TTV or TTV and viral pathogens were present. Similar patterns were observed for subAR but not AR analysed separately (Table 1).
Conclusions: In this retrospective study of TTV dynamics in the context of clinical rejection and infection events, we found that TTV concentration correlates with events such as pathogenic viral infections and allograft rejection. Our results suggest that profiling of viral DNA including TTV in KTRs may serve as a useful biomarker of net state of immunosuppression.

FOCUS GROUPS

Biomarkers and monitoring kidney health

Figure 1:

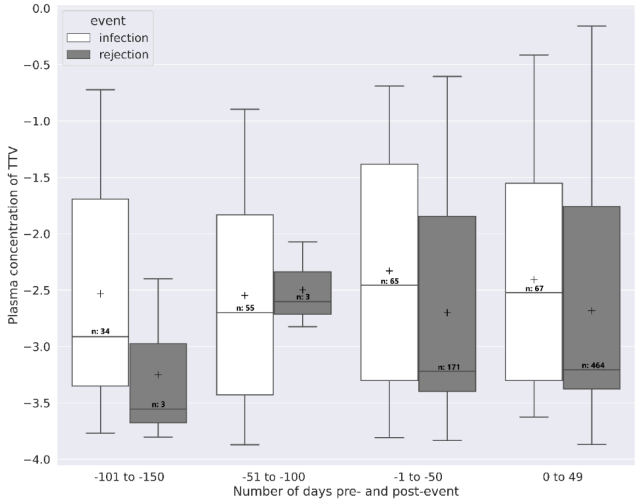

Table 1: Synergy of mNGS viral detection in samples positive for gene expression profile-predicted rejection

	Conditional probability of rejection				
Rejection type	Viral pathogen, TTV absent	TTV absent	GEP[a] positive	TTV present	Viral pathogen and TTV present
subAR[b] or AR[c]	0.568	0.566	0.491	0.415	0.462
subAR	0.362	0.349	0.285	0.220	0.192
AR	0.207	0.217	0.206	0.195	0.269
dd cfDNA > 0.7%	0.466	0.434	0.279	0.122	0.154

[a]Gene expression profiling – TruGraf assay

[b]Subclinical acute rejection

[c]Acute rejection

FG3_8 TORQUE TENO VIRUS VIRAL LOAD PREDICTS SARS-COV-2 VACCINE RESPONSE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Transplant recipients display poor responses to SARS-CoV-2 mRNA vaccines. In this retrospective study, we investigate Torque teno virus (TTV) viral load (VL), a ubiquitous virus reflecting global immune response levels, as a predictive factor of vaccine response in kidney transplant recipients (KTR).
Methods: 459 KTR having received two SARS-CoV-2 mRNA vaccine doses were enrolled, and 241 of them subsequently received a third vaccine dose. Anti–receptor-binding domain (RBD) IgG response was assessed after each vaccine dose and TTV VL was measured in pre-vaccine samples.
Results: Pre-vaccine TTV VL >6.2 log10 copies (cp)/mL was independently associated with non-response to two doses (Odds Ratio (OR)=6.17, 95% confidence interval (CI95)=2.42–15.78) as well as to three doses (OR=3.62, 95% CI95=1.55–8.49). In non-responders to the second dose, high TTV VL in pre-vaccine samples or measured before the third dose were equally predictive of lower seroconversion rates and antibody titers.
Conclusions: High TTV VL before and during SARS-CoV-2 vaccination schedules are predictive of poor vaccine response in KTR. This biomarker should be further evaluated regarding other vaccine responses.

Do we need incompatible kidney transplant

FG4_1 IS UNSPECIFIED (NON-DIRECTED) KIDNEY DONATION JUSTIFIED? RESULTS FROM A PROSPECTIVE STUDY OF 837 DONORS

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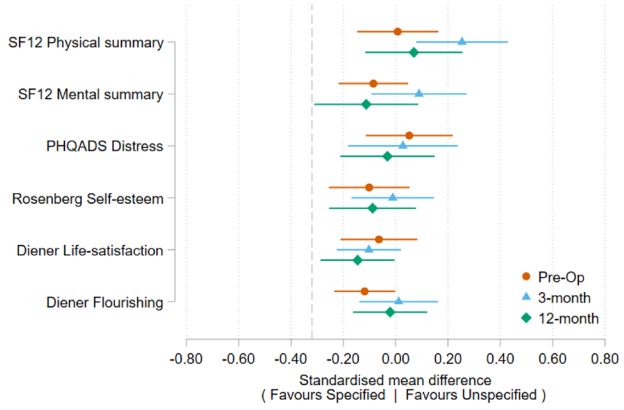
Background: Unspecified Kidney Donation (UKD) is a practice which remains illegal in most countries across the world. UKD in the United Kingdom (UK) has grown into an established practice, with donors making an increasingly valuable contribution to the UK living donor programme. We present the results from a national, multicentre, prospective study conducted as part of the Barriers and Outcomes in Unspecified Donation (BOUnD) study to compare outcomes between specified (SKDs) and unspecified kidney donors (UKDs).
Methods: Participants of BOUnD were recruited from all 23 kidney transplant centres in the UK. Longitudinal physical and psychosocial outcome data were collected over 12 months and were correlated with national data from NHS Blood and Transplant (NHSBT). The primary aim was to establish whether there were differences in outcome between UKDs and SKDs.
Results: 837 participants were recruited to BOUnD, of which 373 proceeded to donation. There was no statistically significant difference in donation rates between the two groups (44.6%; 204 SKDs vs. 169 UKDs; p=0.944). UKDs were more likely to be male, single and without children or dependents. There was no significant difference in age between the two groups. Both groups were equally motivated to donate by the desire to help someone in need (SKD 96.6% vs. UKD 98.9%; p=0.157). There were no statistically significant differences in any of the psychosocial outcome measures (figure 1; p>0.05), including regret (p=0.453). At 12 months there were statistically significant differences in creatinine, glomerular filtration rate and systolic blood pressure, however the differences were small and therefore unlikely to be of clinical significance (Cr SKD 105.9 vs UKD 102.4; p=0.032; GFR SKD 59.5 vs UKD 61.3; p=0.014; Systolic BP SKD 128.4 vs 123.7; p<0.001).
Conclusions: This study has demonstrated some demographic differences between UKDs and SKDs. However, there are no statistically significant differences in psychosocial outcomes, including regret. Physical outcomes are also comparable. This data hopefully provides reassurance to those performing UKD and to those who may be considering establishing a practice in their country.



FG4_2 THE IMPACT OF NON-DIRECTED ALTRUISTIC DONORS (NDAD) IN LIVING KIDNEY EXCHANGE IN THE UK

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Background: The first kidney transplants from NDADs happened in the UK in 2007, following a change in legislation. Until 2012, NDADs donated directly to the deceased donor waiting list (DDWL), following the deceased donor offering scheme to identify the recipient. In 2012, NDADs could choose to donate to DDWL or into the UK Living Kidney Sharing Scheme (UKLKSS), whereby they would donate into a chain of incompatible (and some compatible) pairs, enabling a chain of 2 or 3 transplants, completing with a recipient on the DDWL. Since 2018, NDADs have been included in the UKLKSS by default, to maximise transplants. This is subject to not matching with a high priority recipient on the DDWL. If they are not matched in a chain, then they have the choice of donating direct to DDWL.
Methods: This study examines the benefit that NDADs have made to the kidney exchange programme in the UK (ie UKLKSS), by looking at donor and transplant activity.
Results: In 2012, the first year in which donors could choose to donate into the UKLKSS to create chains of transplants, there were 60 donors, only 3 (5%) of whom donated into the pool. These 3 donors each generated 2 transplants, involving one pair in the UKLKSS and one recipient on the DDWL. In 2013, 21% of 107 NDADs donated to create a chain, rising to 57% of 70 NDADs in 2022 resulting in 130 transplants. In total, between 2012 and 2022, there were 887 NDADs in the UK donating either direct to the DDWL (n=577, 65% of donors) or into the UKLKSS and creating a chain of transplants (n=310, 35% of donors). Taking into account the additional 443 transplants generated by the chains, this resulted in a total of 1330 transplants. This included 176 recipients with more than 5 years waiting time on the DDWL and 30 paediatric recipients.
Conclusions: NDADs are an important contributor to living donor kidney transplantation in the UK and in the last 5 years, 55% of 344 NDADs have created a chain of 2 or 3 transplants rather than a single transplant through donation direct to the DDWL. The 631 transplants resulting from the 344 NDADs in the last 5 years, represent 15% of all living donor transplants in the UK in that time.

FG4_3 COMPARING OUTCOMES OF KIDNEY EXCHANGE PROGRAMMES WITH DIRECT LIVING DONOR KIDNEY TRANSPLANTATION IN A COUNTRY WITH HIGH LIVING DONATION RATES

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Background: Kidney exchange programmes (KEP) provide an option for transplantation for patients who cannot find a compatible or suitable living donor. Compared to non-KEP, these patients are often higher risk patients on baseline due to higher sensitization, longer dialysis vintage and other risk factors resulting in challenges around their transplants. In KEPs, either the donor's kidney is transported to the recipient centre, or the donor travels to the recipient centre for the nephrectomy. Importantly, the cold ischaemia time (CIT) is prolonged when the graft is transported to another hospital, and it is unknown if any mode of transportation is favoured above the other. In our national KEP, the donor travels to the recipient center. In this study, we assessed the differences in graft outcomes between KEP and non-KEP living donor kidney transplants (LDKT).
Methods: All LDKTs performed nationally from 2004 - 2021 were included. The primary outcome measures were 5- and 10-year death censored graft survival (DCGS). The secondary outcome measures were delayed graft function (DGF), rejection rates and patient survival. We used propensity score-matching to account for differences in pre-transplant covariates.
Results: 7536 LDKTs were included of which 694 (9.21%) transplanted via KEP. There was no difference in DCGS at 5 year (survival probability 0.916 (95% CI: 0.894 - 0.939) for KEP versus 0.919 (0.912 - 0.926, p = 0.82) for non-KEP) and 10 year DCGS (survival probability 0.883 (95% CI: 0.857 - 0.910) for KEP and 0.882 (95% CI: 0.874 - 0.890, p < 0.01) in non-KEP, figure 1). We found significant differences in DGF (11.85% versus 5.17%, p < 0.01), 5 year rejection (11.76% versus 7.09%, p < 0.001) and 5 year patient survival: 0.839 (95% CI: 0.812 - 0.868) in KEP and 0.895 (95% CI: 0.887 - 0.902, p < 0.001) in non-KEP. The significant difference in patient survival turned not significant after propensity score-matching.
Conclusions: The excellent results of patients transplanted through KEP highlights the unique option for patients without a compatible or suitable living donor that would otherwise not have been possible without specific and more invasive pre- and post-transplant treatments. The long-term transplant outcomes of KEP are comparable to non-KEP LDKTs and this takes away another level of reluctance to further develop KEPs.

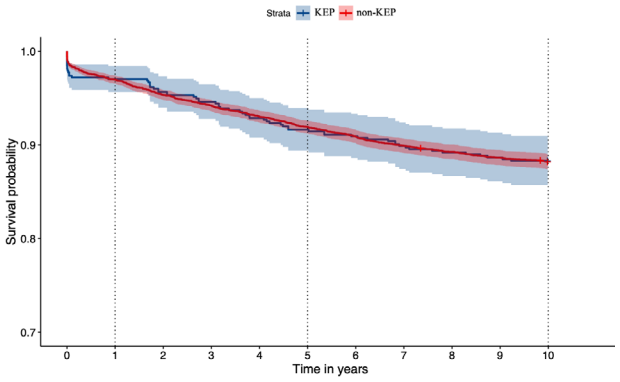

Figure 1. Kaplan-Meier survival estimates for 10-year death censored graft survival.

FG4_5 DESENSITIZATION AND IMMUNOMODULATION IN SENSITIZED KIDNEY TRANSPLANT RECIPIENTS: A DELPHI METHOD CONSENSUS FROM THE ENGAGE WORKING GROUP OF ESOT

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Background: The objective of the EuropeaNGuidelines for the mAnagementof Graft rEcipients (ENGAGE) working group was to obtain a consensus among European experts on desensitization and immunomodulation of kidney recipients, according to defined pre-transplantation patient humoral risk profiles.
Methods: ENGAGE working group included leading experts in the field of transplantation (3 surgeons, 5 nephrologists and 2 immunologists) and performed a systematic literature search through the formulation of PICO (patient/population, intervention, comparison, outcomes) questions, evaluating antibody removal strategies, induction therapies, biological drugs and maintenance immunosuppression in 5 immunological risk categories following cytotoxic/flow cytometry crossmatches and solid phase assay results. Subsequently, 43 statements based on opinion and clinical experience were produced and proposed to a panel of 53 experts, using the DELPHI Methodology. The questionnaire was administered twice (1st and 2nd wave). aiming to reach at least a 75% consensus agreement for each statement.
Results: After two rounds of voting, 41/43 statements reached an overall agreement > 75% on the following themes: first line desensitization strategy with plasma exchange and intravenous immunoglobulin, lymphocyte depleting agents vs IL-2 receptor monoclonal antibodies, role of Rituximab to prevent Ab-mediated injury, role of Imlifidase as a desensitizing agent in recipients from deceased donors, maintenance immunosuppression with tacrolimus, mycophenolic acid and steroid vs minimization and use of mTOR-inhibitors. Consensus was not reached for 2 statements related to the use of complement-inhibitors as a prophylaxis of antibody-mediated rejection
Conclusions: This methodology has allowed to reach a high degree of consensus among the experts in the management of desensitization and immunomodulation strategies of stratified immunological risk kidney transplant recipients

FG4_6 CLINICAL OUTCOMES OF ABO- AND HLA-INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION: A NATIONWIDE STUDY

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Background: ABO-incompatible (ABOi) or Human leukocyte antigen-incompatible (HLAi) living donor kidney transplantation (LDKT) is increasing, however, still inferior to immune-compatible transplantation. We aimed to analyze clinical outcomes of ABOi or HLAi LDKT using nationwide cohort data.
Methods: We utilized the nationwide data repository from the Korean Organ Transplantation Registry (KOTRY) with the cases of LDKT between 2009 and 2018. The kidney transplants were classified according to the presence of anti-A/B or donor-specific anti-HLA (HLA-DSA) antibodies. We compared the incidence of biopsy-proven acute rejection (BPAR), graft survival, and patient survival.
Results: A total of 5046 patients were classified into three groups: transplants in recipients with HLA-DSA (DSA+, n=512), transplants in recipients without HLA-DSA and ABOi donors (DSA- & ABOi, n=1188), and transplants without HLA-DSA and ABO compatible donors (CONTROL, n=3346). The incidence of acute antibody-mediated rejection (AABMR) was the highest in the DSA+ group, followed by DSA- & ABOi group, both higher than the CONTROL group (p<0.001, DSA+ vs. CONTROL; p=0.017 DSA- & ABOi vs. CONTROL). The overall graft survival was superior in the CONTROL group compared to other groups (p=0.005, DSA+ vs. CONTROL; p=0.039, DSA- & ABOi vs. CONTROL). The overall patient survival was superior in the CONTROL group compared to DSA- & ABOi group (p=0.020). For subgroup analysis of the DSA+ group, no statistical difference in BPAR, graft survival, and patient survival was revealed between ABO-incompatible and compatible groups. For DSA- group, the incidence of AABMR and graft loss was higher in ABOi than ABO-compatible group. The multivariable analysis resulted that positive T cell crossmatch (HR 1.962, 95% CI 1.036-3.715, p=0.039), ABOi (HR 1.496, 95% CI 1.041-2.151, p=0.030), AABMR (HR 2.901, 95% CI 1.751-4.807, p<0.001), and ATCMR (HR 3.987, 95% CI 2.634-6.036, p<0.001) were risk factors of graft loss.
Conclusions: The presence of anti-A/B or donor-specific anti-HLA(HLA-DSA) antibodies had unfavorable impacts on clinical outcomes in living donor kidney transplantation. The suspicion of hostile events and appropriate management for AABMR should be undertaken to improve graft and patient survival.

FG4_7 CLINICAL OUTCOMES IN ABO MISMATCHING KIDNEY TRANSPLANTATION IN PATIENTS WITH HIGH BASELINE ANTI-A/B ANTIBODY TITER

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Background: ABO incompatible (ABOi) kidney transplantation (KT) has been considered to overcome donor shortage. We investigated the long-term clinical outcomes in ABOi KT in patients with high baseline anti-A/B antibody titer.
Methods: We retrospectively included 271 patients who had undergone ABOi KT from May, 2009 to November, 2020. One hundred and ninety-one patients with a baseline immunoglobulin G (IgG) titer of ≥1:128 were assigned to the high-titer group and 80 patients with a baseline titer of ≤1:64 were assigned to the low-titer group. We used a protocol composed of rituximab, plasmapheresis, and intravenous immunoglobulin (RTX/PP/IVIG). We compared the clinical outcomes of the two groups
Results: The median follow-up periods were 59.12 months (high titer group) and 41.53 months (low-titer group) (p = 0.003). The high titer group required more sessions of PP/IVIG than the low titer group (7.50±2.47, 3.39±1.30, p < 0.001, respectively). Patient survival at 5 years was 93.80% in high titer and 96.30% in low-titer group (p = 0.178). Graft survival at 5 years was 90.00% in high titer and 92.60% in low-titer group (p = 0.563). During the follow-up period to five years, antibody titer remained higher in the high titer group. And serum creatinine showed no difference between two groups up to 9 years (p for interaction = 0.171). No significant differences were detected in the graft survival rate, patient survival rate and rejection free survival rate between two groups. However, the infection free survival rate was significantly lower in the high-titer group (p = 0.049). The incidence of bacterial infection was higher in high-titer group (45.00% vs. 28.27%, p = 0.008).
Conclusions: Patients with high baseline anti-A/B IgG isoagglutinin titers had equally successful long-term outcomes as those with low titers. However, ABOi KT in the high-titer group may require greater caution compared to the low-titer group because of the higher tendency of infection

FOCUS GROUPS

Do we need incompatible kidney transplant

FG4_8 ENZYMATIC CONVERSION OF HUMAN BLOOD GROUP A KIDNEYS TO UNIVERSAL BLOOD GROUP O

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Background: The ABO blood group restriction on allocation of donor organs leads to waiting time disadvantages for individuals of more restrictive blood types. Here, we outline the first preclinical use of two enzymes from *Flavonifractor plautii* to convert human blood group A kidneys to the universal blood group O.
Methods: Six pairs of human kidneys rejected for transplantation and offered for research were used to in this study with approval from the National Research Ethics committee and Research and Development office (NRES: 15/NE/0408). Three pairs were perfused for 6hrs using normothermic machine perfusion (NMP), and three pairs were perfused for 24hrs using hypothermic machine perfusion (HMP), with one kidney per pair randomised to enzyme treatment. Cortical biopsies collected throughout perfusion were examined for antigen loss using immunofluorescence microscopy.
Results: After 2hrs of NMP, a significant loss of 83.4±10.2% blood group A antigen expression was observed compared to pre-treatment levels (p=0.012), while no significant changes were observed in control kidneys (p=0.999). For HMP, a maximal loss of 71.2±21.9% was observed after 6hrs (p=0.066), with no decrease observed in the contralateral controls (p=0.977). Haemodynamic perfusion parameters were stable in both cohorts, with no significant difference between control vs treated kidneys.
Conclusions: Our results show a loss of 70-80% of blood group A antigens in as little as 2hrs of NMP, and 6hrs of HMP. These approaches pave the way for the first clinical studies that could herald the start of a new era that transforms donor organ allocation in kidney transplantation.

The clinical spectrum of kidney transplant rejection

FG5_1 MICROVASCULAR INJURY, EITHER IN DSA POSITIVE OR NEGATIVE ANTIBODY-MEDIATED REJECTION (ABMR), DETERMINES THE PROGNOSIS IN RENAL ALLOGRAFTS

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Background: ABMR has well-defined histomorphological lesions, like C4d staining or microvascular (MV) inflammation [(g + ptc) ≥ 2]. Although these histologic features of ABMR (ABMRh) are usually compatible with donor-specific antibodies (DSA), it is demonstrated that recipients can develop ABMRh in the absence of DSAs. Indeed, DSA can not be found in 40-60% of patients with marked microvascular inflammation (MVI). We aimed to investigate the relationship between PTC macrophage (M), neutrophil, and HLA-DR positive cell infiltration with variable clinical presentations of ABMR.
Methods: A total of 125 cases with acute ABMR categorized into 4 groups; Group 1: DSA(+) ABMR, Group 2: DSA(-) ABMR, Group 3: DSA(+) mixed rejection (ABMR+vascular rejection), and Group 4: DSA(-) mixed rejection. Glomerular and PTC macrophage, neutrophil, and HLA-DR positive cells were graded.
Results: The type of ABMR showed a significant correlation with PTC C4d expression, TMA, PTC destruction, microvascular macrophage, neutrophil, and DR+ cell infiltration (p<0.01 for all). Group 3 showed the highest MV inflammation, PTC destruction, C4d expression, and TMA. Groups 4, 1, and 2 followed Group 3, respectively, and Group 2 showed the best outcome. Also, patients in Group 3 developed the highest and earliest IF and TG development during follow-up (p<0.01). Similarly, Groups 4, 1, and 2 followed Group 3 regarding the development of IF and TG. PTC C4d expression significantly correlated with PTC destruction and DSA positivity (p<0.001). Overall 5-year graft survival was 86%, 51%, 45%, and 26% for Groups 2, 1, 4, and 3, respectively (p<0.001). Overall 5-year graft survival was 87%, 54%, and 20% for patients with grades 1, 2, and 3 PTC destruction, respectively (p<0.001). Additionally, overall 5-year survival was 100%, 81%, and 21% for grades 1, 2, and 3 C4d depositions in PTCs, respectively (P<0.001).
Conclusions: ABMRh comprising characteristic histologic findings without detectable DSA represent a distinct phenotype with superior allograft survival than ABMRh with positive DSA. The grade of PTC C4d expression and PTC destruction significantly indicate poor prognosis independent of the DSA. Therefore, we concluded that ABMR should be divided into different subgroups for treatment, considering the presence of DSA and vascular rejection.

FG5_2 NEXT GENERATION SEQUENCING: ANTIBODY-MEDIATED REJECTION MOLECULAR SIGNATURE AND MACHINE LEARNING CLASSIFIER

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Background: Molecular description of kidney rejection leaded to the derivation of new diagnostic tools. However, the sequencing technologies engaged in the previous studies had access to a restrained transcriptome. The EU-TRAIN consortium sought to discover new predictive transcripts for antibody-mediated rejection (AMR) that could improve molecular diagnostic tools.
Methods: EU-TRAIN (NCT03652402) is a prospective multicentric study including unselected kidney transplant cohorts from 11 centers from 4 countries (France, Spain, Germany, Switzerland). We performed an Illumina bulk RNA sequencing on 770 kidney biopsies (n=540 kidney recipients) prospectively collected between 2018 and 2021. We derived differentially-expressed genes (DEGs) for AMR against all the other diagnoses and performed feature selection (top 30 DEGs overall, top 30 DEGs BHOT-specific and ElasticNet) to train 4 binary classifiers (Naïve Bayes, Extreme Gradient Boosting, Linear Support Vector Machine (LSVM) and K-Nearest Neighbours) to predict the probability of AMR.
Results: We identified 6,141 differentially-expressed transcripts. 358 (5.8%) were from the Banff Human Organ Transplant (BHOT) panel, 5,180 (84.4%) from the pathogenesis-based transcripts (PBTs) and 603 (9.8%) corresponded to new genes. Pathway analysis revealed consistent functions with activation of both innate and adaptive immune systems (chemokines, interleukins, interferon, TCR/BCR signalling). Lastly, the ElasticNet selected 105 genes with 29 (27.6%) being NGS-specific. In all settings, the LSVM leaded to the best precision-recall area under the curve (ElasticNet: 0.983; top 30 overall: 0.810; top 30 BHOT: 0.841) and calibration, assessed using the Hosmer and Lemeshow goodness of fit test p-values (ElasticNet: 0.947; top 30 overall: 0.063; top 30 BHOT: 0.141). The NGS-specific ElasticNet-selected genes comprised 20 non-coding genes, 2 pseudogenes (*SUGT1P1*, *ANAPC1P2*), 1 tRNA (*TRI-TAT2-1*) and 6 coding genes (*TNFSF13*, *ELMOD1*, *LSM8*, *TRGV4*, *ANKDD1B*, *IGHV3-43*).
Conclusions: We discovered non-coding genes associated with AMR and consistent biological functions. Leveraging new transcripts, we trained accurate classifiers to predict AMR. These new transcripts represent potential molecular levers for drug designing and repurposing.

FOCUS GROUPS

The clinical spectrum of kidney transplant rejection

FG5_3 PROTOCOL BIOPSIES IN PATIENTS WITH SUBCLINICAL DE NOVO DSA AFTER KIDNEY TRANSPLANTATION: LONG TERM DEATH CENSORED GRAFT SURVIVAL

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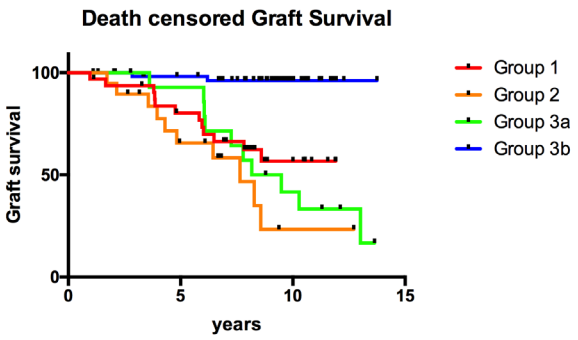
Background: De novo donor-specific antibodies (DSAs) are associated with antibody-mediated rejection (AMR) and allograft loss. Whether monitoring of subclinical de novo DSA (dnDSA) paired with systematic kidney biopsy should become routine remains to be established and long-term graft survival according to the results of this biopsy is not, so far well reported.
Methods: Retrospective multicentric study: 123 patients without graft dysfunction were biopsied because of the presence of dnDSA (One Lambda, mean fluorescence intensity [MFI], >1000). Fifty-one subclinical ABMR (sABMR) (41.4%) were diagnosed, of which 32 (26%) active (group 1) and 19 (15.5%) chronic active sABMR (group 2). In 72 patients (group 3), biopsy did not show any lesions of ABMR. We report here the long-term follow-up of the three groups.
Results: In group 1, after a median follow up of 7.8 years (IQR: 4.8-9.7), we reported 12 graft losses (12/32:37.5%). In group 2, after a median follow-up of 6.1 years (IQR: 3.5-7.6), we noticed 10 graft losses (10/19: 52.6%). In group 3, during a median follow up of 9.2 years (IQR: 6.8-10.3), 15 patients (15/72: 20.8%) presented an episode of clinical ABMR (group 3a) confirmed by a graft biopsy (4/15: active and 11/15 chronic active), and 57 (79.2%) did not (group 3b). In group 3a we reported 10 graft losses (10/15: 66.7%) and in group 3b only 2 graft losses (2/57: 3.5%). Ten-years death censored graft survival was significatively higher in group 3b than in group 1, than in group 3a, than in group 2 (p<0.0001, Figure 1). In group 1, death censored graft survival was not significatively between those receiving a specific therapy for ABMR (IvIg and/or plasmapheresis and/or rituximab) or not.
Conclusions: The results of a biopsy performed for a subclinical dnDSA has an impact on the long-term death censored graft survival. Clinicians have to be cautious with patients with initial normal biopsy, because up to 20% of them could present an episode of clinical ABMR in the follow-up. Finally, we did not find that the treatment of an early active subclinical ABMR could improve the long-term graft survival.

Figure 1. Death censored graft survival according to the results of the first protocolar biopsy in subclinal de novo DSA.



FG5_4 IMPACT OF PREFORMED DONOR-SPECIFIC HLA-CW AND HLA-DP ANTIBODIES ON ACUTE ANTIBODY MEDIATED REJECTION IN KIDNEY TRANSPLANTATION

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Background: Given the risk of rejection, the presence of preformed anti-HLA antibodies in the recipient directed against an HLA-A, HLA-B, HLA-DR or HLA-DQ donor's antigens contraindicates the transplant in most allocation systems. However, very few data exist concerning HLA-Cw and -DP DSAs regarding the risk of post-transplant rejection.
Methods: We performed a multicentric observational study, in which the objective was to determinate risk factors of acute antibody-mediated (aABMR) rejection in recipients transplanted with preformed isolated Cw- or DP-DSA the day of transplantation, between 2010 et 2019.
Results: 183 patients were included and were transplanted with a preformed isolated Cw- or DP-DSA (92 Cw-DSA ; 91 DP-DSA). 63 patients (34.4%) benefited from a prophylactic treatment the day of transplant, consisting in rituximab, IgIVs, plasmapheresis and/or eculizumab. At 2 years, the prevalence of aABMR was 12% in the Cw-DSA group, versus 28% in the DP-DSA group. Using multivariable Cox regression model, the presence of a preformed DP-DSA was associated with an increased risk of aABMR(HR= 2.32 [1.21-4.45 (p = 0.001)]) compared to Cw-DSA. We also observed a significant association between the DSA MFI the day of transplant and the risk of rejection, whatever the DSA was (HR= 1.09 [1.08 - 1.18], p=0.032). Interaction term analysis found an increased risk of aABMR in the DP-DSA group compared to Cw-DSA only for MFI below 3000, and an equivalent risk over 3000. We did not see any effect of the type of DSA or the MFI on death-censored graft survival. There was also no effect of prophylactic treatment on the risk of post-transplant rejection.
Conclusions: In this study, Cw-DSA pathogenicity was dependent on the MFI and was clinically significant over 3000, whereas the risk of rejection was present with DP-DSA whatever the MFI. These results may plead for taking these antibodies into account in the allocation algorithm, in the same way as the other anti-HLA antibodies.

FG5_5 CLINICAL UTILITY ASSESSMENT OF ANNUAL SYSTEMATIC SCREENING OF POST KIDNEY TRANSPLANT DE NOVO DONOR SPECIFIC ANTIBODIES

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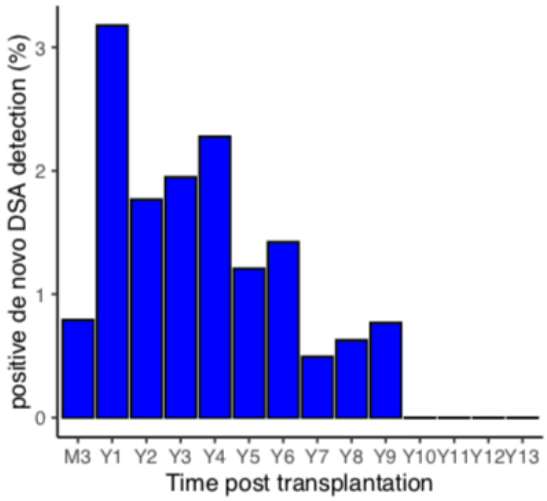
Background: De novo DSA is a strong biomarker associated with the development of chronic antibody mediated rejection and graft loss after kidney transplantation. Although expensive, a systematic annual screening was proposed by some organ transplant agencies, while clinical utility of this recommendation is not clearly supported by the literature.
Methods: To address this question, we retrospectively assessed the incidence of de novo DSA in a cohort of low-immunological risk (first kidney transplant, non-sensitized) patients.
Results: A total of 1072 non-sensitized kidney transplant recipients were included, receiving 4611 tests during the following period. The median number of anti-HLA screening per patient was 4 (IQR 3; 6), during a median follow-up of 8 (IQR 5; 11) years. During the follow-up, seventy-seven recipients presented de novo DSA (7.2%). Systematic screening represented 4267 tests and detected a de novo DSA in 46 cases (1.08%). A large majority (95%) of patients with de novo DSA presented a post-transplant immunizing event in their medical records. Histological findings at DSA detection were similar whatever the indication of DSA screening (antibody-mediated-related lesions found in 59.0% and 70.4%, chronic antibody mediated changes respectively 15.4% and 11.1% after systematic or clinically indicated).
Conclusions: Our results suggest that detection from protocol annual screening does not seem to help in diagnosing AMR at earlier stages than with for cause screening. A close monitoring of selected patients with posttransplant immunizing factors or assessment of others earlier injury markers, should be tested.

The clinical spectrum of kidney transplant rejection

Figure 1: Rate of detection of dnDSA during the follow-up.



FG5_6 DEVELOPMENT OF DE NOVO DONOR-SPECIFIC HLA ANTIBODIES AND ABMR IN RENAL TRANSPLANT PATIENTS DEPENDS ON CYP3A5 GENOTYPE

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Background: The single-nucleotide polymorphism *CYP3A5* rs776746 is related to a reduction in the metabolizing activity of the *CYP3A5* enzyme. Persons carrying at least one copy of the wild-type allele, defined as *CYP3A5* expressers, exhibit higher clearance and lower trough concentrations of tacrolimus than homozygous nonexpressers, and this difference may affect alloimmunization and allograft function.
Methods: We retrospectively studied 400 kidney transplant recipients treated with a tacrolimus-based immunosuppression regimen to detect *CYP3A5* genotype, *de novo* formation of human leukocyte antigen (HLA) antibodies and donor-specific antibodies (DSA), and clinical outcome up to 5 years after transplant.
Results: We found that 69 (17%) of the 400 patients were *CYP3A5* expressers. During the first 3 years after transplant, *CYP3A5* expressers tended to have lower tacrolimus trough levels than non-expressers, even though their tacrolimus dosage was as much as 80% higher. *De novo* DSAs were found more frequently in *CYP3A5* expressers than in nonexpressers (13/69 [19%] vs. 33/331 [10%], $p = 0.02$). *De novo* DSA-free survival rates ($p = 0.02$) were significantly lower for expressers than for nonexpressers. *CYP3A5* genotype had no effect on allograft failure, but *CYP3A5* expressers exhibited a significantly higher frequency of antibody-mediated rejection. *CYP3A5* expresser status was an independent risk factor for the development of *de novo* DSAs (relative risk, 2.34, p= 0.01).
Conclusions: Early detection of *CYP3A5* expressers, enabling genotype-based dose adjustment of tacrolimus immediately after renal transplant, may be a useful strategy for reducing the risk of *de novo* DSA production and antibody-mediated rejection.

FG5_7 DISTINCT EFFECTOR CD28-CD8 T CELL POPULATIONS DIFFERENTIALLY CONTRIBUTE TO KIDNEY ALLOGRAFT REJECTION

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Background: CD8 T cells can mediate allograft inflammation and damage. Although effector CD28$^-$ CD8 T cells were previously shown to be associated with both antibody-mediated rejection (ABMR) and T-cell mediated rejection (TCMR), comprehensive immune phenotyping and molecular profiling of such cells is lacking.
Methods: In a cohort of 76 kidney transplant recipients (stable, N=41; ABMR, N=23; TCMR, N=12) and 16 healthy controls, we used high dimensional flow cytometry and single-cell RNA seq to deeply profile peripheral blood CD8 T cells at the time of allograft biopsy. Concomitantly, we assessed CD8 T cell gene expression profiles in allograft biopsies using bulk RNAseq.
Results: Compared to stable and TCMR subjects, ABMR patients displayed significantly expanded cell populations of resting naïve and proliferating effector memory CD45RO$^+$CD28$^-$ CD8 T cells. TCMR patients showed specific expansion of CD45RO$^-$CD28$^-$ terminally differentiated effector memory (TEMRA) CD8 T cells expressing IL-21R and CXCR5. At the single-cell transcriptional level, ABMR was characterized by elevated transcripts related to T-cell receptor activation and FcγRIIIA pathways, while TCMR was associated with enrichment in cell cytotoxicity transcripts, and IL-21 and Th1 signaling pathways in CD28$^-$ CD8 T cells. Consistently, ABMR biopsies were enriched for antibody-dependent cytotoxicity related transcripts and TCMR biopsies for *TBX21* gene expression and cell-dependent cytotoxicity related transcripts.
Conclusions: We identified predominant effector memory differentiation with antibody-dependent cytotoxicity potential in CD28$^-$ CD8 T cells during ABMR, while TCMR was characterized by type-1 and IL-21 driven CD28$^-$ CD8 T cell changes. Thus, our study identifies novel CD28$^-$ CD8 T cell populations with potential for allograft injury which may be therapeutically targeted for treatment of kidney allograft rejection.

FG5_8 SUBCLINICAL REJECTION-FREE DIAGNOSTIC AFTER KIDNEY TRANSPLANTATION USING BLOOD GENE EXPRESSION

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Background: Spontaneous and rare cases of patients undergoing a functional renal transplant in the absence of immunosuppression represent a particular situation of immune tolerance. We previously established a blood score of operational tolerance (cSoT) which was reversed in patients developing anti-HLA and donor-specific antibodies (DSAs), suggesting that this biomarker could be associated with immunological events and risk of rejection.
Methods: We measured the 6 genes composing the cSoT using quantitative PCR (qPCR) and NanoString enzyme-free methods in an independent multicenter cohort of 588 renal transplanted patients with paired blood samples and biopsies at 1 year after transplantation.
Results: We validated its association with pre-existing and *de novo* DSA. In addition, from the 441 patients with protocol biopsy, we evidenced a significant decrease of the cSoT in the 45 patients with biopsy-proven subclinical rejection (SCR), a major threat associated with pejorative kidney allograft outcomes that prompted us to refined a SCR score (SCR-S), with only two genes, *AKR1C3* and *TCL1A*, and 4 clinical parameters. The SCR-S was able to identify patients unlikely to develop SCR with an AUC of 0.864 and a negative predictive value of 98.3% and also reclassifying patients with discrepancies between the presence of DSA and the histological diagnosis of antibody mediated rejection. The SCR-S was technically validated with two methods (qPCR and NanoString), externally validated on 447 patients from the independent and multicenter cohort of the KTD-Innov consortium and reproduced in an independent and external laboratory.
Conclusions: The presentation will describe a composite score that could improve detection of subclinical rejection to allow a closer and noninvasive patient monitoring, allowing early medical management of these kidney transplanted patients.

FG6_1 FIVE-YEAR OUTCOMES OF KIDNEY TRANSPLANTATION FROM DONORS AFTER CIRCULATORY DEATH OLDER THAN 65 YEARS OLD

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Background: The age of donors after circulatory death has increased in our country allowing an expansion in the number of kidney transplants performed. The aim of our study is to compare the short- and medium-term results of transplants performed with donors after circulatory death older than 65 years vs. younger ones.
Methods: Retrospective, single-center study including all kidney transplantation recipients of donors after circulatory death performed in our center between April 2015 and December 31, 2021. Data was analized using logistic and Cox regression for multivariable analysis and survival was analized using Kaplain-Meier curves and long rank. The mean follow-up time was 33 months.
Results: 96 renal transplants were performed with donors after circulatory death, 20 of which with donors ≥ 65 years old. Recipient age was significantly higher in the group of patients with donors ≥ 65 years (67.7 vs. 52.4 p<0.05), as well as pre-transplant comorbidity. Renal function at 1 year was significantly lower in recipients with donors ≥ 65 years (cr 1.9 vs. 1.6 mg/dl, p<0,05) presenting no differences at 3 (cr 1.8 vs. 1.7 mg/dl, p=0,4) and 5 years (cr 1.2 vs. 1.6 mg/dl, p=0,15). There were no differences in patient survival (69% vs. 85% p=0.09) or graft survival, death-censured (100% vs. 83% p=0.11) or not death-censured (69% vs. 70%) at 5 years. They presented more delayed graft function (70% vs. 48.7%, p<0.005), but less acute rejection (0% vs. 7.9%, p<0.05). In the multivariate analysis, donor age was not related to worse graft survival or worse renal function at one year.
Conclusions: The use of donors after circulatory death older than 65 years is an adequate source of kidneys for patients awaiting renal transplantation.

FG6_2 KIDNEY OUTCOMES FROM UNCONTROLLED DONATION AFTER CIRCULATORY DEATH: A LONGITUDINAL COHORT

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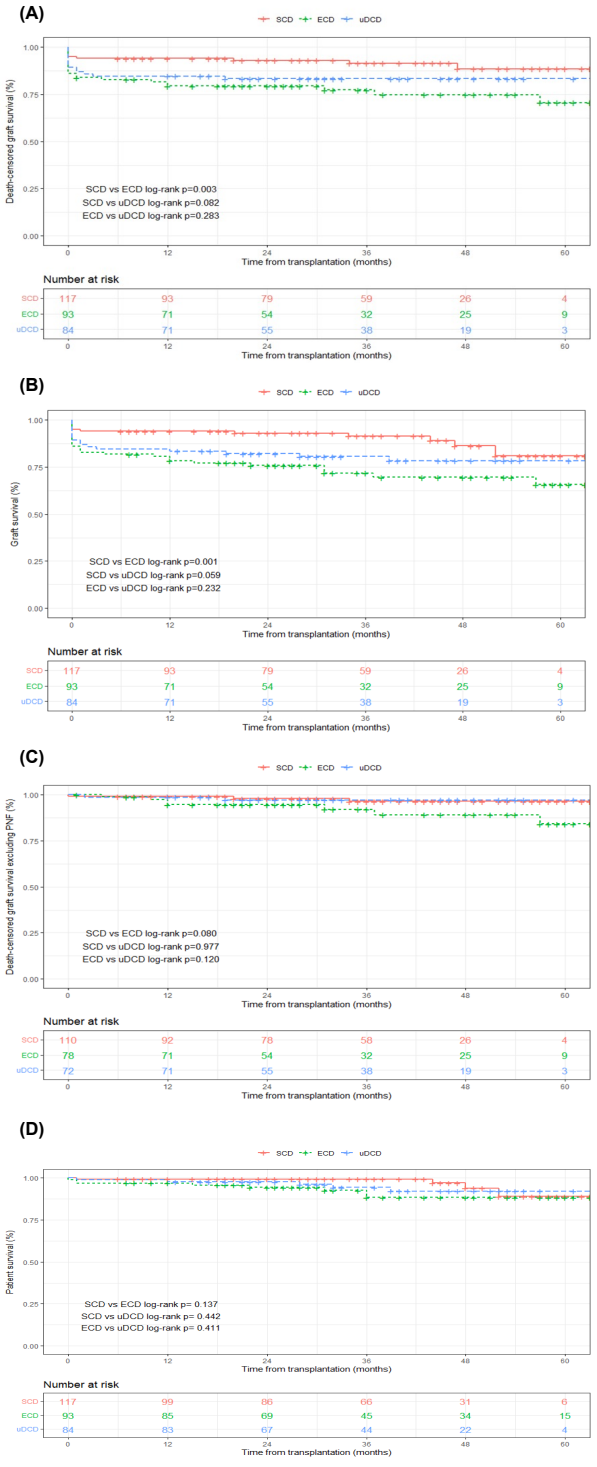
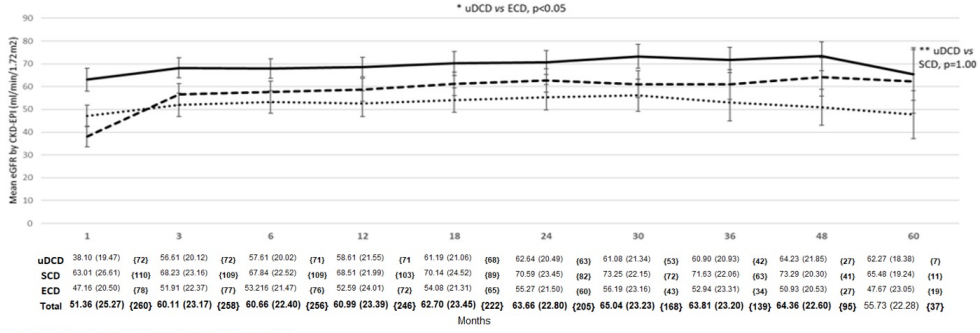
Background: In January 2016, our hospital started a program of uncontrolled donation after circulatory death (uDCD) to increase organ availability for kidney transplantation.
Methods: We longitudinally analysed the results of 294 consecutive recipient's kidney transplant (KT) performed from January 2016 to December 2020 in our centre and compared the outcomes of 84 KT from uDCD donors maintained by normothermic extracorporeal membrane oxygenation (nECMO) with those from 117 KT from standard-criteria brain-death donors (SCD) and 93 KT from expanded-criteria brain-death donors (ECD).
Results: Primary non-function (PNF) was more common in both uDCD (14.3%) and ECD (16.1%, p=0.895) groups than in SCD (6.0%) group (p=0.081 and p=0.03). In addition, delayed graft function (DGF) was more frequent in uDCD group (79.2%) than in ECD (59.0%) and SCD (31.8%) groups (p=0.008 and p<0.001). However, estimated glomerular filtration rate (eGFR) at 5 years was higher in uDCD (62.27±18.38 mL/min/1.73m^2) than in ECD (47.67±23.05 mL/min/1.73m^2, p<0.001) and similar to SCD (65.48±19.24 mL/min/1.73m^2, p=1) group. When excluding PNF, uDCD and SCD groups had similar 5-year death-censored graft survival (97.1% vs 96.4%; p=0.977).
Conclusions: Despite the increased risk of PNF and DGF, functional and survival outcomes of uDCD KT at 5 years were comparable to those of SCD, thus supporting the use of uDCD kidneys maintained under nECMO support as a successful resource to address organ scarcity.





* From 18 months forward eGFR of uDCD is significantly higher than ECD.
** At 5 years there are no differences between uDCD and SCD. SCD is always significantly higher than ECD.
Figure 3. Longitudinally estimated glomerular filtration rate by donation type.

FG6_3 BIOLOGICAL INJURY ASSOCIATED WITH DECEASED DONOR PATHWAYS REFLECT DIFFERENCES IN THE DONOR KIDNEY PROTEOME AND CELLULAR STRESS RESPONSES

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Background: Deceased donation remains the primary source of organs for transplantation, yet short- and long-term outcomes remain difficult to predict. Brain stem death characteristic of the deceased after brain death (DBD) pathway induces haemodynamic and metabolic dysregulation and systemic inflammation in the donor, inducing injury. Whilst lengthy ischaemia inherent to the deceased after circulatory death (DCD) pathway correlates with increased incidences of delayed graft function and early graft loss. Organ specific injury in deceased donors remains under explored and may provide tangible targets for intervention pre or posttransplant. Here, we analysed the proteome of DBD and DCD kidneys to identify differences in pathophysiological processes associated with donor type.
Methods: Kidney biopsies from DBD (n=100) and DCD (n=85) donors were provided by the Quality in Organ Donation biobank. Biopsies were selected based on paired recipient eGFR outcomes at 12mths posttransplant and their proteomes analysed using mass spectrometry. We explored protein expression differences that separated donor type using partial least square discriminant analysis (PLS-DA).
Results: We quantified n=2984 protein groups (5% FDR). Supervised analysis comparing the DBD and DCD proteome using PLS-DA showed incomplete separation of the samples by donor type (Figure 1a); the first latent variable (LV) separated a subset of DCD donors, and the second LV separated a subset of DBD donors, suggesting that a fully discriminatory comprehensive model may involve non-linear and/or interaction terms, but would require a much larger cohort to validate. Analysis of the top 50 proteins contributing to variable importance across both LVs were mapped using STRING, revealing links to reactive oxygen species regulation, ageing and cellular response to stress (Figure 1b). Notably, the first LV that separated DCD donors had a weakly significant negative correlation with the length of functional warm ischaemia (rho=-0.26, p=0.051).
Conclusions: Proteomes of deceased donor kidneys partially separate based on donor type by a linear combination of protein abundances. Our analysis highlights changes in cellular and metabolic stress responses, indicating that injury and repair mechanisms may differ between donor types.

Figure 1a

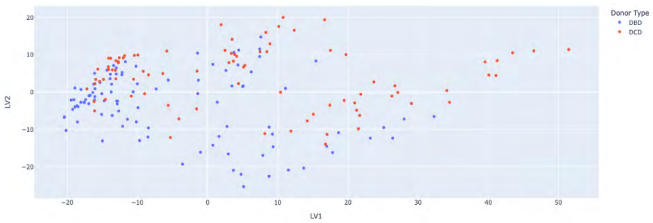
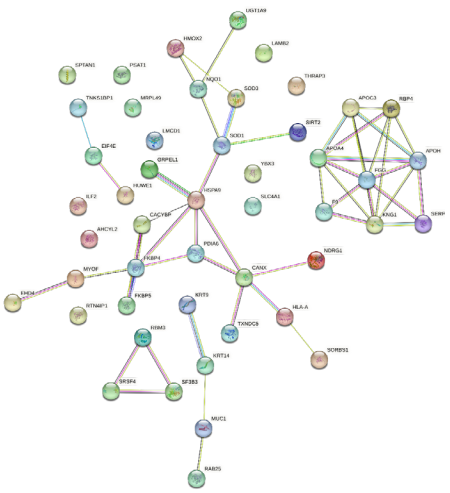


Figure 1b



FG6_4 RISK FACTORS OF ACUTE KIDNEY INJURY IN DECEASED KIDNEY DONORS

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Background: Acute kidney injury (AKI) in deceased donors affects kidney graft outcome. Little is known about risk factors associated with AKI in deceased donors.
Methods: In this prospective single center study, procurement biopsies of each kidney were performed in all deceased donors referred to our center in May 2021 - December 2022. AKI was defined by AKIN criteria. Clinical data were collected and AKI markers in urine were measured.
Results: 196 deceased (DBD 188, DCD 8) kidney donors were included in the analysis; 9 donors were excluded for insufficient data to determine AKI. AKI occurred in 89 donors (AKI+, 45.5%). AKIN stage 1 was observed in 69 donors (77.5%), AKIN stage 2 in 16 (17.9%) and stage 3 in 4 (4.4%) donors, respectively. AKI+ donors had higher BMI (27.3 (IQR 24.28–31.75) vs. 25.4 (22.35–29.80), p = 0.018) as compared to AKI-. There were no significant differences in age, gender, diabetes and hypertension. The procurement biopsies in AKI+ donors displayed higher cv (p = 0.002), ah (p = 0.02) and IF/TA scores (p = 0.019), and higher ATN rate (p = 0.002). We found higher urinary NGAL/creatinine (20.03 µg/mmol (IQR 6.37– 48.66) vs. 8.47 (3.35–27.27) p=0.001) and alpha-1-mikroglobulin/creatinine (12.94 (6.26–22.87) vs. 8.74 (4.67–16.92), p=0.04) ratio in AKI+ compared to AKI- donors respectively. There were no significant differences in other urinary AKI markers such as NAG, beta-2-mikroglobulin, alpha-2-mikroglobulin and albumin. AKI was associated with ATN (OR 1.55, 95% CI 1.03 – 2.45, p=0.044), cv score (OR 1.29, 95% CI 1.09 – 1.53, p=0.003) IF/TA score (OR 1.37, 95% CI 1.05 – 1.80, p=0.020), and highest NGAL/creatinine ratio tercile (>22.3 µg/mmol, OR 2.86, 95% CI 1.41 – 5.93, p=0.004) in logistic regression. Body mass index and diabetes status were not significantly associated with AKI.
Conclusions: Deceased donors with AKI were more likely to have kidney structural abnormalities and AKI was independent on BMI, hypertension, diabetes status and other donor categories. Procurement biopsies and urinary NGAL assessment allows the identification of deceased donors at risk of AKI which might have implications for kidney transplantation outcomes.

FG6_5 DONOR CHARACTERISTICS ASSOCIATED WITH EARLY THROMBOTIC MICROANGIOPATHY AFTER KIDNEY TRANSPLANTATION AND OUTCOMES: A SINGLE-CENTER EXPERIENCE

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Background: Thrombotic microangiopathy (TMA) is a serious complication that significantly affects allograft survival. Endothelial injury is one of the pathogeneses of TMA. Donor factors with the consequence of ischemic reperfusion injury might be the risk of early TMA after transplantation.
Methods: A retrospective cohort study of patients who underwent deceased donor kidney transplantation at Siriraj hospital between 2006 and 2020 was conducted. The definition of early TMA was biopsy-proven TMA within one month after transplantation. We determined incidence, risk factors of early TMA and its effect on graft outcomes.
Results: Of all 412 patients, the incidence of early TMA after kidney transplantation was 12.4% (51 patients). The median time to diagnosis was 7 days after transplantation. Only 20 patients (39.2%) developed TMA with evidence of antibodies-mediated rejection in graft biopsy. Donor profiles in TMA patients showed higher KDPI scores, including an increased number of hypertension and cerebrovascular accidents. The cold ischemic time over 20 hours [OR, 2.51(95%CI 1.44, 4.39); p=0.001], anastomosis time over 60 minutes [OR 2.11, (95%CI 1.17, 3.79); p=0.013] and donor with hypertension [OR, 2.80 (95%CI 1.06, 7.43); p=0.038] were significant independent risk factors for developing early TMA. Patients with TMA had significantly lower 5-year graft survival than patients without TMA (57.2% and 93.4%, p<0.001).
Conclusions: Early TMA post-transplantation is associated with limited donor characteristics including hypertension and cerebrovascular accident. This condition is aggravated by longer cold ischemic time and anastomosis time, leading to premature graft failure.

Table 1. Factors associated with early TMA post-transplantation

	Univariate		Multivariate	
Factors	Odd ration (95%CI)	p-value	Odd ratio (95%CI)	p-value
Recipient age (years)	1.02 (0.99, 1.05)	0.072		
Donor age; ≥39 years	1.85 (1.03, 3.31)	0.039		
Donor hypertension	2.36 (1.34, 4.16)	0.003	**2.80 (1.06, 7.43)**	**0.038**
Donor with cerebrovascular accident	1.74 (0.99, 3.03)	0.05		
Thai kidney donor profile index; ≥80	1.96 (1.13, 3.39)	0.016		
Cold ischemic time; ≥20 hours	2.32 (1.34, 4.02)	0.003	**2.51 (1.44, 4.39)**	**0.001**
Anastomosis time; ≥60 minute	1.86 (1.06, 3.24)	0.03	**2.11 (1.17, 3.79)**	**0.013**

FG6_6 NON-IMMUNOLOGICAL RISK FACTORS AND CLINICAL OUTCOME OF SLOW GRAFT FUNCTION AFTER DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: The slow graft function (SGF) is associated with an increased risk of acute rejection and inferior long-term outcome after kidney transplantation. The exact mechanism whether the SGF might influence long-term outcome immunologically or non-immunologically, is still unclear. In order to find the non-immunological risk factors of the SGF, we selected the study population with the kidney recipients from deceased donors with immunological low risks.
Methods: Total 363 recipients underwent deceased donor kidney transplantation at Ajou university hospital between March 2010 and December 2020. Among these recipients, 137 recipients with extended criteria donor transplantation, re-transplantation, positive donor-specific antibody, delayed graft function were excluded. Two hundred twenty-six recipients were finally included in this study. Study population was divided into immediate recovery of graft function (IGF, n=190) and slow graft function (SGF, n=38) according to serum creatinine (3mg/dL) at post-operative day 5. Clinical parameters were analyzed and compared between the two groups, and we attempted to identify the risk factor of developing SGF in immunological low risk deceased donor kidney transplantation.
Results: There were significant differences in recipient's body mass index (BMI), total ischemic time. Other factors were not associated with developing SGF. A multivariate analysis of risk factors for SGF showed recipient's BMI >25 kg/m^2 (odds ratio=2.229, p=0.044) and total ischemic time (odds ratio=1.004, p=0.032) to be the independent risk factors. The estimated glomerular filtration rates (eGFRs) at 1-year post-transplantation were significantly higher in IGF group. There was one graft failure in IGF group and no graft failure in SGF group within 1-year post-transplantation. The 1-year acute rejection rates were not statistically different between the groups
Conclusions: The recipients with SGF showed significantly low eGFR at 1-year post-transplantation. The factors of recipient's high BMI and prolonged ischemic time were independent risk factors of developing SGF in deceased donor kidney transplantation with low immunological risk. To improve long-term graft function, donor selection is important in terms of high BMI and prolonged ischemic time.

FG6_7 KIDNEY TRANSPLANT SURVIVAL ANALYSIS AND PROGNOSTIC FACTORS AFTER 10 YEARS OF FOLLOW-UP

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Background: To analyse overall and implant survival after kidney transplant in a 3-year cohort and to identify predictive factors of both in patients with at least 10 years of follow-up.
Methods: retrospective consecutive cohort study of 250 kidney transplant recipients operated between 2010 and 2012 (excluded paediatric patients). Multiorganic transplants and both dead-donor and living-donor transplants were included. Data were collected from clinical records and introduced in an Excel-designed database. A survival analysis was conducted using the Kaplan-Meier method and a Cox proportional-hazards multivariate model. A p-value < 0.05 was considered statistically significant.
Results: mean follow-up was 8.1 ± 3.2 years. Implant survival at 2, 5 and 10 years was 89%, 85.1% and 78.4% respectively. The multivariate model identified the following risk factors for implant loss: diabetic nephropathy (HR 3.17 CI95% [1.07-9.41]), delayed graft function (HR 3.84 CI95% [1.99-7.4]), chronic kidney rejection (HR 3.72 CI 95% [1.21-11.43]), and early surgical complications (HR 2.62 CI95% [1.35-5.06]). Conversely, combined transplant (kidney-pancreas and kidney-liver) was found to be a protective factor for graft loss (HR 0.08 CI95% [0.01-0.45]). Overall survival was 94.3%, 90% and 76.6% at 2, 5 and 10 years respectively. The model identified the following mortality risk factors: recipient older age (HR 1.12 CI 95% [1.07-1.2]), combined transplant (HR 7.55 CI 95% [1.65-34.5]) and opportunistic infections (HR 2.55 CI 95% [1.32-5]).
Conclusions: 10-year overall and implant survival was 76.6% and 78.4% respectively. Main mortality risk factors were recipient older age, opportunistic infections and multiorganic transplant. Main implant loss risk factors were diabetic nephropathy, delayed graft function, chronic kidney rejection and early surgical complications.

FOCUS GROUPS

Deceased donor kidney transplantation issues

FG6_8 TRANSPLANT OUTCOME FROM OCTOGENARIAN DONORS: SINGLE KIDNEY TRANSPLANT VERSUS DUAL KIDNEY TRANSPLANT

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Background: Kidney transplantation (KT) is the treatment of choice for end-stage renal disease (ESRD). New strategies have been adopted for increasing donor pool, including the use of kidneys from extended criteria donors (ECD). An increasing number of studies are evaluating the outcome of KT from donors > 60 years, but only few of them considered donors older than 80 years. The aim of this study was to assess the outcome of Single Kidney Transplantation (SKT) and Dual Kidney Transplantation (DKT) performed from donors > 80 years.

Methods: Data about all patients who underwent a KT form donor more than 80 years old in a single-centre between 2011 and 2022 were collected. Patients were divided in two groups according to the type of KT: SKT group and DKT group. Decision to perform SKT or DKT was based on the histological evaluation of graft (Karpinski score) and clinical donor evaluation (past medical history, kidney function and cause of death). Tab.1 depicts recipient characteristics, serum creatinine at discharge, delayed graft function, acute rejection and graft failure. Comparison in terms of transplant outcome and graft function between the two groups was carried out.

Results: Between January 2011 and December 2022, 100 kidney transplants using grafts from octogenarian donors were performed. Thirty-one of them were SKT and 69 were DKT. Median donor age was significantly higher for DKT (83.8 ± 2.5 years) compared to the median age for SKT (81.5 ± 1.7 years). Median kidney biopsy score was 3.44 ± 0.6 in SKT group and 3.96 ± 0.9 for right kidney and 4.55 ± 1.7 for left kidney in DKT cohort. A statistically significant difference in serum creatinine at discharge was observed between the two groups (210 ± 88 umol/L for SKT and 164 ± 84 umol/L for DKT). Five-year graft survival showed a significant better survival in DKT cohort (see Fig.1).

Conclusions: Histological and clinical selection for the allocation of kidneys from octogenarian donors can safely increase transplant activity with acceptable long-term outcome. Our preliminary results demonstrate that grafts recovered from donors older than 80 years perform better when used for DKT. Therefore, data suggest that DKT is an appropriate strategy to address the growing graft shortage.

Figure 1. Graft Survival of Kidneys from Donors ≥ 80 Years

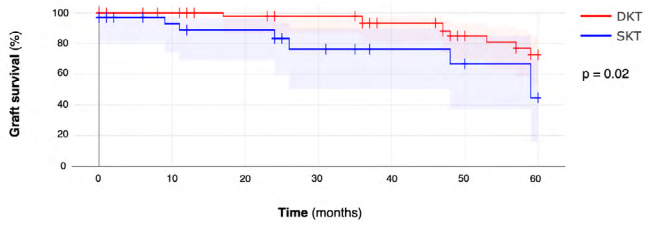

Table 1. Donor and Recipient Data

Donors

	SKT (n.31)	DKT (n.69)	*p-value*
Age(years, mean ± DS)	81.8±1.7	83.8±2.5	**< 0.001**
Cause of death (n%) Cerebrovascular disease Trauma Post anoxic injury	 28 (90) 2 (6.5) 1 (3.5)	 60 (87) 8 (11.6) 1 (1.4)	0.62
Renal function S-Creatinine < 1.5 mg/dL (n%) S-Creatinine 1.5-2.5 mg/dL (n%)	 29 (94) 2 (6)	 61 (88) 8 (12)	0.42
Karpinski Score (mean ± DS)	3.44 ±0.6	R: 3.96±0.9 L: 4.55±1.7	

Recipients

	SKT (n.31)	DKT (n.69)	*p-value*
Age at transplant (mean ± DS)	65.7±6.4	65.1±6.5	0.84
S-Creatinine at dischrge (umol/L, mean ± DS)	210.4±88	163.7±84	0.008
DGF (n%)	5 (16)	5 (7)	0.17
Acute rejection(n%)	1 (3)	3 (4)	0.79
Graft loss (n%)	0	2 (2.9)	0.92

Kidney machine perfusion and ischemia reperfusion injury

FG7_1 TRANSPLANT OUTCOMES AFTER EXPOSURE OF DECEASED KIDNEY DONORS TO CONTRAST MEDIUM

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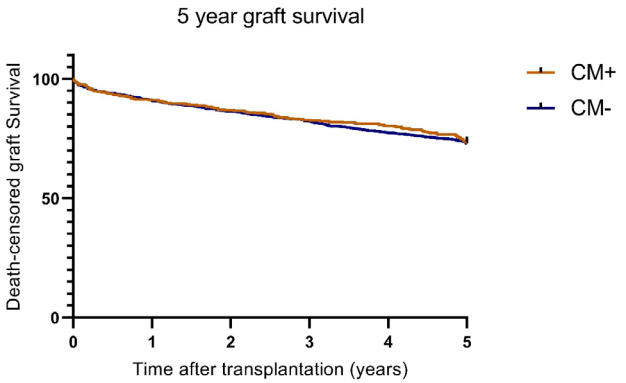
Background: In 18% of deceased donors in The Netherlands a CT scan is performed during the screenings process, using intravenous contrast medium (IV-CM) for enhancement. Potential heart donors are evaluated with Coronary Angiography (CAG) using intra-arterial CM (IA-CM). Administration of IV- and IA-CM has been associated with acute kidney injury, but the effect of CM exposure of a deceased organ donor on kidney transplant outcomes has been poorly studied. This study aims to investigate the effect of administration of IA- and IV CM in deceased kidney donors on transplant outcome after kidney transplantation.

Methods: All deceased kidney donors in the Netherlands between 2011-2021 were retrospectively reviewed on CM exposure. Donor characteristics and follow-up data on kidney recipients were obtained from the Eurotransplant and Dutch Transplantation Foundation Database respectively. Multivariable analyses were performed to assess associations between CM exposure and Delayed graft function (DGF) / death-censored graft survival. Linear mixed models were used to assess difference in mean eGFR values in recipients 1 to 8 years after transplantation.

Results: In total 2177 deceased kidney donors and 3638 corresponding kidney graft recipients were included. Twenty-four percent of the donors (n=520) were exposed to CM, corresponding to 23% of recipients (n=832) included. Delayed graft function (DGF) was observed in 36% (n=1321) and primary non function in 3% (n=106) of recipients. Analysing DGF rates separately for Donation after Brain death (DBD) and Donation after Circulatory Death (DCD) donors showed no significant effect of CM exposure (p=0.15 and p= 0.60 respectively). In multivariable analyses CM administration was not significantly associated with a higher DGF risk (OR 1.06; 95% CI 0.86-1.36, p=0.63), nor a significant predictor for death-censored graft failure (HR 1.01; 95% CI 0.77-1.33, p=0.93). Linear mixed models showed no difference in mean eGFR values in recipients 1-8 years post transplantation (p=0.78).

Conclusion: This study indicates that CM administration in DBD and DCD donors has no negative effect on early and long-term kidney graft function and is safe to use during the organ donor evaluation process.

Figure 1: Death-censored graft survival according to CM exposure of the donor



Time point	0 year	1 year	2 years	3 years	4 years	5 years
CM-, Numbers at risk	1827	1164	1576	1503	1415	1340
CM +, Numbers at risk	446	406	387	369	358	328

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FG7_2 THE SETUP USED FOR EX VIVO RENAL NORMOTHERMIC PERFUSION INFLUENCES A KIDNEY'S BEHAVIOR ON THE MACHINE

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Background: Along with a growing interest in renal normothermic machine perfusion (NMP) came an increase in the number of different clinically available perfusion devices. While all perfusion systems have the same aim, there are significant differences in the circuit, pumps, sensors, and software. Also, the NMP protocols used in combination with these devices vary. Therefore, we evaluated three different NMP protocols using porcine and human kidneys, hereby assessing two clinically approved perfusion devices.
Methods: Twelve porcine kidneys were subjected to 30min of warm ischemia, 24h of static cold storage, and subsequently exposed to 6h of NMP. Four kidneys were perfused on the Kidney Assist (KA, XVIVO) with a mean arterial pressure (MAP) of 75 mmHg (Figure 1A-B). Four kidneys were perfused on the KA device incorporating several workaround improvements to the standard protocol and a MAP of 85mmHg (KA+WA, Figure 1A-B). Four kidneys were perfused with the Perlife perfusion device (PL, Aferetica, Figure 1C-D). To validate findings, six human discarded kidneys from DCD donors were perfused on the KA (KA-h) or KA+WA (KA+WA-h) (n=3 per group) protocol.
Results: Kidneys of the PL group reached the device's upper flow limit of 500ml/min after 1h of NMP and were consequently pumped with a significantly lower pressure compared to KA and KA+WA ($p<0.0001$). The arterial pO2 was significantly lower in the PL group ($p<0.0001$). Yet, the Hb increased over time, and the oxygen consumption was significantly higher ($p<0.001$). Fractional sodium excretion was significantly lower in the PL group ($p<0.01$). Tissue ATP levels, urine production, and creatinine clearance rates did not differ between groups. The KA+WA-h group showed a significantly lower vascular resistance, higher oxygen delivery, and lower levels of injury markers in the perfusate compared to the KA-h group.
Conclusions: This study shows that differences in NMP protocols and machines can have a relevant influence on perfusion characteristics and kidney function on the pump, which should therefore be interpreted with caution. There is a need to develop optimized consensus protocols for renal NMP to obtain comparable results between centers.

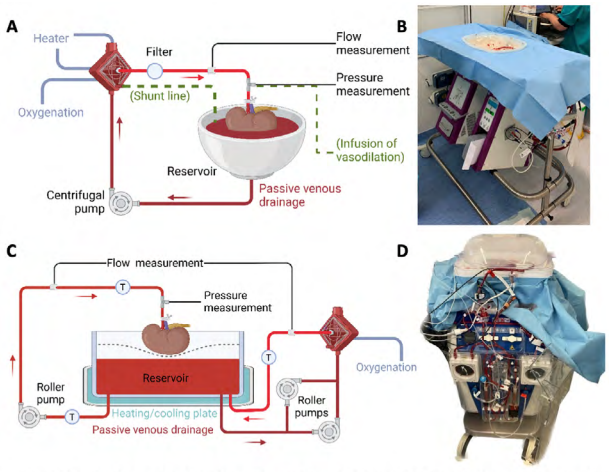

Figure 1. Perfusion setup. A. Schematic overview of Kidney Assist perfusion setup. The extra shunt line and the infusion of vasodilation of the 'workaround' protocol shown in green. **B.** Picture of Kidney Assist perfusion setup. **C.** Schematic overview of PerLife perfusion setup. **D.** Picture of PerLife perfusion setup. T = temperature sensor, D = pressure dome.

FG7_3 NORMOTHERMIC KIDNEY PERFUSION PHASE 1 – A CLINICAL TRIAL OF UP TO 24-HOUR NORMOTHERMIC MACHINE PERFUSION PRIOR TO TRANSPLANTATION

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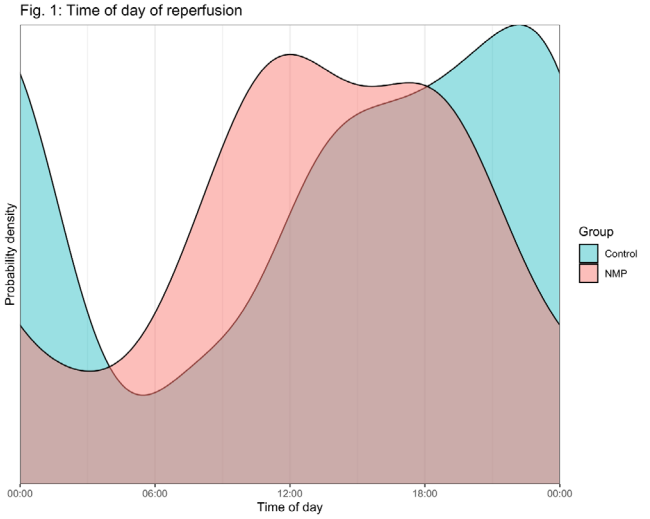
Background: Normothermic Machine Perfusion of the Kidney (NMP-K) prior to transplant offers multiple potential domains of benefit, including reduction of preservation injury, organ assessment, optimisation of logistics, and as a platform for delivery of therapeutics. Previous clinical reports have been limited to a short duration of perfusion, and anatomically suitable organs. Normothermic Kidney Perfusion Phase 1 (NKP1) is a single centre trial investigating the safety and feasibility of prolonged duration NMP-K following static cold storage, using an automated mobile system (OrganOx, UK) designed for 24-hour perfusion.
Methods: All kidneys accepted for transplantation in Oxford were potentially eligible. Perfusion duration was determined primarily by logistical considerations, with maximum permissible perfusion times increasing from 6 to 12 to 24 hours in consecutive study phases (each n=12). Kidneys were prepared, cannulated, and then perfused at 37°C with red cell based perfusate, and urine recirculation. Immediately prior to implantation, the kidney was removed from the device and cold-flushed. The primary endpoint was 30-day graft survival. Comparison was made to historical controls with similar risk profiles and cold ischaemia times, ratio 1:2, selected by a pre-defined matching algorithm.
Results: 36 patients were transplanted with kidneys that underwent NMP-K. Minimum normothermic perfusion time was 2h11, maximum 23h22. One kidney was discarded due to markedly abnormal perfusion parameters. 9/36 perfused kidneys had multiple renal arteries; in one case a vascular injury sustained at retrieval was identified and repaired following ex-vivo reperfusion. All transplanted grafts met the primary endpoint. Functional outcomes were similar to those of the control cohort, despite the much longer overall preservation time (Table 1). This facilitated a shift towards daytime operating (Fig. 1). There were no adverse events related to the technique.
Conclusions: Prolonged duration NMP-K is safe and feasible. In a real-world setting it enables a reduction in cold ischaemia time as well as a prolongation of total preservation time, thereby facilitating daytime operating. The platform also provides opportunities for assessment and treatment of deceased donor kidneys prior to transplantation.

Fig. 1: Time of day of reperfusion



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FG7_4 MAGNETIC RESONANCE IMAGING ASSESSMENT OF FUNCTIONAL DIFFERENCES BETWEEN KIDNEYS IN VIVO AND DURING EX VIVO NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) is a promising method for pre-transplant donor kidney quality assessment. Although its potential is increasingly being recognized, it remains unclear which NMP parameters convey information about graft viability. This is largely due to our limited understanding of ex vivo organ physiology. To increase our knowledge about organ biology during NMP, we combined non-invasive functional magnetic resonance imaging (MRI) with renal normothermic perfusion in a porcine model. This project aimed to determine the differences between *in vivo* and *ex vivo* regional renal tissue oxygenation and diffusion patterns.
Methods: Pigs (n=30) were anesthetized and brought into a clinical-grade MRI. In vivo MRI scans were performed to provide information about regional tissue oxygenation using T2* mapping and water diffusion patterns using diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) maps. Subsequently, a bilateral nephrectomy was performed to retrieve kidney pairs, which were randomized to sustain either minimal warm ischemia (WI) or 75 min WI. After WI and 4-5 hours of cold preservation, both kidneys were connected to an MRI-compatible NMP circuit and perfused for 6 hours. Hourly, T2* maps and DWI images were acquired from both kidneys. Regions of interest were drawn in the cortex and medulla to calculate the mean signal intensity.
Results: *In vivo* mean T2* corticomedullar (CM) ratio (1.71±0.21) differed significantly from the mean *ex vivo* CM ratio of the minimal WI group (0.60±0.13, $P < 0.0001$) and the 75 min WI group (0.62±0.16, $P < 0.0001$). In vivo cortical ADC values (2.1±0.15 x 10^{-3} mm^2/s) were significantly higher compared to the minimal WI group (1.46±0.25, $P < 0.0001$) and the 75 minutes WI group (1.76±0.09, $P = 0.002$).
Conclusions: This study provides the first evidence for the existence of remarkable differences in regional tissue oxygenation and diffusion patterns between a normal physiological *in vivo* environment and during *ex vivo* normothermic machine perfusion. These findings highlight that renal function during *ex vivo* perfusion is very different from what we are used to in our *in vivo* reference frame. Therefore, organ viability assessment during NMP should likely consider other parameters than those functional markers that are common *in vivo*.

FG7_5 KIDNEY TRANSCRIPTOME VARIES BETWEEN DONOR TYPES, WITH A DIFFERENTIAL REPONSE TO ISCHEMIC PRECONDITIONING

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Background: The prevention/attenuation of graft ischemic injury is a challenge in kidney transplantation. We developed two rat models to investigate the impact of mesenchymal stromal cells (MSCs) in the ischemic preconditioning of kidneys from Donors after Circulatory Death (DCD) and Donors after Brain Death (DBD).
Methods: Under general anesthesia, rats underwent iv injection of saline (S-groups) or 1.5 10^6 MSCs (MSC-groups) followed by either DBD (6hr of brain death) or DCD (6hr of anesthesia and 20min warm ischemia) models, resulting in 4 groups (S-DBD, S-DCD, MSC-DBD, MSC-DCD). Kidneys were then procured after IGL1 flush. One kidney was directly fixed and the other one immersed for 14 hours in IGL1 at 4°C. Serum samples were collected before treatment (baseline) and at the time of kidney collection. Urine samples were collected by bladder puncture at the time of kidney collection. Renal function was evaluated. Kidney histology was assessed by PAS staining and KIM1 immunostaining. Total RNA was extracted from S-DCD vs S-DBD kidneys for RNAseq.
Results: BUN was increased after 6h of anesthesia (DCD) or brain death (DBD) ($p<0.01$). SCr increased in both S-DBD and MSC-DBD but was lower in MSC-treated rats (MSC-DBD 0.5±0.2mg/dL vs S-DBD 0.7±0.1mg/dL; p=0.037). Urinary KIM1 was lower in MSC-treated DBD (S-DBD 10.9±4.5 vs MSC-DBD 7.1±1.7; p=0.03). Acute Tubular Injury (ATI) and KIM1 expression were higher in S-DBD (ATI: S-DBD 65±24 % of surface vs S-DCD 39±27 % of surface (p=0.03) and KIM1: S-DBD 0.39±0.24 % of surface vs S-DCD 0.10±0.09 % of surface (p=0.0002)). In MSC groups, there was no difference in both ATI extension and KIM1 expression. There was no difference in KIM1 expression between S-DBD and S-DCD groups. RNAseq showed that proinflammatory and proapoptotic pathways were upregulated in DBD, whereas transmembrane transport and metabolic pathways were downregulated, compared to DCD.
Conclusions: The RNA profiles of the kidneys are different upon donor types, which may impact the response to MSC-based ischemic preconditioning.

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FG7_6 FASTING PORCINE KIDNEYS DURING NORMO-THERMIC MACHINE PERFUSION DOES NOT AFFECT MITOCHONDRIAL FUNCTION

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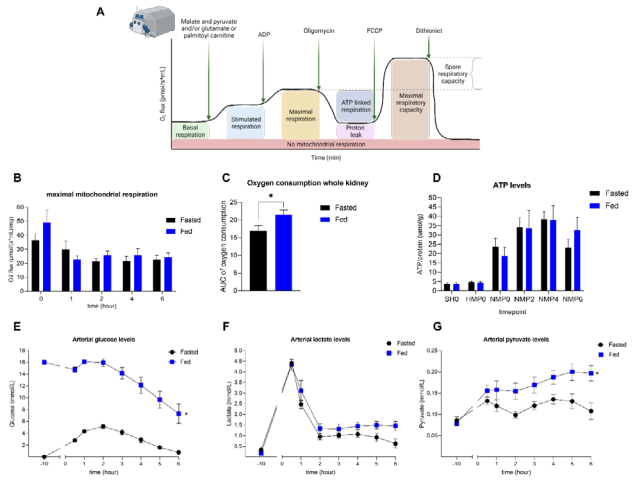
Background: Normothermic Machine Perfusion (NMP) enables assessment and reconditioning during the preservation period due to full metabolic activity. However, knowledge of mitochondrial metabolism and how to sustain this during NMP is lacking. Oxygen and nutrients are the two important sources for aerobic metabolism in mitochondria. It is known that oxygen is needed during NMP, but not much is known about the need for nutrients. Therefore, this study aims to investigate the effect of the presence or absence of nutrients in the perfusate during NMP on mitochondrial function.
Methods: Porcine kidneys were procured at a local slaughterhouse. After 30 minutes of warm ischemia the kidneys were perfused with oxygenated hypothermic machine for 24 hours. Thereafter, kidneys were normothermically perfused for 6 hours, during which they were either fed (n=6) with glucose, fatty acids and glutamine, or fasted (n=6) without any nutrients. Every hour biopsies were taken to assess mitochondrial respiration, using the Oxygraph-2k *(figure 1A)*. Moreover, metabolites and adenine triphosphate (ATP) were measured in tissue, perfusate and urine samples.
Results: No differences in mitochondrial function, reflected by their respiration, were observed between the groups *(figure 1B)*. However, oxygen consumption of the whole kidney was higher during NMP in the fed group compared to the fasted group *(figure 1C)*. During the first two hours of NMP the fasted kidneys were able to produce ATP from their remaining sources, as reflected by the increasing glucose levels and decreasing pyruvate and lactate levels. This is different in the fed group where stable glucose and pyruvate levels and decreasing lactate levels are observed. In the remaining four hours of NMP the metabolites show a similar pattern in both groups *(figure 1E,F,G)*. Furthermore, a trend towards higher ATP levels after 6 hours of NMP was seen in the fed group *(figure 1D)*. Kidney function, reflected by the fractional sodium excretion, was not significantly different between the groups.
Conclusions: No differences in mitochondrial function were observed between groups despite significant differences in oxygen consumption, glucose and pyruvate levels during NMP. More in depth analyses about the resources for ATP production of fasted kidneys during NMP are currently executing.



FG7_7 RENAL ARTERY FUNCTIONS IN KIDNEYS AFTER THREE MONTHS FOLLOWING RECONDITIONING IN PORCINE EXTENDED UDCD MODEL

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Background: Today, kidney transplantation is a successful treatment of chronic renal failure, with more than 90% graft survival after 1 year in most parts of the world. Unfortunately, the waiting lists are long. Decreased renal blood flow is an early sign of graft failure. Several factors contribute to an increased renal resistance to flow, including micro thrombi in the renal circulation and tone of the renal vessels. Preserved vascular function is critical for adequate kidney recovery after transplantation. The importance of contractile function of renal blood vessels should not be underestimated during evaluation of general transplant outcome. The study is focused on the properties of porcine renal arteries in a transplantation context.
Methods: Porcine renal arteries were compared between: 1. *Normal* - obtained immediately before euthanasia, 2. *Machine-perfused* - kidneys isolated from animals after 4-5 h WIT and reconditioned ex-vivo, 3. *Nephrectomised* - one kidney was removed and the artery of the remaining kidney was analysed after 3 months, 4. *Living-donor* - animals were nephrectomised on the right side and after 15-16 h under anaesthesia left kidney was transplanted to the right side and observed for 3 months, 5. *Transplanted* - reconditioned kidney after 4-5 h WIT was transplanted and observed for 3 months. From each animal, 2-4 ring preparations were obtained and mounted for isometric force recording in open organ baths at 37 °C in normal Krebs solution.
Results: The mean value for active wall tension following activation with high-K^+ in the living-donor group was lower, but not significant. For activation with noradrenaline the difference in active stress between living-donor and other groups was less prominent. The extent of substance P induced relaxation was higher in the normal group, but no significant differences were observed between groups.
Conclusions: No major differences in the passive properties of the vessels was observer which may exclude significant changes in the biomechanics of the vessel wall in any of the conditions. The maximal wall tension after activation with a saturating concentration of the physiological agonist noradrenaline (NA) was similar in the different groups. Transplanted vessels reacted similar to normal which confirms expected effect of ex-vivo reconditioning process.

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FG7_8 REAL-TIME ASSESSMENT OF KIDNEY ALLOGRAFTS DURING HOPE USING FLAVIN MONONUCLEOTIDE (FMN) - A PRECLINICAL STUDY

Richard Sousa Da Silva[*1], **Tom Darius**[2], **Leandro Mancina**[3], **Janina Eden**[3], **Kendra Wernlé**[3], **Ahmed Ghoneima**[4], **Adam Barlow**[4], **Pierre-Alain Clavien**[3], **Philipp Dutkowski**[5], **Philipp Kron**[5]

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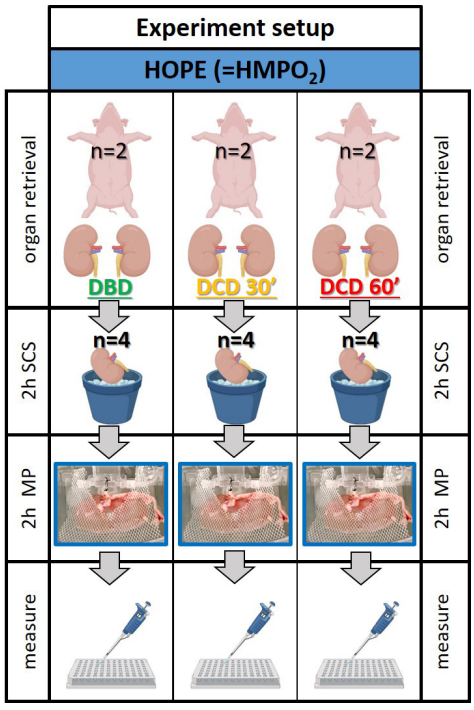
Background: The gap between available donor grafts and patients on the waiting lists is constantly growing, leading to an increased utilization of high-risk kidney grafts. The use of these organs requires new strategies of organ optimization and assessment before transplantation. Hypothermic machine perfusion (HMP) is standard for kidneys obtained from donation after circulatory death (DCD), whereas evidence for additional oxygenation to HMP is still very limited and an objective assessment of HMP-perfused kidneys is lacking. This study aims to determine whether Flavin mononucleotide (FMN) is a feasible and suitable marker for the assessment of kidney injury.
Methods: In a porcine model, the feasibility of assessing DCD kidney grafts during hypothermic oxygen perfusion (HOPE) was explored. A DCD group with warm ischemia times (WIT) of 30 and 60 minutes, mimicking a clinically relevant scenario, and a DBD group (donation after brain death) as control (*see Figure*). Kidneys were subjected to two hours of static cold storage (SCS) followed by two hours of end-ischemic HOPE with real-time FMN measurement. FMN values were then related to initial ischemic damage.
Results: We demonstrate, first, feasibility of FMN measurement in perfused kidneys, and secondly its correlation with the WIT. Accordingly, perfusate FMN was significantly higher in the 60-minute WIT group (n=4) compared with the 30-minute WIT (n=4) and DBD group (n=4). FMN release also correlated with DAMP signaling. Finally, ATP replenishment was best in DBD kidneys, followed by DCD kidneys with 30 and then by 60 minutes of WIT.
Conclusions: This study proves feasibility of FMN measurement in kidneys during HOPE. In addition, we reveal a correlation between FMN quantification and pre-existing kidney injury. Based on this, real-time FMN measurement during HOPE may be an objective assessment tool in the near future to accept high-risk kidneys for transplantation while minimizing post-transplant dysfunction.



Living donation

FG8_1 USEFULNESS OF LIVER VOLUMETRY BASED ON HEPATIC VENOUS TERRITORY AS PREOPERATIVE EVALUATION FOR LIVING DONOR LIVER TRANSPLANTATION

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Background: To evaluate whether volumetry based on middle hepatic venous (MHV) territory is useful as a preoperative examination to select patients who require a interposition venous graft (IVG) replacing a MHV in right liver living donor liver transplantation (LDLT).
Methods: This retrospective study was conducted with 79 donors and recipients. Volumetry of MHV territories was performed by using a 3-D volumetric software (Hepatic VCAR; GE Healthcare). If the MHV territory was more than 30% of total volume of the graft, IVG was recommended. The subject was classified into four groups. Groups 1 was the patients whose MHV territory was less than 30% in the RL, so IVG was not connected; group 2 was the patients whose MHV territory was less than 30%, but IVG was connected by surgeon's decision; groups 3 was the patients whose MHVT was more than 30%, but IVG was not connected or closed by thrombosis; and group 4 were patients whose MHV territory was more than 30%, and IVG was connected. To explore the usefulness of this technique, the volume changes of MHV territory were examined before and after surgery. Graft regeneration ratio (GRR) was calculated according to the following formula. [GRR (%) = (volume after surgery - volume before surgery) / volume before surgery] The GRRs were compared among the patients group by using Kruskal-Wallis test. Given that graft-to-recipient weight ratio (GRWR) is an important factor related to regeneration, the analyses were conducted by dividing < 1.0 of GRWR or other.
Results: The number of patients in each group was as follows: 21 in group 1; 17 in group 2; 7 in group 3; and 34 in group 4. In the patients whose GRWR was ≥1.0, the GRR of group 3 was significantly lower than that of group 4 (-21.5% vs. -2.7%; p = 0.041). In case of <1.0 of GRWR, the GRR of group 3 was 3.0%, and that of group 4 was 24.4% (p = 0.052). In contrast, the GRR in group 1 was not different from that of group 2 (9.5% vs. 8.7% in ≥1.0 of GRWR; 24.9% vs. 2.2% in <1 of GRWR; all p >0.05).
Conclusions: Volumetry based on MHV territory is useful to determine whether IVG is needed to ensure regeneration of the MHV territory. Especially, in patients of which MVH territory was >30% and the GRWR was less than 1.0, the connectivity of IVG was crucial to graft regeneration.

FG8_2 RISK FACTORS ASSOCIATED WITH SURGICAL MORBIDITIES OF LAPAROSCOPIC LIVING LIVER DONORS

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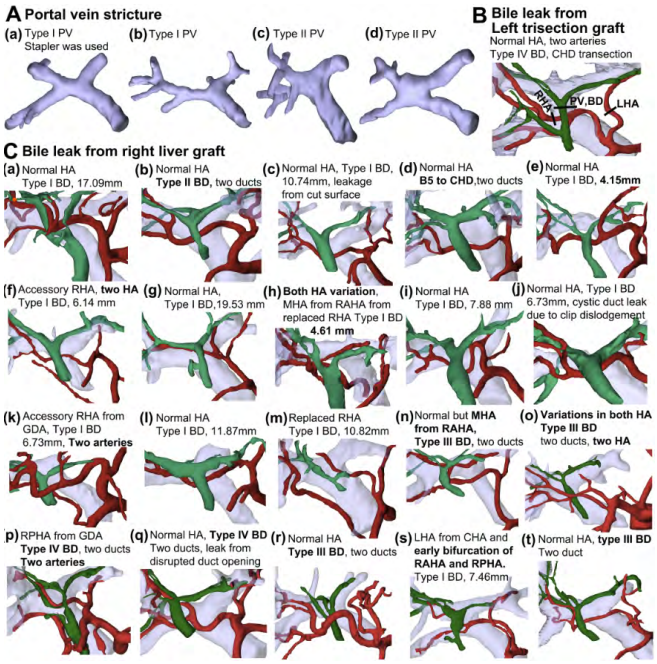
Background: This study analyzed incidence and risk factors for surgical morbidities of laparoscopic living donors. Although laparoscopic living donor program has been safely established in leading centers, donor morbidities have not been sufficiently discussed.
Method: Laparoscopic living donors operated during May 2013 to June 2022 were reviewed. Donors' complications were reviewed, and factors related to bile leakage and biliary stricture were analyzed using multivariable logistic regression method.
Results: A total of 636 donors underwent laparoscopic living donor hepatectomy. Open conversion rate was 1.6%. Thirty-day complication rate was 16.8%. (n=107) Grade IIIa and IIIb complication occurred in 4.4% (n=28) and 1.9% (n=12), respectively. The most common complication was bleeding (n=38, 6.0%). Fourteen donors (2.2%) required reoperation. Portal vein stricture, bile leakage and biliary stricture occurred in 0.6% (n=4), 3.3% (n=21), and 1.6% (n=10) of cases. Readmission rate and reoperation rate was 5.2% (n=33) and 2.2% (n=14), respectively. Risk factors related to bile leakage were two hepatic arteries in liver graft (OR=13.836, CI=4.092-46.789, P<0.001), division-free margin <5mm from main duct (OR=2.624, CI=1.030-6.686, P=0.043) and estimated blood loss during operation (OR=1.002, CI=1.001-1.003, P=0.008) while Pringle maneuver (OR=0.300, CI=0.110-0.817, P=0.018) was protective for leakage. Regarding biliary stricture, only bile leakage was the only significant factor (OR=11.902, CI=2.773-51.083, P=0.001).
Conclusion: Laparoscopic living donor showed excellent safety for majority of the donors and critical complications were resolved with proper management. To minimize bile leakage, cautious surgical manipulation should be made on donors with complex hilar anatomy.



FG8_3 DUAL GRAFT LDLT HAS A ROLE IN AVOIDING SMALL-FOR-SIZE SYNDROME

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Background: Live donor liver transplantation(LDLT) is established as a complementary method to the scarceness of deceased donors. Many technical improvements were developed to expand the donor pool. But 22% of donor candidates were rejected due to various causes, small remnant liver volume or small graft size for recipient were most common. To get sufficient graft volume and donor safety, we developed dual grafts LDLT, using two grafts from different donors.
Methods: From Mar. 2000 to Dec. 2018, we performed 593 dual grafts LDLTs out of 5121 cases of total LDLTs(11.5% of LDLTs). 9% of donor candidates were selected for dual donor LDLT(RL 31.5%, LL 2%, complete rejection 39.4%). Most common combination of grafts were left and left graft, due to small remnant liver volume in donor(70.5%). Right and left graft were used in 29.5%. Various grafts, ABOi donor, split graft from deceased donor, and from donor exchange program, were included in this graft combinations.
Results: Mean GRWR from dual grafts was 1.03 similar with single right lobe graft (1.04). overall donor morbidity of dual graft(1.5%) was not significantly different from single graft(2.2%). There was no significant different of recipient survival rates(1, 5, 10years, 89.3%, 83.9%, 80.1%) between dual and single graft LDLTs. Single graft atrophy were developed in 47 recipient, predominantly in right side which was suboptimal graft, without severe sequalae. Recipient complications associated technical problems were higher in early cases but with improvement in technique and experiences, recently its complications are similar with single graft recipients.
Conclusions: Live donor liver transplantation using dual grafts is a requisite option for selective patients who has no conventional suitable donor. With this innovative technique, we can expand donor pool about 10% in LDLT.

FG8_6 REVOLUTIONIZING LIVER TRANSPLANT: THE JOURNEY FROM LAPAROSCOPIC LDLT TO ROBOTIC LDLT

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Background: Minimally invasive surgery (MIS) is becoming increasingly popular in various surgical fields. Within the field of living donor liver transplantation (LDLT), MIS has been historically thought challenging due to worries regarding excessive bleeding and complexity. Hybrid techniques of LDLT have been documented, showing MIS may be possible with the right patient selection. We described various trials, errors, and established techniques of minimally invasive LDLT. We compared each method's differences, technical merits, and drawbacks.
Methods: From June 2020 to August 2021 we performed 14 minimal invasive LDLTs, including robotic hybrid LT. We attempted each procedure in a stepwise manner and, after completing explant by laparoscopy then attempted engraftment through laparoscopy or robotic surgery.
Results: The recipients' average age was 54.1 ± 9.4 years. All underwent modified right liver grafts; 7 (half) were Child-Pugh A, with an average MELD score of 10.8 ± 3.7 and GRWR of 1.13 ± 0.33. Total operative time was 471.9 ± 216.2 minutes; explant time 119 ± 46.6 minutes; engraftment time 201 ± 93.3 minutes. Early complication rate 28.6%; late complication rate 14.3%. Average ICU stay 3.9 ± 0.6 days; total hospital stay after surgery 11.5 ± 4.1 days. 12 underwent engraftment using an upper midline incision after laparoscopic explant. Successful right and left mobilization were achieved in the first 4 cases, with one case requiring open conversion due to bleeding. Subsequently, successful totally laparoscopic mobilization and hilar dissection were performed in 2 cases. The next 3 cases were successful in totally laparoscopic explant, and engraftment was achieved using the upper-midline incision. The 10th case was the first to attempt robotic anastomosis, and the 11th case was the first to successfully perform robotic engraftment. The last 2 cases underwent laparoscopic explant followed by Pfannenstiel incision and robotic anastomosis.
Conclusions: MIS LDLT requires patient selection and offers smaller wounds and faster recovery than open surgery. It can be performed via laparoscopic and robotic surgery, with precautions and initial experiences for each step described. This perspective provides a reference for future transplant surgeons to quickly reach the learning curve.

FG8_7 POST-LIVER TRANSPLANT LONG-TERM SURVIVAL IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE: LIVING-DONOR VERSUS DECEASED-DONOR LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is a life-saving treatment for patients with acute-on chronic liver failure (ACLF). In patients with ACLF, early LT is crucial to ensure the success of LT, therefore, the decision to LT and donor-organ should be taken rapidly. We compared post-LT long-term survival in patients with ACLF: living-donor versus deceased-donor LT.
Methods: Of 3686 LT recipients between 2008 and 2019, consecutive 854 patients who met the criteria for ACLF (363 ACLF-1, 276 ACLF-2, 215 ACLF-3 grade) were retrospectively evaluated in a large volume LT center. In patients with ACLF, urgent living-donor LT program within 24-48 hours was expedited in carefully selected patients, whenever timely allocation of deceased-donor organ was not available. Mortality data was collected and followed up to February 2020 (i.e., at least 1 years and up to 12 years since the date of LT) from the medical record database and Kaplan-Meier cumulative survival curves and log-rank test were evaluated.
Results: Living-donor LT was performed in 483 (56.6%) of patients with ACLF: 261 (71.9%) of ACLF-1, 147 (53.3%) of ACLF-2, 75 (34.9%) of ACLF-3. Living-donor LT showed better overall survival rates compared to deceased-donor LT (P<0.001). When patients were grouped with ACLF grades, living-donor LT showed better survival outcomes especially in patients with ACLF grade 1 and 2 (P=0.025, P=0.0024, respectively), however, in those with ACLF grade 3, the overall survival outcome was numerically higher in living-donor LT but was not statistically significant compared with deceased-donor LT (72% vs. 67.9% at 1 year; 67.5% 57.6% at 5 year; log-rank, P = 0.21)
Conclusions: Whenever timely allocation of deceased-donor organ was not available, urgent living-donor LT program needs to be expedited to improve survival in patients with ACLF.

FOCUS GROUPS

Living donation

FG8_8 *EFFECTIVENESS OF A DESENSITIZATION PROTOCOL ON ANTIBODY-MEDIATED REJECTION IN LIVING DONOR LIVER TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

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Background: Graft failure associated with donor specific antibody (DSA) is rare but consistent in living donor liver transplant (LDLT). This study aims to analyze the outcomes of desensitization protocol according to the preoperative antibody mediate rejection (AMR) risk.
Methods: We reviewed 998 cases of LDLT between January 1, 2012 and December 31, 2021 retrospectively. The desensitization treatment was protocolized for three different risk groups based on crossmatching(CDC), flow cytometry cross-matching (FCXM), and single antigen DSA test results: Rituximab + plasma pheresis for high risk (all positive), Rituximab only for intermediate risk (CBC-, FCXM+, DSA+), no treatment for low risk (only DSA+). The graft and patient survival of those retrospective cohort were analyzed.
Results: From 640 ABO compatible cases, there were 292(45.6%) and 348(54%) cases each before and after desensitization treatment was protocolized, with 2(0.7%) and 4(1.1%) incidents of AMR respectively. From 69 cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69) (Table 1). Among cases with both pre- and post-desensitization DSA measurement, DSA MFI showed significant reduction as a result to desensitization treatment. Crossmatching results showed high correlation(p<0.001) with DSA mean fluorescent intensity(MFI), and also showed high correlation(p<0.05) with AMR incidence.
Conclusions: AMR incidence remaining relatively similar despite the significant increase in number of high-risk group recipients post protocol initiation, suggests that the desensitization treatment might be effective. Studies including larger number of cases are needed to prove the necessity of desensitization protocol in clinical settings.

Table 1. Presumed risk level seems viable, but the proportion showed no significant difference.

		DSA level				
	AMR positive / total cases	High	Intermediate	Low	No risk	Total
AMR risk level by Crossmatching	High	2 / 20	0 / 2	0 / 1	0 / 0	2 / 23
	Intermediate	1 / 17	0 / 11	1 / 9	0 / 0	2 / 37
	Low	0 / 0	0 / 2	0 / 6	0 / 1	0 / 9
	No risk	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
	Total	3 / 37	0 / 15	1 / 16	0 / 1	4 / 69

Oncology - it's time for wider access

FG9_1 ONCOLOGIC RESULTS AFTER TEN YEARS OF SYSTEMATIC APPLICATION OF LOCO REGIONAL THERAPIES FOR HEPATOCELLULAR CARCINOMA

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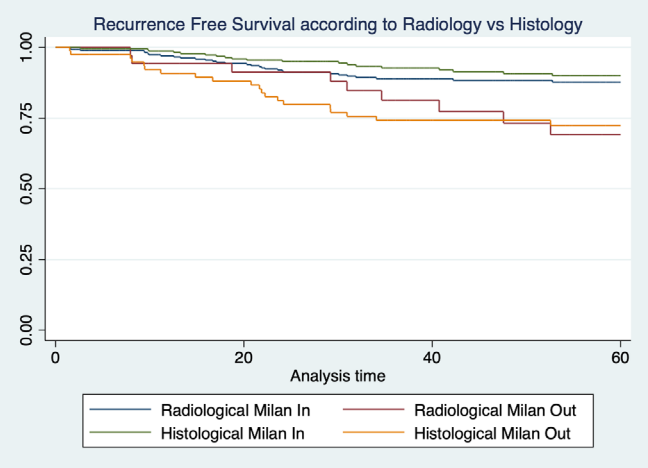
Background: after the definition of Milan Criteria (MC) the effort to find patients who, despite being MC Out (MO), could benefit from LT without significant effect on Recurrence Free Survival (RFS) led to the development of Down-staging (DS). The main objective of the study is to compare the Recurrence Free Survival (RFS) of Milan IN (MI) and Milan Out within the DS group at the last pre-LT Radiological Imaging (RI). The secondary aim is to compare the RFS of patients In/Out Milan stratified by last pre-LT RI or explant pathology (EP).
Methods: a retrospective analysis of consecutive liver recipients after LRT for HCC between 2011 and 2020. LRT included Liver Resection, Ablation, Trans-Arterial Chemoembolization or Radioembolization. Considering the features of HCC at the diagnosis and at the last pre-LT RI, we identified 3 groups: MI at diagnosis and at last pre-LT RI (Group A), MO at diagnosis but MI at last pre-LT RI (Group B) and MO at pre-LT RI (Group C). We compared the RFS of the groups using Cox regression and multivariable logistic regression models. We also compared the RFS of patients In/Out MC at the pre-LT RI with those In/Out MC at EP.
Results: We included 293 patients, of which 191 (65.19%) were in Group A, 69 (23.55%) in Group B and 33 (11.26%) in Group C. The median waiting time in the list was 9.5 months (IQR 4.4 - 17.3). No difference between groups regarding LRT in type and number was observed. However, patients in Group B received more frequent multimodal LRT with respect to Group A but without reaching statistical significance (p=0.062). The median time between the last imaging and LT was 2.39 months (IQR 1.2 - 4.4) and the follow-up (FU) after LT was 55.3 months (IQR 30.1 - 72.8). After COX-regression analysis, alpha-fetoprotein (AFP) at diagnosis (p<0.001), the need for multiple types of LRT (p=0.024), being MO at last imaging (p=0.014) and AFP levels (p=0.008) at LT resulted significantly associated with RFS. Conversely, initial MC status at diagnosis did not impact RFS (p=0.132). Finally, no differences were observed after stratification, MI at pre-LT RI vs EP (p=0.3) and MO at pre-LT RI vs EP (p=0.9).
Conclusions: Patients who underwent successful DS at LT have similar RFS to those always within the MC. Thus, LRT plays an important role in increasing eligible patients for LT and maintaining similar long-term outcomes.



FG9_2 LAPAROSCOPIC ABLATION AND SALVAGE TRANSPLANTATION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Background: No studies evaluate a strategy based on laparoscopic microwave ablation followed by salvage liver transplantation (LT) for patients with hepatocellular carcinoma (HCC).
Methods: Between 2014 and 2020, 512 HCC patients were treated with laparoscopic ablation, followed by transplantation in case of a transplantable recurrence or liver failure. All patients enrolled were diagnosed as HCC within the Milan criteria, with Child A-B cirrhosis, and were judged unsuitable for liver resection or percutaneous ablation.
Results: Ablation was complete for 90% of nodules. No mortality occurred. Over a median follow-up of 51 months for survivors, 243 patients (47%) had new treatments for HCC recurrences, 161 (31%) were listed for LT, and 113 (22%) had LT. One-hundred-six patients (21%) were alive without recurrence more than 24 months after ablation. The intention-to-treat survival rates at 1, 3, and 5 years were 88%, 79%, and 68%, respectively. The primary survival predictors at multivariable analysis were child B class liver function and alpha-fetoprotein levels higher than 400 ng/ml.
Conclusions: First-line laparoscopic ablation followed by salvage LT achieves intention-to-treat survival figures similar to other radical therapies for HCC while limiting the number of grafts required.

FG9_4 LIVER TRANSPLANTATION FOR HCC BEYOND MILAN CRITERIA AFTER DOWN-STAGING WITH STEREOTACTIC RADIOTHERAPY OR TRANSARTERIAL RADIOEMBOLIZATION

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Background: Liver transplant (LT) is the first-line therapy (tx) for early HCC, but it can be offered also for HCC outside LT-criteria if successfully down-staged. According to Barcelona Clinic Liver Cancer (BCLC) staging system, transarterial chemoembolization (TACE) and systemic therapy (ST) are recommended for intermediate (BCLC B) and advanced HCC (BCLC C), respectively. We reported pre- and post-LT characteristics of pts undergoing stereotactic radiotherapy (SABR) or transarterial radioembolization (TARE) for Milan-out HCC.
Methods: pts transplanted from 01/01/2019 to 30/09/2022 after HCC down-staging from Milan out to Milan/Up-to-7 in by SABR or TARE were enrolled. Follow-up (FU) was closed on 31/12/2022.
Results: In the study period 573 LTs were performed; 257 (44.9%) were affected by HCC and 15/257 (5.8%) pts fit our inclusion criteria. Median age 56 years, median biochemical MELD 9. All except 2 pts were Child A. 11 pts were BCLC-B and 4 pts BCLC-C (vascular invasion). Median baseline AFP 62 IU/mL. 8 pts (53.3%) underwent TARE (unilobar infiltrative HCC w/o portal trunk invasion) and 7 SABR (subglissonian or hypovascularized HCC). After a median of 8.9 [4-16] months since tx, pts were registered on the LT-waiting list (14 pts Milan-in and pt #3 Up-to-7-in). LT was performed after a median time of 23 days. At histological examination of the explanted livers, 4 pts had no HCC; pt #7 had cholangiocarcinoma and pt #11 both HCC and mixed cholangio-HCC. Six pts (54.4%) had poorly differentiated G3-HCC and 3 showed microvascular invasion (Table 1). 9 pts received everolimus + tacrolimus (1 acute rejection 1 month after LT) and 6 tacrolimus + mycophenolate. After a median FU of 1.8 years [1-2.6] pt #1 died from metastatic HCC 1.8 year after LT, while 14 pts (93.3%) were still alive, 12 (80%) without recurrence. Pt #10 underwent TACE plus ST for HCC recurrence 1 year after LT and pt #12 adrenal metastasectomy at 6 months; both underwent pre-LT TARE for HCC with portal invasion.
Conclusions: Our 15 HCC pts (11 BCLC-B, 4 BCLC-C) underwent LT after an overage time of 8.9 months from a successful down-staging with SABR or TARE. Fourteen out of 15 (93%) pts are still alive after a post-LT follow-up of 1.8 years; 1 pt died from HCC. 2/4 (50%) pts with baseline portal invasion showed HCC recurrence after LT.

Patient	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15
AT DIAGNOSIS															
N° HCC	3	2	2	4	6	2	3	3	2	4	4	1	2	2	3
Max diam HCC (mm)	80	48	55	54	47	65	60	50	Infiltrative	Infiltrative	54	60	82	77	50
AFP (IU/mL)	6.3	10070	2.7	4	8.4	23.6	613	40.7	1915	40000	NA	906	83	10	756.4
Milan out	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Up-to-7 out	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
Portal Invasion	N	N	N	N	N	N	Y, Lobar	N	Y Lobar	Y Lobar	N	Y Segmental	N	N	N
HCC THERAPY	SABR	SABR	SABR	TARE	SABR	TARE	TARE	SABR	TARE	TARE	TARE	TARE	TARE	SABR	SABR
AT LT															
N° viable HCC	1	0	2	1	2	0	0	1	0	1	1	0	1	2	3
Diam max HCC (mm)	20	0	50	20	15	0	0	40	0	14	20	0	11	22	24
AFP (IU/mL)	4.6	3.5	2.5	2.9	6.8	5.4	3.1	11.4	26.7	5.6	7.3	1.6	0.7	6	274.8
Milan out	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N
Up-to-7 out	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Portal Invasion	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
EXPLANTED LIVER															
Viable HCC	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	N	N	Y	Y
Differentiation grade	G3	/	G3	G3	G1	G1	G2	G2	/	G3	G3	/	/	G2	G3
Microvascular invasion	N	/	Y	N	N	N	N	N	/	Y	Y	/	/	N	N
POST LT															
Recurrence	Y	N	N	N	N	N	N	N	N	Y	N	Y	N	N	N
Death	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N

FG9_5 EVALUATION OF A DELAYED LIVER TRANSPLANT STRATEGY FOR PATIENTS LISTED FOR HCC TREATED WITH RESECTION OR THERMO-ABLATION AS A BRIDGE TO LT

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Background: To maximize utility and prevent premature liver transplantation (LT), a delayed transplant strategy (DS) was adopted in France in 2015 in patients listed for any single hepatocellular carcinoma (HCC) treated with surgical resection (SR) or thermo-ablation (TA) during the waiting phase, postponing LT until recurrence. It is crucial to make sure that pre and post-LT outcomes of patients entering DS are not negatively impacted. The purpose of this study was to evaluate this DS.
Methods: Study population: patients listed for HCC in France between 2015 and 2018, with an AFP score ≤2. After data extraction from the national LT database, Cristal, 2025 patients were classified according to 6 groups: single tumor entering DS, single tumor not entering DS (NDS), multiple tumors (MT), other loco-regional therapies (LRT) with no DS, untreatable HCC (UH) and T1 tumors (T1). 18-months Kaplan-Meier estimates of drop-out before LT and 5-year post-LT recurrence and survival rates were compared.
Results: The patients' features are shown in the table. Pre-LT drop-out probabilities were 13, 18, 21, 22 and 25% in DS, LRT and MT, UH, NDS and T1, respectively (p =0.05), significantly lower in DS, and higher in T1. Post- LT 5-year survival and recurrence rates did not differ among groups.
Conclusions: The DELTAS HCC study shows that: **a.** DS can be considered in around 20 % of HCC candidates (DS and NDS groups). **b.**DS in patients amenable to curative treatments pre-LT has no negative impact on pre- and post-LT outcomes. **c.**DS has the potential to redistribute organs to patients in more urgent need and can reasonably be pursued. The unexpected high drop-out in T1 patients seems related to a combination of purely MELD–based driving rules, with a 15 median MELD at listing, hampering bridging treatments and access to LT. It calls for revision of allocation rules in this subgroup.

	DS N = 341 (16.8%)	NDS N = 74 (3.7%)	MT N = 238 (11.7%)	LRT N = 879 (43.4%)	UH N = 346 (17.1%)	T1 N = 147 (7.3%)	p
MELD (median)	8.47	10.25	8.95	9.93	15.54	13.21	<0.0001
Tumor size (cm) (median)	2.5	2.55	2.4	3.0	2.3	1.5	0.0005
Number of tumor (median)	1.0	1.0	2.0	2.0	2.0	1.0	0.006
AFP (ng/mL) (median)	7.95	7.00	9.25	9.30	5.71	7.00	1
Time from treatment to LT (days) (median)	910	285	666	442		717	<0.0001

This study benefited from a grant the French Organ Sharing Organization.

FG9_6 LIVER TRANSPLANTATION SURVIVAL BENEFIT OVER RESECTION FOR COLORECTAL METASTASIS IN PATIENTS WITH HIGH TUMOR LOAD: MULTICENTER RETROSPECTIVE ANALYSIS

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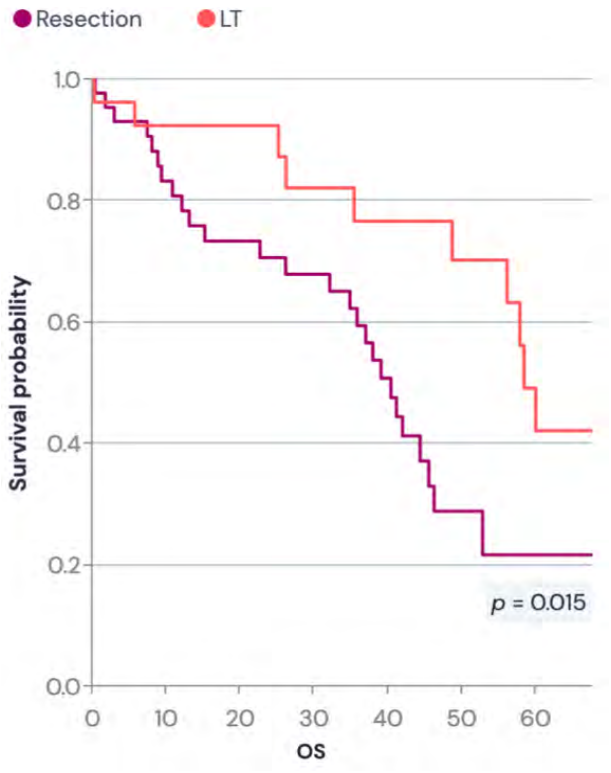
Background: Liver resection (LR) is standard of care for technically resectable colorectal liver metastases (CRLM). High number of lesions and bilobar disease is, however, associated with high recurrence rates and low 5-year overall survival (OS). Liver transplantation (LT) may yield 5-year OS rates from 60-80% for selected patients with unresectable CRLM. The role of technical resectability as a biological predictive factor is limited, since this is an anatomic-technical parameter displaying high variability among centres and individual surgeons. Hence, we tested the hypothesis that LT could offer better OS than resection in technically resectable patients when hepatic tumor load (HTL) is above a threshold (i.e.: max number of lesions ≥ 8), in patients that otherwise satisfy the inclusion criteria for LT according to the SECA-I study.
Methods: LR performed at 10 tertiary HBP centres in CRLM patients between 2002 and 2021, were compared with LT for unresectable CRLM performed at 7 of the centres between 2006 and 2021. Exclusion criteria were age ≥ 71 years, weight loss > 10%, ECOG score > 1, standard contraindications to LT, other malignancy, liver first approach, neoadjuvant chemotherapy <6 weeks, extra-hepatic tumour.
Results: 1144 CRLM patients underwent 1060 LR and 84 LT. 723 patients were eligible: 641 underwent LR and 82 LT. 5-year OS after LR and LT was 42.7% and 54.9% (p = 0.077). Patients were stratified according to favourable prognostic features for transplant (Tx-pos) by max diameter < 5.5 cm and CEA < 80 µg/L. Overall, 47 (57.3%) LT satisfied Tx-pos and 5-year OS after LT within and outside Tx-pos criteria was 61.7% and 38.7% (p < 0.006). High HTL were found in 98 (66.2%) LR and 50 (33.8%) LT patients with corresponding 5-year OS of 15.7% and 48.6% respectively (p < 0.001). In the cohort with Tx-pos features and HTL (i.e.: 46 [7.2%] LR and 27 [33%] LT) the 5-year OS after LR and LT was 21.7% and 49.2% (p = 0.015); disease-free survival (DFS) 17.8% and 17.9% (p = 0.593); and survival after recurrence (SAR) was 15.7% and 31% (p = 0,157). Table 1 shows different recurrence pattern after LR and LT in this cohort.
Conclusions: About 7% of liver resected CRLM patients have high tumor load and favourable prognostic criteria for LT. This selected group could possibly obtain better survival outcomes with LT compared to standard of care LR.

Table 1. Recurrence pattern after LR and LT in Tx-pos & HTL cohort

Recurrence site	LR n = 31	LT n = 20
Liver only	7 (22.6%)	3 (15%)
Lung only	1 (3.2%)	4 (20%)
Liver & Lung	11 (35.5%)	4 (20%)
Multisite	12 (38.7%)	9 (45%)



FG9_7 VON WILLEBRAND FACTOR ANTIGEN ALLOWS IMPROVED DECISION MAKING IN HCC PATIENTS SUBJECTED TO SURGICAL TREATMENT OPTIONS

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Background: Liver transplantation (LTx) and liver resection (LR) are potential treatment options for patients with hepatocellular carcinoma (HCC). We previously reported on von Willebrand factor antigen (vWF) as a predictor of post-hepatectomy liver failure (PHLF) and early mortality on the waiting list for LTx. In this study, we explore the use of vWF as a tool for perioperative decision-making in patients with HCC.
Methods: Included patients were diagnosed with HCC and underwent either LR or listing for LTx at Medical University of Vienna (MUV) and Mayo Clinic Rochester (MCR) between 2004 and 2022. VWF was evaluated prior to LR or at listing for LTx, respectively. The previously evaluated cut-offs at 182% and 291% vWF were used to divide the cohort into low- (≤ 182%), intermediate- (183% - 291%) and high-risk (> 291%) groups. Clinical course and overall survival (OS) were prospectively documented and retrospectively analyzed.
Results: 443 patients were included: 106 patients underwent LR (MUV: 72, MCR: 34); 337 patients were listed for LTx (MUV: 214, MCR: 123), of those 199 underwent LTx (MUV: 124, MCR: 75). Patients in intermediate- and high-risk groups undergoing LR displayed higher incidences of PHLF (4.0% vs 27.5% vs 53.3%, p<0.001). Further, postoperative OS was significantly reduced in both these cohorts (median in months: 95.5 vs 46.7 vs 13.7, p=0.006). As previously reported, HCC patients with increased vWF had reduced survival on the waiting list (p=0.01). Yet, no difference in post-LTx OS was observed when comparing risk groups according to vWF (median in months: not reached vs 130.4 vs 116.6, p=0.343). Similarly, OS from listing was comparable between vWF risk groups (median in months: 108.7 vs 131.8 vs 90.0, p=0.390).
Conclusions: We here present an international bicentric evaluation of vWF as a perioperative decision-making tool for patients with HCC. Patients with high vWF prior to LR show an increased risk for PHLF and reduced OS and therefore seem to derive limited benefit from surgery. Further, increased vWF is associated with early mortality on the LTx waiting list. As post-LTx and post-listing OS was comparable between risk groups according to vWF, patients presenting with HCC and high vWF values may benefit from LTx listing. We conclude that vWF can optimize LR and LTx decision-making for patients with HCC.

FG9_8 DE NOVO CANCERS AFTER LIVER TRANSPLANTATION: A FRENCH NATIONWIDE COHORT

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Background: *De novo* cancer (DNC) following liver transplantation (LT) have been reported as one of the major causes of post-transplant mortality. Everolimus is frequently prescribed to patients presenting *de novo* cancer after LT and those who are at risk of cancer recurrence. With this study we aimed to estimate the cancer burden after LT at a nationwide level and to evaluate the potential role of everolimus in *de novo* cancer occurrence.
Method: The French national health data system (SNDS), linked with the national hospital database (PMSI), contains information on at least 99% of the French population, concerning ICD-10 codes, medical procedures (MP), prescribed drugs and vital status. 8658 patients having received LT for hepatocellular carcinoma (3902) or decompensated cirrhosis were identified from 2009 to 2019. Algorithms combining ICD and MP identified post-transplant neoplasia at different sites. Cox models including competitive risk, everolimus as time-dependent exposure and propensity score analysed cancer incidence and mortality.
Results: With a median follow-up of 4.6 [2.2, 6.8] years after LT, 1119 (13 %) patients developed DNC, of which 232 (2.7%) dysmyelopoiesis, 216 (2.5%) head and neck, 213 (2.5%) skin cancer, 184 (2,1%) metastatic cancer, 180 (2.1%) lung cancer, 100 (1.2%) lymphoma, 88 (3.3%) colorectal cancer, 87 (1.0%) prostate cancer and 50 (0.6%) bladder cancer. Age, tobacco, alcohol, diabetes and cancer before LT were significantly associated to *de novo* cancer for most studied sites. Three groups of DNC were identified according to survival: blood, skin and prostate cancer with good survival; lymphoma and colorectal cancer with medium survival; ORL and lung cancer with poor survival. During the follow-up, 2588 patients were exposed to everolimus including 997 before the detection of any cancer. In all sites both using landmark analysis (everolimus given or not before DNC) or time-dependent exposure, everolimus was associated neither to a lower incidence nor to a better survival after occurrence (figure).
Conclusion: DNC occur in at least 13% of adults after LT. Systematic screening is clearly insufficient in view of the poor survival. More surprisingly, the antitumoral action of everolimus recipients to prevent de novo malignancies is not clearly demonstrated.

FOCUS GROUPS

Public perception in organ donation: multi-stakeholder vision and work team

FG10_1 ORGAN DONATION AFTER BRAIN-DEATH - FAMILY DYNAMICS, FACTORS FOR CONSENT AND ATTACHMENT OF MEANING AS A WAY TO PROCESS LOSS

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Background: Donation after brain death presents an extremely stressful event with significant impact on the entire donor family, which is faced with multiple challenges being called to manage the loss of a loved one and make a decision regarding the donors´ life and body.
Methods: The current study investigates via semi-structured interviews the experience of family members who consented to organ donation of a brain-dead relative. Specifically, the study aims to understand the: (1) manner and degree of involvement of first-degree relatives in the consent, (2) factors influencing the decision to donate, (3) meaning participants attach to donation, (4) effect of donation on the perception of self and others, (5) relationship dynamics within the family. Corbin and Strauss' grounded theory was applied for the research design and data analysis.
Results: All participants attach significant meaning to their decision, describing donation as the supreme gift of life and do not regret the decision, despite difficulties managing the loss. The decision was made on two levels: an individual and a collective one involving discussions with friends and relatives. Determinants for consent were: the health personnel´s attitude, the level of understanding brain death, trust in the medical team, past donation experience, the ability to attach meaning to donation, belief in the continuation of the deceased's life through the recipients, the knowledge of the donor´s attitude towards donation, specific donor characteristics and the agreement and cooperative decision-making within families. Most participants show signs of personal growth, despite adjustment difficulties and bereavement. The loss challenged religion-affine individuals who distanced themselves from religion after donation. Already strained family relationships suffered or broke after donation, while stable relationships helped maintain family homeostasis.
Conclusions: The study adds to our knowledge regarding personal growth, decision-making and family dynamics in organ donation. It highlights factors contributing to donation consent and its effect on the family. It reveals the necessity of expanding support structures for the donor family, and contributes to empirically based recommendations for an adequate approach and support of the donor family.

FG10_2 RELATIVES' DECISION PROCESSES AND PERCEPTIONS IN THE CONTEXT OF INTENSIVE CARE FOR ORGAN DONATION: RESULTS OF A QUALITATIVE STUDY

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Background: Spain world leading donation rates depend, among other factors, on the implementation of the protocol called Intensive Care for Organ Donation (ICOD), meaning the initiation/continuation of intensive care measures in patients with devastating brain injury when any curative treatment is deemed futile, incorporating the option of donation into their end-of-life care plans. ICOD protocol requires families to grant permission for its application and, after the death of the relative, confirm their willingness to donate their organs. This qualitative research investigates information and decision process of 24 family units that gave consent for ICOD and for the extraction of organs.
Methods: An interview script "focused on the problem" was followed with 9 topics addressed in chronological order. Interviews were recorded on audio, with prior informed consent. With the verbatim statements of the informants, content analysis was carried out with the systematic Constant Comparative Method on 6 main themes: a) Medical information received at the beginning of the crisis; b) Communication of the irreversible state of the patient; c) request for ICOD or donation; d) Factors influencing the decision; e) Assessment of health personnel; f) Assessment of the decision taken at the time and its influence on the grieving process.
Results: Results identify a general hypothesis based on the interaction between the expressed or inferred will of the potential donor and the previous or emerging attitudes of the decision-making relatives towards organ donation, health personnel and the care received by the deceased. Transplant coordinators have an important mission to facilitate the understanding of the whole process and promote the emergence of wills and positive attitudes towards donation, explicit or implicit. The effects of donation on the grieving process are mostly positive when linked to positive ethical and pragmatic assessments, shared by the relatives present or by a broader affective environment.
Conclusions: Family decision process in the context of ICOD are similar to those experienced in other donation procedures and can be approached by transplant coordination taking as reference other normalized practices. FUNDING: ISCIII-PI18/00403-Co-funded ERDF/ESF and Fundación Mutua Madrileña.

FG10_3 OUTCOME TO DEVELOPING EDUCATION PROGRAMS TO ADVANCE ORGAN DONATION ACTIVITY IN THE ORGAN PROCUREMENT ORGANIZATION: A SIX YEAR DATA

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Background: The organ transplantation program of Southern Philippines Medical Center (SPMC) started in 2003 with the kidney transplant at 20 cases per year using living donors. In 2017, SPMC together with University of Barcelona was granted by the International Society of Nephrology and The Transplantation Society the Sister Transplant Center Program (ISN-TTS STC) which aims to promote partnerships to increase transplantation rates. SPMC has no proper education, training and experience in the deceased donation process. It welcomed the support and partnership of University of Barcelona and the Donation and Transplant Institute (DTI) was integrated in the program as part of capability building. The objective of this study is to evaluate the outcome of the training and education on the donation activities in SPMC.
Methods: Five intermediate Transplant Procurement Management (TPM) courses were carried out from 2017 to 2022 together with online mentoring by experts and assistance in the development of a transplantation and donation manual. Data on the deceased donation activity was collected from the hospital from 2016 to 2022
Results: At the start of the Sister Transplant Center Program, there were only 4 deceased donor referrals per year, and no deceased donation was done. A total of 2317 health professionals (46% Doctors, 54% nurses) had been oriented and trained, with 180 participants underwent the 3 day intermediate TPM courses from DTI, and the others received a one day Potential Multiple Organ Donor Management Training Course. Increase in the donation activities was observed with the start of training in 2017. The hospital achieved its record high in the numbers of referrals (n=389) in 2019. The number of referrals dropped from 127 in 2020 to 14 referrals in 2021. In 2022, with additional intervention to include evaluation of the donation process and improvement of the pandemic protocol resulted to 50 referrals with one utilized donor and increase transplantation rates from deceased donor to 200%. This has yield a total of 1121 donation activities for the last 6 years.
Conclusions: Outcome of training and educational support to health professionals improved all aspects of donation activity from referral, family approach to donor utilization and provides evidence that this has improved the donation activity of SPMC

FOCUS GROUPS

Public perception in organ donation: multi-stakeholder vision and work team

FG10_4 ICU STAFF'S SELF-REPORTED NEED FOR SUPPORT AND EDUCATION IN ORGAN DONATION

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Background: Within organ donation (OD) ICU staff members play a key role in identification and management of potential organ donors, as well as the care of relatives. However, OD is a rare event in many centers. This often makes it challenging to achieve and maintain competence needed to fulfill their responsibility in providing a caring environment and in ensuring the availability of organs for patients awaiting transplantation. The aim of this study was to map self-reported educational and supportive needs among ICU staff involved in the OD process.
Methods: A cross-sectional survey was conducted in a large university hospital with 63 ICU-beds and approximately 40 actual donors a year. Around 200 physicians and 800 nurses in 11 ICU departments received an electronic survey. The survey included items about level of experience, educational and supportive needs, and professional competence in OD. Educational need was measured from "no need" to "great need", and professional competence was measured on a Likert scale (1-5), with ranging from "to a small extent" to "to a great extent". Descriptive and comparative analyses were performed.
Results: A total of 211 ICU staff (physicians 57, nurses 154) responded. Mean experience in ICU was 15 years (SD=9,5). The majority had participated in OD management (70%) and in approaching relatives (59%) more than 5 times. Guidance from colleagues specialized in OD (72%) and being relieved from other tasks (62%) were reported as most important supportive measures in the OD process. Physicians' mean score (4.3) was slightly higher (p=0.001) than nurses' (4.1) on feeling competent in caring for an organ donor. Most physicians and nurses reported further educational needs regarding medical management of the donor (79% and 85%, respectively) and in communication (77% and 79%, respectively).
Conclusions: The participants were highly experienced in OD. This indicates that the responders have an interest in OD that may not be representative of all staff in ICU. The results demonstrated the importance of strengthening professional support in OD and providing regular education in medical management and communication skills. A national survey is needed to investigate the level of professional competence in OD and compare educational and supportive needs between university and local hospitals.

FG10_5 IMPROVING DECEASED DONATION THROUGH AN INTERNATIONAL COOPERATION TRAINING FOR HEALTH PROFESSIONALS

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Background: Nurturing a culture and enhancing the knowledge of donation among health professionals appears to be a crucial factor to improve donation. A Belt and Road Organ Donation Capacity Improvement Cooperation Training Project training was an initiative made to educate health professionals in the practice of donation which includes donor evaluation and management, family communication and organ allocation. The study aimed to evaluate the effectiveness of the training by using pre- and post-tests.
Methods: Personnel who directly or indirectly involved in donation and transplantation were enrolled. The training was conducted virtually with an interactive modality that comprised roundtable, clinical case discussion and quiz. The content was developed by experts to include the best practices of donation processes. Participants were required to complete 25 questions before and after the training. Changes in scores were analyzed with 2-tailed Wilcoxon signed rank test. The satisfaction of the participants with the training was collected with the administration of a post-training survey.
Results: Four editions of 3-day training and one edition of 4-day training were conducted in 2021 and 2022. A total of 271 individuals consists of 77% Chinese and 23% international participants from 43 countries were trained. Health professionals from the donation team formed most of the participants (34%), 21% were from the anesthesia department and 19% were from the transplant team. Analysis of the 241 participants who completed both pre-test (median= 6.8/10.0) and post-tests (median= 7.6/10.0) revealed significant difference in score, Z= -7.26, p<0.001. Generally, rating of participants with the training were positive.
Conclusions: The training helped strengthening knowledge and understanding of health professionals. The virtual modality increased accessibility that could reach out and train more individuals. It can be complemented with practical training to further improve the confidence and skills of the practitioners. As a training program based on international cooperation, it promotes participants' understanding on both international standards and local practices and facilitate mutual understanding on organ donation among Belt and Road countries.

FG10_6 MASS MEDIA CAMPAIGNS SENSITIZE BUT FAIL TO INCREASE ACTUAL ORGAN DONATION RATE

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Background: Media campaigns aimed at increasing non-living organ donors (OD) for transplantation have demonstrated increasing intention to donate in their target population, but their effectiveness for increasing donation rates is not clear. The largest broadcasting corporation in Chile conducted a one-year national mass media campaign (2016-2017) intended to decrease familial refusal to donation (FR). It included prime time TV coverages, advertising with well-known personalities, and web, radio, and social media content. In 2016 Chile reached an OD rate of 7.9 donors per million population (dpmp) and 50% FR; and in 2017, 10 dpmp, and 46% FR.
Methods: With the aim of studying the effect of the campaign over OD figures, we analyzed if there were changes in FR and OD between 2016 and 2017 and between the year before and during the campaign, using ANOVA.
Results: For FR we found no statistically significant difference between 2016-17, yearly (p=0,16), semesterly (p=0,28), nor quarterly (p=0,54). Same happened when comparing the period of the campaign (year p=0,17, semester p=0,62, quarter p=0,39). Nonetheless, we found significant differences in OD for both yearly periods (p<0,01; p=0,01). Semesterly, we found significant differences just comparing calendar years (p=0,048), but not campaign years (p=0,09). We found no significant differences in the quarterly analyses (p=0,16; p=0,15).
Conclusions: Even though FR did not change, OD increased. This, because more potential donors reached the donation request stage of the procurement process, which may have been due to more detection and referral, or better care of patients. Both things are the responsibility of the healthcare professionals (HCP) inside the hospitals, so maybe the campaign sensitized HCP, but not its target population. Media campaigns are attractive in the short run, but they are unsustainable and ineffective in the long run. Looking for other interventions, like those targeting HCP should be explored.

FOCUS GROUPS

Public perception in organ donation: multi-stakeholder vision and work team

FG10_8 OLDER LIVING LIVER DONORS CAN ENLARGE THE DONOR POOL: A SYSTEMATIC REVIEW AND META-ANALYSIS

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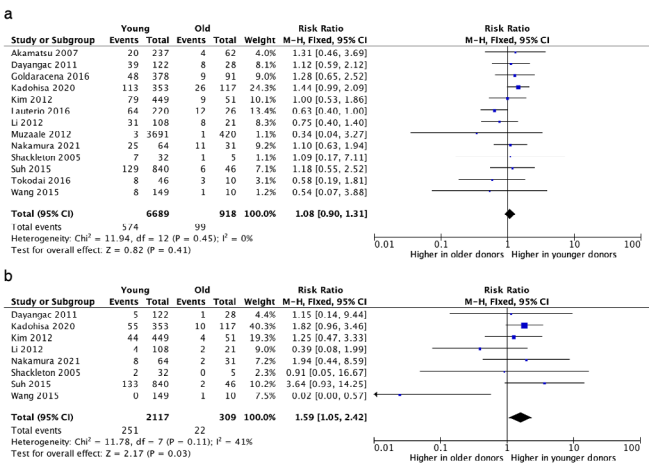
Background: Living donor liver transplantation (LDLT) is an option to solve the donor liver shortage. Due to the aging population, older potential donors are increasingly willing to donate. This study aims to systematically assess the differences in donor peri- and postoperative complications, mortality, and quality of life (QoL) between younger (≤50 years) and older (>50 years) living liver donors.
Methods: Embase, Medline, and Cochrane Central Register of Controlled Trials were searched for studies published between 2002 and August 3, 2022. Studies' methodological quality was assessed using the Newcastle Ottawa Scale. For donor complications and major complications, meta-analyses were conducted, donor mortality and QoL results were systematically described.
Results: The literature search resulted in 7838 studies, of which 17 were included (13 on complications, 2 on mortality, 2 on QoL). In 673/7607 (8.8%) donors, complications occurred, 85.4% in younger and 14.6% in older donors. The risk ratio (RR) for complications in younger donors was 1.08 [0.90, 1.31] (P=0.41). Risk ratios for major complications in younger donors were 0.98 [0.64, 1.48] and 0.89 [0.50, 1.57] using Clavien-Dindo ≥III and ≥IIIb as a major complication, respectively. RR for biliary complications in younger donors was 1.59 [1.05, 2.42] (P=0.03). In 60/14227 (0.4%) donors, mortality occurred, 47 (78.3%) in younger and 13 (21.7%) in older donors. One study on early mortality reported a RR in younger donors of 0.28 [0.06, 1.46], and 1 study on long-term mortality a RR in younger donors of 0.23 [0.12, 0.44]. QoL data was recorded for 414 (72.9%) younger and 154 (27.1%) older donors. Mean physical summary score in younger donors was 51.87 and in older donors 51.29. Mean mental summary score in younger donors was 52.93 and in older donors 55.40.
Conclusions: Older donors do not have a higher complication rate or mortality rate than younger donors after LDLT. They do have a lower rate of biliary complications. In addition, older donors have a similar QoL after LDLT compared to younger donors. With careful selection, older donors can be included in screening programs for living liver donation to expand the donor pool.

Figure 1. (a) Donor complications and (b) donor biliary complications in younger and older living liver donors.



Digital Health for personalized care

FG11_1 DEVELOPMENT AND VALIDATION OF ANTIBODY-MEDIATED REJECTION PREDICTION MODEL ON AUGMENTED DATA USING GENERATIVE MODEL IN KIDNEY TRANSPLANT PATIENTS

Daniel Yoo*[1], Valentin Goutaudier[1], Marta Sablik[1], Blaise Robin[1], Fariza Mezine[1], Jessy Dagobert[1], Esteban Cortes Garcia[1], Marc Raynaud[1], Gillian Divard[1], Vanderlene Kung[2], Edmund Huang[2], Mehdi Maanaoui[3], Jean-Baptiste Gibier[3], Arnaud Lionet[3], Aurélie Sannier[1], Alba Torija[4], Oriol Bestard[4], Carmen Lefaucheur[1], Olivier Aubert[1], Alexandre Loupy[1]

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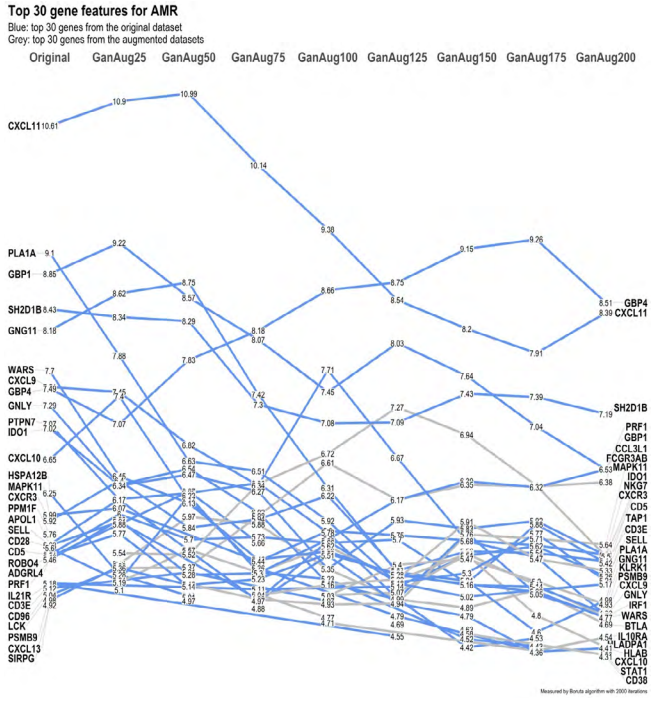
Background: Generative adversarial networks (GAN) are increasingly used in clinical studies, yet evidence of its usage in data augmentation for transcriptomic data is unclear. We aimed to compare the performances of an antibody-mediated rejection (AMR) prediction system based on generated synthetic transcriptomic data, to those based on the original data.
Methods: We prospectively monitored 709 patients from 8 centers in Europe and the US between November 2004 to May 2021, for clinical, biological, immunological, histological, and transcriptomic data. We used the Banff Human Organ Transplant panel on the Nanostring nCounter platform to analyze FFPE biopsies. The outcome was AMR defined by the Banff 2019. The cohort was split into train and test sets in 8:2 ratio. Using GAN based on the train set, 8 synthetic cohorts were generated, each sample size gradually augmented by 25%, which augmented the train set by merging. Random forest (RF) models were developed on the original (train set) and augmented cohorts and were assessed in area under the curve of receiver operating characteristics (ROCAUC) and precision-recall (PRAUC) curves on the test set.
Results: A total of 787 kidney transplant biopsies were included. The RF model on the original cohort had the best ROCAUC of 0.824. Stable ROCAUCs were achieved across all original and augmented cohorts. The 75% augmented cohort (GanAug75) had the best PRAUC of 0.760, compared to 0.722 in the original cohort. GanAug75 showed the best brier score of 0.140. Genes related to AMR signatures (CXCL11, GBP4, GBP1, SH2D1B, GNG11, CXCL9, PLA1A, IDO1, PRF1, CXCR3, GNLY, WARS, CD5, and PSMB9) were consistently predictive to AMR across all original and augmented cohorts while biological and immunological genes for B-cell activations, T-cell, innate immune activation, NK-specific activation, cellular injury, and adaptive immune were captured as important features in the augmented cohorts only.
Conclusions: The study demonstrated that use of generative model (GAN) could augment data and result in comparable stability and partial increase of performance in predicting AMR in ROCAUC and PRAUC, respectively, compared to the original cohort. This study shows that augmenting real-world data with synthetic data can significantly aid in the development of more generalizable and robust models.

Figure 1. Top 30 gene features for AMR. Feature importance analyses were performed on each cohort. Augmented cohorts are inclusive (i.e. Gan SO includes Gan25 dataset). GanAug datasets are augmented datasets including the original train set plus the synthetic dataset.



FG11_2 DEEP LEARNING MODELS OF REAL-TIME NON-INVASIVE IMAGING DURING WARM PERFUSION OF EXPANDED CRITERIA DONOR KIDNEYS POTENTIALLY PREDICT ACUTE REJECTION

Iacopo Cristoferi[*1;2], Farhan Akram[3], Dafsy Bouari[1], Yitian Fang[1], Elsaline Rijkse[1], Martin Hoogduijn[4], Ron de Bruin[1], Carla Baan[4], Marian Clahsen-van Groningen[2;5], Andrew Stubbs[3], Robert Minnee[1]

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Background: Normothermic machine perfusion (NMP) recreates a more physiologic environment that could allow for better organ preservation and objective graft evaluation which are key for the use of expanded criteria donor (ECD) kidneys. However, an objective graft assessment tool for ECD kidneys undergoing NMP is missing. Useful information could be acquired through laser speckle contrast imaging (LSCI), a novel non-invasive imaging technology that provides high-resolution information about microcirculatory perfusion and oxygen delivery. In this study, we investigated the potential use of real-time-available LSCI of ECD kidneys undergoing NMP for post-transplant outcome prediction.
Methods: Fifteen ECD kidneys underwent 2 additional hours of NMP prior to transplantation. Nine kidneys were included in the training/validation set and six kidneys were included in the test set. Oversampling techniques were applied to the individual frames of each sample within the training/validation set to compensate for the low sample size and increase variability and generalizability. LSCI data was acquired during NMP after 15, 75, and 105 minutes. Multiple convolutional neural network-based deep learning models were developed to predict the future development of acute rejection within the first three months after kidney transplantation (AR) or the development of delayed graft function (DGF), separately. Positive predictive value (PPV), negative predictive value (NPV), and weighted F1-score (WF1) were chosen as performance metrics.
Results: Among the included kidneys, nine developed DGF and five developed AR. LSCI performed after 105 minutes of NMP was able to discriminate kidneys within the test set that will develop AR (PPV = 0.80, NPV = 1.00, WF1 = 0.81). The same data collected at earlier time points failed to identify these kidneys. LSCI data at any of the assessed time points was not able to identify kidneys that will develop DGF.
Conclusions: In our cohort, LSCI was able to discriminate kidneys that will develop AR before the donor kidneys were transplanted in the recipient. This novel insight needs to be verified in other studies with larger cohorts. LSCI shows potential for real-time-available graft assessment of ECD kidneys undergoing NMP for periods longer than 90 minutes.

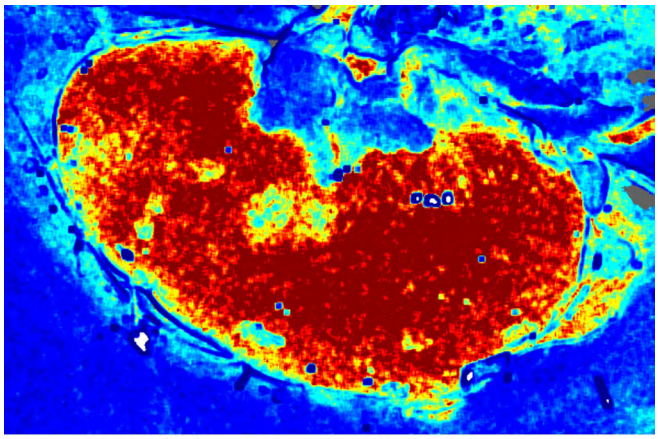

Figure. **Laser Speckle Contrast Imaging of a human kidney undergoing normothermic machine perfusion**

FG11_3 PANCREATIC STEATOSIS AND TRANSPLANT SUITABILITY ASSESSMENT WITH IMAGE BASED MACHINE LEARNING MODELS

Georgios Kourounis[*1], Pierre Ezuma[2], Mark Turner[2], Sorina-Maria Cornateanu[3;4], Lucy Bates[2], Emily Thompson[1;2], Samuel Tingle[1;2], Gourab Sen[1], William E Scott III[2], Steve White[1;2], Colin Wilson[1;2]

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Background: Assessment of donor organ quality in pancreas transplantation is currently qualitative and reliant on the transplant surgeons' experience and subjective decision-making. Limited inter-rater consensus may limit organ utilisation, especially with 'marginal' organs. This study aimed to investigate inter-rater consensus and use machine learning (ML) to develop an objective organ quality assessment tool to evaluate pancreatic steatosis (PS) and suitability for transplant.
Methods: 214 images from 66 separate donor pancreases were assessed independently by three transplant surgeons for PS and transplant suitability. Six convolutional neural network models were selected to evaluate these images. They were each trained with 200 images and tested on the remaining 14 images. 9 organs were also fully analysed by microscopic histological assessment. Correlation between macroscopic and microscopic PS was defined in this subset.
Results: Accuracy during training for PS and transplant suitability respectively was 48.7-53.8% and 55-75%. Accuracy during testing increased for both variables to 71.4% and 78.6% respectively. Model testing for PS found sensitivity, specificity, and area under receiver operating characteristic (AUROC) to range between 41.7-50.0%, 77.7-84.1%, and 0.33-0.4 respectively. Model testing for transplant suitability found sensitivity, specificity, and AUROC to range between 78.6-83.3%, 0-50% and 0.24-0.7 respectively. Macroscopic visual assessment and microscopic histological analysis for PS was strongly positively correlated, r=0.7650, p=0.0082. Testing 14 images for PS required 0.369 seconds per model.
Conclusions: A quantitative and automated ML model for evaluating donor pancreas organ quality is feasible. Increased accuracy between the training and test phase demonstrates a desired generalisability to novel test images. Low sample size, especially in the test dataset may have limited analysis and performance.

Table 1. Inter-observer reliability for macroscopic visual assessment of PS and transplant suitability.

	Value	p-value
Pancreatic Steatosis (Kendall's W)	0.641 Moderate consensus	p<0.0001
Transplant Suitability (Fleiss' kappa)	0.310 Poor consensus	p<0.0001

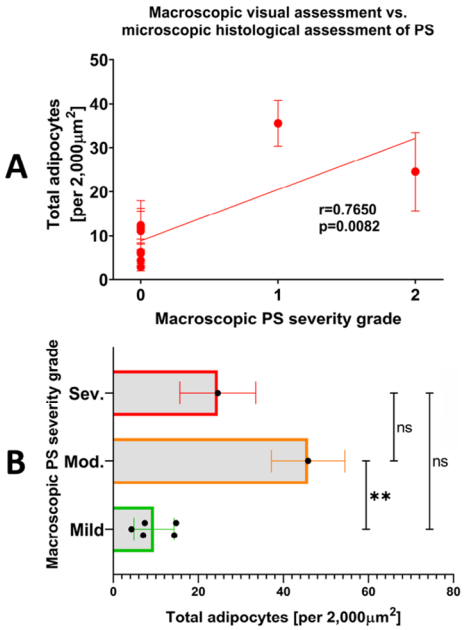
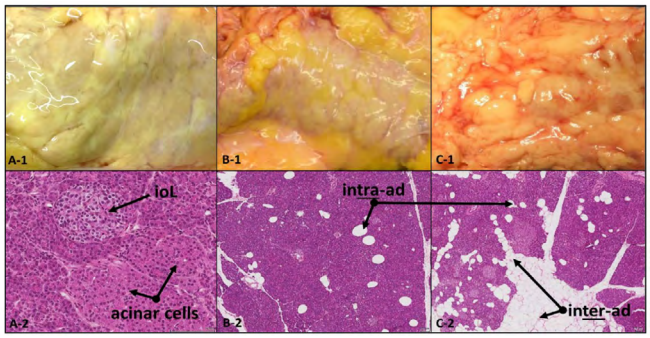


Figure 1. Relationship between macroscopic and microscopic assessment of PS.

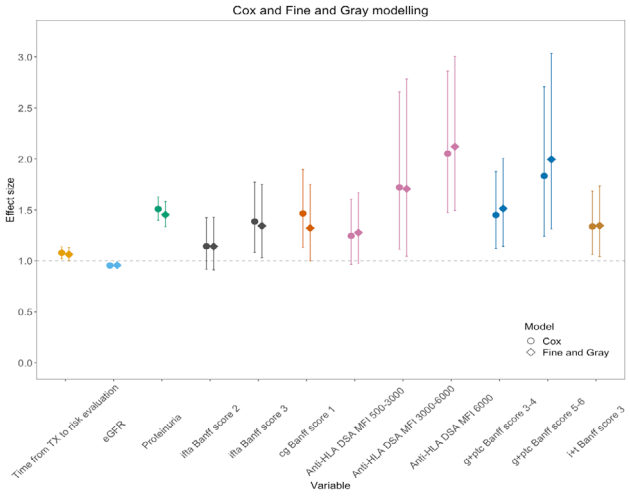


FG11_4 THE IMPACT OF DEATH IN PREDICTING KIDNEY-ALLOGRAFT FAILURE: A COMPETING RISK ANALYSIS STUDY (NCT03474003)

Agathe Truchot[*1], **Marc Raynaud**[1], **Gillian Divard**[1], **Charlotte Debiais-Deschamps**[1], **Sofia Naser**[1], **Carmen Lefaucheur**[2], **Olivier Aubert**[1], **Alexandre Loupy**[1]

[1]Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM U-970, AP-HP, Paris, France, [2]Saint-Louis Hospital, Kidney Transplant Department, Paris, France

Background: The occurrence of clinical outcomes can be precluded by competing risks (e.g death with a functioning graft). In kidney transplantation, a graft failure model censoring for death tends to overestimate the risk of graft failure, which can generate inaccurate predictions. We aimed to compare the predictive performances of a graft failure model censoring for death to those of a model accounting for the competing risk of death.
Methods: We included 4,000 kidney transplant recipients prospectively enrolled in 4 French centers. Death-censored graft failure was estimated using a Cox model, and graft failure accounting for the competing risk of death with a Fine-Gray model. Candidate predictors included recipient, donor and transplant parameters, histology (Banff lesions and diagnoses) and functional and immunological parameters. The prediction performances were assessed with the discrimination (C-index), calibration (calibration plots) and overall accuracy (Integrated Brier Score and Index of Predictive Accuracy).
Results: 549 patients (13.7%) lost their graft and 425 (10.6%) died with a functioning graft after a median post-transplant follow-up time of 7.65 years (IQR 5.39-8.21). The Cox and Fine-Gray models integrated 8 independent factors including the time from transplant to risk evaluation, functional factors (eGFR, proteinuria), histological findings (IFTA, g+ptc, i+t, cg Banff scores) and anti-HLA DSA. The models were highly similar in terms of parameters coefficients, as Fine-Gray's coefficients were all comprised within the 95% CIs of the Cox's. At 7 years post risk evaluation, the models showed similar discrimination (C-index 0.81 for the Cox model and 0.80 for the Fine-Gray model) and overall accuracy (Integrated Brier Score 0.054 for both models). The Index of Predictive Accuracy was higher for the Cox model (31.9% versus 24.8% for the Fine-Gray model). Both models showed good and similar calibration at 3, 5 and 7 years post risk evaluation.
Conclusions: In the setting of graft failure prediction after kidney transplantation, we showed that competition with patient death did not affect the predictive performances of a Cox model. This study shows that a prediction model may not always benefit from a competing risk approach and should be developed based on its final predictive performances.

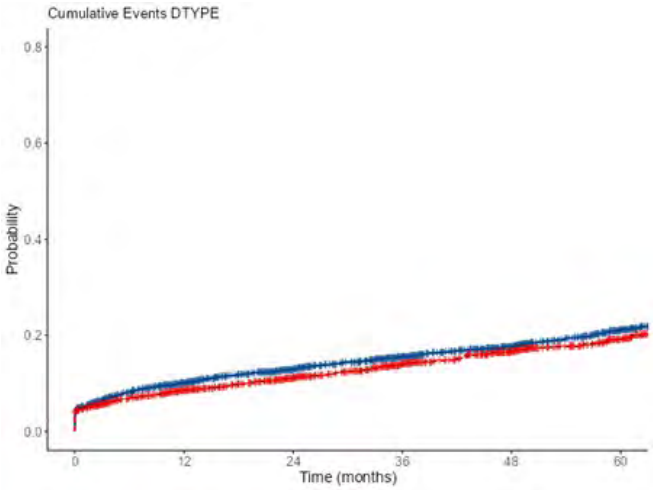


FG11_5 PREDICTORS OF OUTCOMES OF DCD VERSUS DBD KIDNEY TRANSPLANTATION FROM SUPRA MARGINAL DONORS (D4). A MACHINE LEARNING ANALYSIS OF NHSBT REGISTRY DATA

Hemant Sharma[1,2], **Bhavesh Devkaran**[1], **Kunal Kapoor**[1,3], **Thilina Gunawardena**[1], **Abhishek Sharma**[4], **Sanjay Mehra***[1]

[1]Royal Liverpool University Hospital, Transplant and Vascular Access Surgery, Liverpool, United Kingdom, [2]Ochsner Medical Center, Transplant Surgery, New Orleans, United States, [3]University of North Carolina, Transplant Surgery, Chapel Hill, United States, [4]Loyola University Chicago, Reserach Analytics, Chicago, United States

Purpose: Marginal Donor 4- D4 (Donor Risk Index ≥1.50) Matching was introduced as a part of new Kidney allocation scheme in the UK in 2018. The focus is primed at recipient matching but the role of types of transplants for these donors is unreported. The aim of our study is to assess predictors associated with survival outcomes for DCD and DBD transplants from D4 Donors.
Methods: We harmonized the NHSBT Data to shortlist the D4 criterion kidneys. The Predictors of Transplant outcomes were evaluated by five classifiers including logistic regression, SVM, random forest, K-Nearest neighbour matching and adaptive boosting. Random Forest Model had the best performance validated by RMSE. Survival outcomes and predictors data mined from MLA were further mined with Cox Regression.
Results: 6254 D4 donors had 3793 (DBD) and 2461 (DCD) Kidney transplantation between 2000 -2018.. The Odds of DGF and PNF in DCD Kidneys was significant (1.7 (1.5-1.44) p <0-001, 1.2(1.1- 1.6) p=0.02 respectively. There were minor but statistically insignificant difference in regional outcomes across the UK. The Model used 70% of data for testing, 15% for validation and 15% for testing. The Validation accuracy was 91% and testing accuracy was 83.%, AUC was 0.714. In regards to survival at 3 & 5 years post transplant, Serum Creatinine >100 mmol/L at 12 months, Donor Creatinine <100 mmol/l at procurement, Serum Creatinine >100 mmol/L at 3 months, no rejection within 12 months and CIT <12 hrs were the variable of importance in order. The 1,3,5 year survival for DBD versus DCD transplants was 90%, 85%, 81%; 89, 84%, 80% respectively
Conclusions: The MLA accurately predicts variable of importance. There is no statistical difference in DCD verus DBD transplant survival outcomes for D4 kidneys though DCD kidneys with CIT >12 hrs do have a significant risk of DGF and PNF



Variable Importance

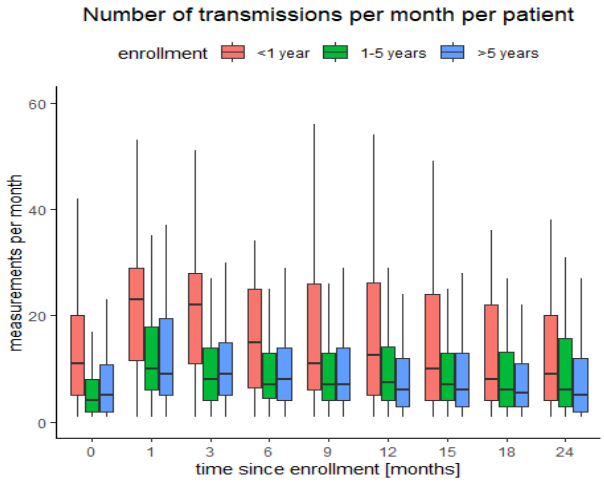
	Total increase in node purity
Serum Creatinine12 Mo <100mmol/l	0.080
Donor Creatinine <100 mmol/l	0.011
Serum Creatinine 3 months <100 mmol/l	0.011
Rejection Count – 12 months	0.007
CIT Min <12 Hr	0.006
Donor BMI <30	0.003
Donor Past History Smoking - No	0.002
HLA MM	0.001
Donor Past History DRUG ABUSE -No	0.000
Functional WIT >60 min	-4.978e-4
Donor Past History Diabetes - Yes	-8.076e-4
Rejection Count – 3 months	-0.002
Recipient Age >60 years	-0.005

FG11_6 MEASUREMENT FREQUENCY OF BLOOD PRESSURE IN NEWLY KIDNEY TRANSPLANTED PATIENTS DROPS OVER TIME IN REGULAR TELEMEDICINE SURVEILLANCE

Marcel Naik[1;2], Verena Graf*[3], Bilgin Osmanodja[1], Georgios Eleftheriadis[1], Wiebke Duettmann[1;2], Matthias Pfefferkorn[1], Klemens Budde[1]

[1]Charite, Medical Department, Division of Nephrology and Internal Intensive Care Medicine, Berlin, Germany, [2]Berlin Institute of Health, Berlin, Germany, [3]Charite, GB - IT, Berlin, Germany

Background: In February 2020 we established a regular telemedicine service for patients after transplantation in order to provide a better follow-up after transplantation and detect problems as early as possible. Here, we report differences in measurement behavior depending on the time after transplantation.
Methods: We included all patients participating in our telemedicine home monitoring project after kidney transplantation from February 2020 until January 2023. Patients submitted their blood pressure measurements, pulse, temperature, personal well-being and weight via smartphone app to the telemedicine center. We analyzed the number of transmissions of blood pressure measurements per month per patient and stratified for time since transplantation and inclusion into telemedicine.
Results: 626 patients were included into the regular telemedicine service, mean age at enrollment 51.5 years. 144.087 blood pressure measurements were submitted since beginning of the project, and patients submitted a median of 8 (IQR 4-19) blood pressure measurements per month. 160 patients (25.6%) were enrolled <1 year, 134 (21.4%) 1-5 years and 332 (53.0%) >5 years after transplantation. Patients transplanted <1 year transmitted more blood pressure measurements than patients during their long-term follow-up (figure 1). After 12 months all groups converged in the number of measurements.
Conclusions: This is a first analysis of the feasibility of blood pressure home monitoring using a telemedicine service with a smartphone patient app. We demonstrate differences in measurement behavior and intensity during telemedicine surveillance depending on the time of enrollment after transplantation. This observation provides first insight into the potential of novel telemedicine services for home monitoring of renal allograft recipients and may help to improve outcomes after transplantation.



FG11_7 EXPECTATIONS, CONCERNS, AND WILLINGNESS TOWARD THE USE OF MHEALTH TOOLS IN LIVER AND KIDNEY TRANSPLANT RECIPIENTS: A PILOT SURVEY STUDY

Justyna Gołębiewska*[1], Eric Buleux-Osman[2], Christophe Duvoux[3], Wojciech Polak[4], Giancarlo La Pietra[5], Jan Raginia[1], Alicja Dębska-Ślizień[1], Vincent Karam[6]

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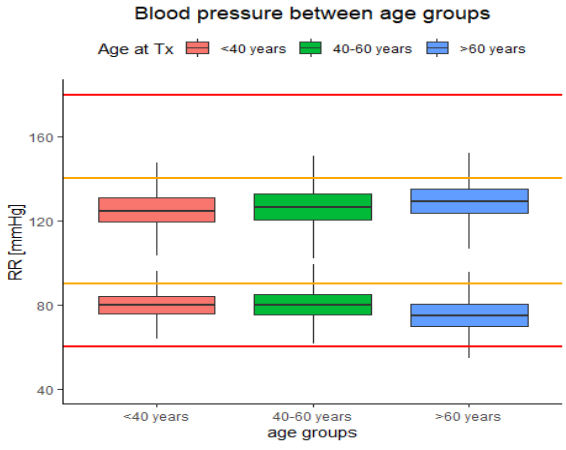
Background: COVID-19 pandemic has accelerated the transformation of healthcare delivery. The aim of this study was to evaluate the attitude of kidney (KTx) and liver transplant recipients (LTx) towards the use of mHealth tools and to identify potential concerns and obstacles in future implementation of digital health solutions in this group of patients in European countries.
Methods: We conducted a cross-sectional survey among French LTx and Polish KTx recipients. The survey comprised 11 questions on sociodemographic data, present use of digital technologies in daily life and for health reasons, overall attitude towards eHealth, specific expectations towards mHealth tools, especially mobile phone applications, and potential barriers to adopting digital health solutions.
Results: Overall, 156 French LTx recipients and 209 Polish KTx completed the questionnaire. Over 60% of respondents were male, mean age of LTx and KTx recipients was 65 ± 11 years and 50 ± 14 years, respectively. Thirty percent of respondents indicated that a health app could have an impact on the medical care and/or health of transplant patients, while 51% of respondents expressed this belief in case of a specific mobile health app connected to their Tx center. Both health apps and wearables were considered useful in engaging in one's own health (49%), improving patient-doctor communication (55%) and understanding one's health condition (43%). Almost 40% of respondents indicated the lack of a mobile app suitable for Tx recipients as a major obstacle towards using mHealth tools. The expectations towards specific functions of an app regarded as useful varied, with the function of scheduling visits at Tx center or access to medical reports, educational resources, monitoring symptoms with the use of wearables and sharing the results with the doctor being most popular. Data privacy and concern of excessive control over one's own health were most common among anticipated considerations expressed in both groups.
Conclusions: Both LTx and KTx recipients expressed a positive attitude towards the use of mHealth tools across all age groups, irrespective of the organ transplanted. The lack of a mobile app suitable for Tx recipients was indicated as a major obstacle towards using mHealth tools.

FG11_8 BLOOD PRESSURE MEASUREMENTS IN A REGULAR TELEMEDICINE SERVICE AFTER RENAL TRANSPLANTATION IN DIFFERENT AGE GROUPS

Marcel Naik[1;2], Matthias Pfefferkorn*[1], Bilgin Osmanodja[1], Georgios Eleftheriadis[1], Wiebke Duettmann[1;2], Verena Graf[3], Klemens Budde[1]

[1]Charite, Department of Nephrology and Medical Intensive Care, Berlin, Germany, [2]Berlin Institute of Health, Berlin, Germany, [3]Charite, GB IT, Berlin, Germany

Background: Renal transplanted patients need a consistent follow-up after transplantation to detect problems as early as possible. Using our telemedicine system with a smartphone app, patients submit their vital signs and well-being into an electronic health record at the telemedicine center. Here we analyzed differences in blood pressure depending on age at transplantation.
Methods: We included all patients participating in our home monitoring after kidney transplantation that started in February 2020 until January 2023. We analyzed all transmitted blood pressure values and averaged per month per patient. Then we stratified for age at transplantation.
Results: 626 patients were included into a regular telemedicine service after renal transplantation, median age at transplantation 44.9 years, 62.5% were male. Time from transplantation until time of enrollment into telemedicine surveillance was 5.5years in median. 249 patients (39.8%) were <40 years, 289 (46.2%) 40-60 years and 88 (14.1%) >60 years. 144.087 blood pressure measurements were submitted since beginning of the project in February 2020 with 10929 patient months. Mean blood pressure values per month were below 140/90mmHg in 88% of all values. There were patients with isolated systolic (6.5%) or diastolic hypertension (3.6%) and in 2.0% combined systolic and diastolic hypertension. Younger patients had lower median systolic and diastolic blood pressure values compared to patients >60 years as shown in figure1 (p≤0.02 between <40 years and >61 years).
Conclusions: Patients had good blood pressure control at home. Self-measured blood pressure values using telemedicine and home monitoring may open new insights into long term blood pressure control outside regular medical institutions. Throughout the observation time as expected younger recipients had lower systolic and higher diastolic blood pressure values than older recipients.



Abstracts of the 21st Biennial European Society for Organ Transplantation (ESOT) Congress, Athens, Greece, 17 – 20 September 2023

BRIEF ORALS

Molecular transplant immunology

BOS1_1 17B-ESTRADIOL THERAPY MODULATES MICROGLIA ACTIVATION AFTER ISCHEMIA AND REPERFUSION REPERCUSSIONS

Fernanda Yamamoto Ricardo-Da-Silva[*1], Pedro Luiz Zonta de Freitas*[*1], Marcelo Sousa[1], Lucas Ferreira Da Anunciação[1], Luiz Felipe Pinho Moreira[1], Cristiano Jesus Correia[1], Ana Cristina Breithaupt-Faloppa[1]

[1]*Laboratório de Cirurgia Cardiovascular e Fisiopatologia da Circulação (LIM-11), Cardiopneumology , São Paulo , Brazil*

Background: Organ transplantation is adopted as the main therapeutic approach for patients without treatment options. In this context, the process of ischemia and reperfusion of the organ during transplant surgery is inevitable. IR induced systemic inflammation is responsible for several systemic physiological changes, including neurological and cognitive complications; those are directly linked to brain parenchyma inflammation, mainly due to the activation of microglia. Studies indicate 17β-estradiol (E2) as a potential therapy to decrease the IR induced inflammatory process. Therefore, here we investigate the effects of E2 treatment on the brain parenchyma after visceral ischemia and reperfusion.
Methods: Male Wistar rats were divided in 3 groups (n= 6/group): (I) sham, surgically manipulated; (II) VIR, animals subjected to ischemia and reperfusion. (III) E2, animals treated with 17β-estradiol (280 µg/Kg, i.v.) after VIR (1h after reperfusion). The visceral ischemia was induced by insertion of a 2-Fogarty® catheter in the descending aorta (aortic occlusion for 20 min, followed by a reperfusion period of 4h). Immunohistochemistry of anti-Iba-1 also know AIF-1 (Allograft inflammatory factor 1) was performed to assess microglia activation in the brain parenchyma (prefrontal cortex, hippocampus, as well as the thalamus and hypothalamus).
Results: The number of active resident microglia cells had greater amounts in the left side of the brain parenchyma of the VIR group compared to Sham (VIR: 25.3 ± 4.1; Sham: 19.4 ± 2.6 active cells/mm²; *p*= 0,04). There was a reduction of active cells count in the E2 group when compared to the VIR group, on the right (E2: 16.36 ± 2; VIR: 25.31 ± 4 active cells/mm²; *p*= 0.02) and left (E2: 17.39 ± 2; VIR: 25.04 ± 5 active cells/mm²; *p*= 0.05) sides of the brain parenchyma.
Conclusions: Our data showed that the systemic inflammation triggered by visceral ischemia and reperfusion was responsible for activating microglia. However, treatment with E2 proved to be an important therapeutic agent, by effectively controlling microglia activation even after reperfusion is initiated.
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BOS1_2 SINGLE CELL RNA SEQUENCING OF DONOR-REACTIVE T CELLS REVEALS ROLE OF APOPTOSIS IN DONOR-SPECIFIC HYPORESPONSIVENESS OF KIDNEY TRANSPLANT RECIPIENTS

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Background: After kidney transplantation (KT) donor-specific hyporesponsiveness (DSH) of recipient T cells develops over time. Recently, apoptosis was identified as a possible underlying mechanism.
Methods: In this study, both transcriptomic profiles and complete V(D)J variable regions of TR transcripts from individual alloreactive T cells of kidney transplant recipients were determined with single cell RNA sequencing. Alloreactive T cells were identified by CD137 expression after stimulation of peripheral blood mononuclear cells (PBMCs) obtained from KT recipients (N=7) prior to and 3-5 years after transplantation with CD3-depleted PBMCs of their donor or a third party control. The alloreactive T cells were sorted, sequenced and the transcriptome and T cell receptor profile analysed using unsupervised clustering.
Results: Alloreactive T cells retain a highly polyclonal TRA/TRB repertoire over time. Clustering based on the transcriptome divided the donor-reactive T cells into three main groups; one cluster of cytotoxic CD8+ T cells and two clusters of CD4+ T cells with distinct activation profiles. Differential expression analysis revealed that donor-reactive CD4+ T cells in both clusters had downregulation of genes involved in apoptosis and intracellular signalling pathways post-transplant. Remarkably, no change in the transcriptome of donor-reactive cytotoxic CD8+ T cells was observed over time. Inclusion of third-party controls enabled us to ascertain that the differences we detected post-transplant were truly donor-specific and not due to the influence of immunosuppression.
Conclusions: Single cell expression profiling demonstrated a loss of activated and pro-apoptotic donor-reactive CD4+ T cell clones after transplantation in stable kidney transplant recipients. This supports a role of apoptosis of highly activated alloreactive CD4+ T cells in the development of donor-specific hyporesponsiveness in stable kidney transplant recipients.

BOS1_3 ELDERLY RENAL TRANSPLANT RECIPIENTS HAVE LESS POLYFUNCTIONAL ALLOREACTIVE CD4 T CELLS PRE TRANSPLANT AND LOWER IL-2 MEDIATED T CELL PROLIFERATION

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Background: Elderly kidney transplant recipients have a lower risk for both early and late acute T-cell mediated rejection (TCMR). Recently, we identified alloreactive memory CD4 T cells expressing at least two pro-inflammatory cytokines (poly-alloCD4) as pivotal cells for TCMR. The decline of poly-alloCD4 after transplantation leads to donor-specific hyporesponsiveness (DSH). Therefore, we hypothesized that the frequency and kinetics post-transplantation of poly-alloCD4 in elderly recipients differs from younger recipients.
Methods: Peripheral blood mononuclear cells (PBMCs) of N=16 young (<45 years) and N=14 elderly (>55 years) stable renal transplant recipients were obtained before, at 6 months, 12 months, and at 3-5 years after transplantation. Expression of the co-stimulatory molecule CD137 identified alloreactive T cells following co-culture of recipient PBMCs with CD3-depleted PBMCs from their donor or third-party control. The phenotype and proportions of cytokine producing alloreactive CD137+ T cells as well as the proliferative capacity of T cells was evaluated using flow cytometry. Cytometric bead array was used to measure cytokines in supernatant.
Results: The frequency of poly-alloCD4 expressing three pro-inflammatory cytokines (IFNγ+IL2+TNFα+) was significantly lower in elderly prior to transplantation (p<0.01). T cells of elderly had decreased capacity to proliferate in response to alloantigen pre-transplantation although only significant within the CD8 T cell compartment (p<0.02). Elderly also had lowered IL-2 production which was correlated with the reduced proliferative response. Post-transplantation, a decline in frequencies of poly-alloCD4 was observed in both age groups with a plateau reached after 12 months with no difference in kinetics.
Conclusions: DSH develops with similar kinetics post-transplant in both elderly and young stable renal transplant recipients through a decrease in frequency of poly-alloCD4. However, prior to transplantation, elderly recipients have lower levels of poly-alloCD4 expressing IFNγ+IL2+TNFα+ and decreased capacity to proliferate which is associated with decreased production of IL-2. Together, these factors can explain the lowered risk of acute TCMR in the elderly and them reaching DSH earlier than younger recipients.

BOS1_4 DUAL INHIBITION OF THE COMPLEMENT SYSTEM AND TOLL-LIKE RECEPTORS PREVENTS SYSTEMIC AND LOCAL KIDNEY INFLAMMATION IN MICE EXPERIENCING BRAIN DEATH

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Background: Brain death (BD) induces a potentially harmful systemic inflammation, which may reduce organ quality for transplantation. The complement system (CS) and Toll-like receptors (TLRs) are key for the innate immune system both for recognition and response. The cluster of differentiation 14 (CD14) is a co-receptor for several TLRs, necessary for TLR signaling. We hypothesized that dual inhibition of CS and TLRs by complement protein 5 (C5) and CD14 inhibition will prevent innate immune-mediated inflammation during BD.
Methods: BD was induced with a fluid-filled intracranial balloon in wild-type C57/BL6 mice. Prior to BD, mice were left untreated (n=8), treated with a C5 inhibitor (n=7), a CD14 inhibitor (n=7), or both inhibitors (n=7). Sham mice did not experience BD and were left untreated (n=8). Blood and kidneys were collected three hours after BD. Inflammatory plasma cytokines were analyzed using a 23-plex immunoassay, kidney mRNA expression by qPCR.
Results: In plasma, BD significantly induced expression of interleukin-6 (IL-6), human IL-8 homolog, IL-12, monocyte chemoattractant protein (MCP-1), macrophage inflammatory protein MIP-1α, and MIP-1β compared to sham (all p<0.01). In kidneys, BD significantly induced IL-6, IL-8, TNF, MCP-1, P-Selectin, and VCAM-1 (all p<0.01). C5 and CD14 single inhibition significantly reduced BD-induced activation of all markers in plasma (all p<0.01) and in kidneys (p<0.01, except C5 inhibition for P-Selectin p=0.06). Dual inhibition of C5 and CD14 further reduced all plasma cytokines to levels comparable with sham animals (all p>0.05). In kidneys, double inhibition was comparable to single inhibition.

Conclusions: The innate immune system is crucial for inducing inflammatory reactions during BD. Inhibition of both the CS and TLRs is necessary to efficiently prevent BD-induced systemic inflammation and to reduce local kidney inflammation. CS and TLR inhibitors are clinically available and clinical studies should be performed on deceased BD donors to enhance donor organ quality.

BOS1_5 RELEVANCE OF THE BANFF HUMAN ORGAN TRANSPLANT CONSENSUS GENE PANEL FOR DETECTING ANTIBODY AND T-CELL MEDIATED REJECTION OF KIDNEY ALLOGRAFTS

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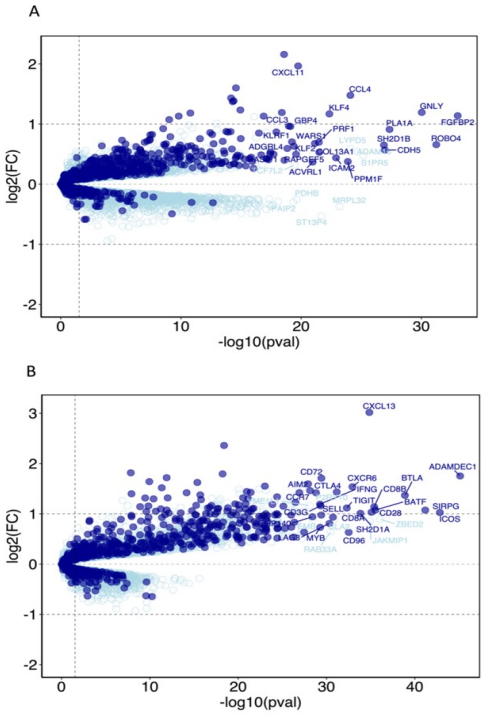
Background: Gene expression studies relying on whole-transcriptome profiling have defined the molecular phenotypes of kidney allograft rejection, but have several barriers limiting its application in clinical practice. The Banff Human Organ Transplant panel (BHOT) was developed to facilitate reproducible gene expression analysis of solid organ allografts, but its relevance to assess antibody-mediated (AMR) and T-cell mediated rejection (TCMR) in kidney allograft biopsies has not been demonstrated.
Methods: We performed *in silico* analysis and projected the BHOT panel on published microarray data of 547 kidney transplant biopsies (AMR, n=129; TCMR, n=77; non-rejection related cases, n=341). We compared expression between whole-transcriptome or BHOT panel genes, and performed differential expression, pathway, and gene network analysis. Finally, we evaluated the performance of BHOT genes to classify AMR and TCMR.
Results: Targeted versus whole-transcriptome analysis demonstrates that the BHOT panel captures the key gene signatures and pathways associated with rejection Figure A (AMR) and Figure B (TCMR). The top significant AMR-associated pathways based on BHOT genes were associated with interferon-gamma and interleukin signaling, toll-like receptor cascade and B-cell activation. For TCMR, the top pathways derived from the BHOT panel were related to PD-1 signal transduction, TLR signaling cascade, phosphorylation of CD3, demonstrating that the panel detects relevant pathophysiological mechanisms. The performance of BHOT-based ensemble classification models for detecting AMR (AUC=0.88; 95% CI=0.85-0.91) and TCMR (AUC=0.85; 95% CI=0.81-0.90) were highly similar to the performance of classifiers based on whole-transcriptome data for AMR (AUC=0.88; 95% CI=0.84-0.91) and TCMR (AUC=0.85; 95% CI=0.80-0.90).
Conclusions: We demonstrate that the BHOT gene panel comprises the relevant genes and pathways associated with AMR and TCMR in kidney allograft tissue. Our findings show that this targeted panel is sufficient and sensitive to serve as a proxy to whole-transcriptome-based analysis for gene expression profiling in kidney allograft biopsies.



BOS1_6 DDPCR DETECTION OF MIRNAS FIBROSIS SIGNATURE IN URINE-EVS FROM KIDNEY TRANSPLANTED PATIENTS: A NON-INVASIVE APPROACH TO DETECT KIDNEY FIBROSIS

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Background: Predicting or diagnosing renal fibrosis (IFTA) to reduce chronic allograft loss is still a major challenge in kidney transplantation. Current analytical standards, such as creatinine, proteinuria or Glomerular Filtration Rate have poor predictability value and the diagnostic still relies on costly and invasive kidney biopsy. Thus, molecular analyses of urinary extracellular vesicles (uEV) have emerged as a possible source of new biomarkers, and as a platform to overcome the risks, costs and sampling limitations of renal biopsy. In this context, in a preliminary study our group isolated uEV by size exclusion chromatography from 6 healthy donors and 11 kidney transplanted patients (kTx) with altered kidney function. RNA sequencing led us to identify a miRNA signature in the kTx patients. Specifically, seven of those miRNAs were found in kTx patients diagnosed with IFTA by renal biopsy. Aiming to explore a possible clinical application, here we validated these results using digital droplet PCR (ddPCR), a technique with higher throughput screening potential.
Methods: miRNAs signature was studied in a new cohort of kTx patients (n=20) using ddPCR. Briefly, the uEV RNA was obtained from 1 mL urine (Urine Exosome RNA Isolation Kit, Norgen Biotek Corp.). After retrotranscription, the ddPCR was performed. For data analysis, patients were divided into non-IFTA (scored as less than 1, 40% of total) and IFTA patients (scored as 1 or more, 60% of total), according to their Renal Biopsy Banff score.
Results: ddPCR results achieved higher technical sensitivity, accuracy and reproducibility compared to real-time quantitative PCR (qPCR). This permitted absolute quantification of miRNAs even in samples with limited target abundance. Furthermore, we mostly validated the previous miRNAs fibrosis signature identified by RNAseq using ddPCR in this new cohort of kTx patients.
Conclusions: ddPCR detection of multiple miRNAs in urine-EVs is a suitable non-invasive approach to monitor fibrosis in kTx patients.

BOS1_7 MEK INHIBITION, A NEW THERAPEUTIC APPROACH IN ORGAN TRANSPLANTATION

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Background: Because graft survival is still impacted by chronic dysfunction related, among other things, to poor control of the alloimmune response, the development of new strategies that would be efficient in preventing rejection and free of toxicity is necessary. As recent studies in mouse models have shown that MEK inhibition is effective in controlling the alloimmune response in experimental GVHD without abrogating anti-tumor and anti-viral immunity, we evaluated the therapeutic potential of MEK pathway inhibition in a preclinical model of allogeneic human skin transplantation in humanized NSG mice.
Methods: Human skin grafted animals, whose immune system was reconstituted with human PBMCs, were treated with trametinib, an anti-MEK molecule already used in the clinic for the treatment of melanoma. Graft survival was evaluated and the effects on the human allogeneic immune response were analyzed.
Results: Experiments performed with 4 human skin donors and 4 human blood donors showed that trametinib-induced MEK inhibition significantly prolonged the survival of allogeneic skin graft compared with untreated controls (30.7 ± 4.3 days, n=17 vs 18.4±3.3 days, n=15, p<0,0001) without interfering in vivo immune reconstitution in the NSG mice. Analysis of PBMCS from these animals showed an increase of the hCD4/hCD8 T cell ratio in trametinib treated mice however we could not detect any difference in the expression of T hCD4 and/or hCD8 inhibitory markers and hCD4 regulatory T cells. To further investigate the effect of trametinib in an unbiased way, we used single cell RNAseq analysis (10X chromium) on spleen hCD45 cells harvested 16 days following reconstitution. Regarding hCD8 T cells, trametinib treated animals presented more early activated cells and less effector cells, suggesting that trametinib inhibited hCD8 T cell differenciation. Regarding hCD4 T cells, trametinib seemed favor hCD4 early proliferation and impede differenciation toward follicular helper T cells and promote TH1.

Conclusions: This study showed that inhibition of the MEK pathway in a preclinical model of allogeneic human skin graft allowed a significant survival of the transplant by acting differentially on CD4 and CD8 T cells, suggesting this new approach could be of interest in solid organ transplantation.

BOS1_8 DECONVOLUTION ANALYSIS REVEALS CHANGES IN IMMUNE CELL SUBSETS IN PERIPHERAL BLOOD FOR MULTIPLE REJECTION PHENOTYPES FOLLOWING KIDNEY TRANSPLANT

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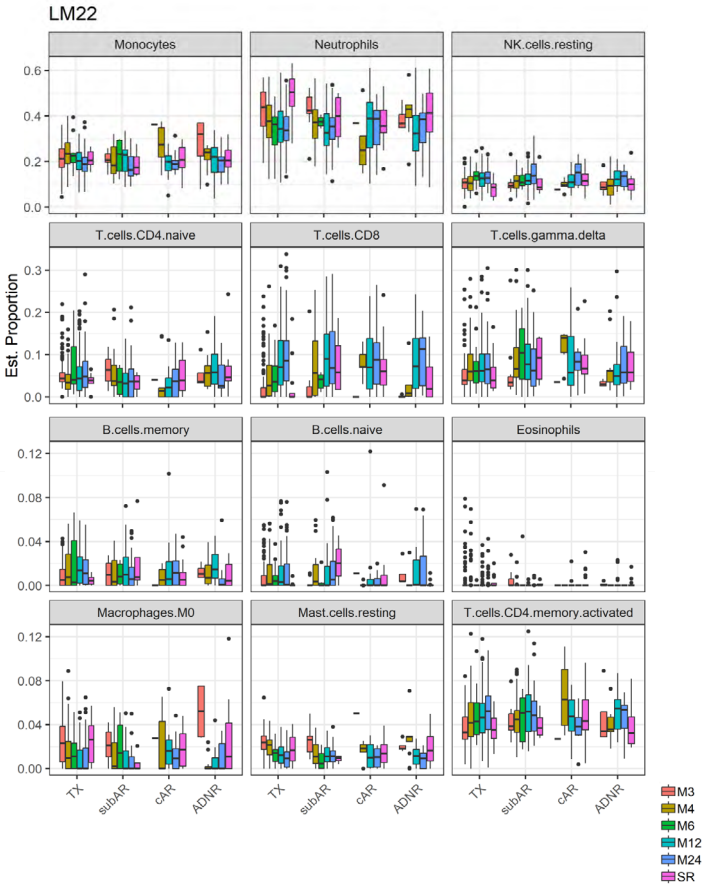
Background: Gene expression microarray data generated from peripheral blood mononuclear cells (PBMCs) quantifies transcript abundance for a combination of multiple cell populations representing varying percentages of all cells. We hypothesized that applying deconvolution analysis to generate estimated cellular proportions in these data can provide insight into the temporal and phenotypic changes associated with rejection that occur in the first 2 years after kidney transplant.
Methods: We generated gene expression data from PBMC preparations collected concurrent with biopsies from patients in the first two years after kidney transplant. The gene expression data covered four biopsy proven phenotypes (Transplant eXcellence – TX; subclinical Acute Rejection – subAR; clinical Acute Rejection – cAR; Acute Dysfunction, No Rejection – ADNR) over 5 post-transplant timepoints (months 3, 4, 6, 12, 24) and unscheduled time points of Suspected Rejection (SR). These data were used as input into the CIBERSORTx webtool to determine the proportions of immune cell types found in each sample based 22 cell types in the LM22 signature matrix.
Results: Of the 22 possible cell types, Monocyte and Neutrophil populations each represented over 20% of the total in a majority of samples. In the TX and subAR sample groups, the Neutrophil proportion showed a significant decrease over time ($p < 0.05$). Resting NK cells were present at more than 10% in a majority of samples with a slight upward trend over time in the subAR samples. Finally, 4 populations of T-cells (CD8 T-cells, Naïve CD4 T-cells, gd T-cells, and activated memory CD4 T-cells) were the next most abundant. For each phenotype, these populations were also increasing over time with that trend significant for the CD8 population in all phenotypes ($p < 0.05$) except for cAR.
Conclusions: We identified changes in the identity and proportions of cell populations in the peripheral blood in the first two years following kidney transplant. These changes correlate with both the biopsy determined state of the transplanted organ as well as the interval following transplant. Future studies looking at correlation of other factors like age, biological sex, race, and treatment as well as serially collected samples in the interim between biopsies will be informative.

Table 1

Biopsy Timepoint	TX Samples	subAR Samples	cAR Samples	ADNR Samples
Month 3 (M3)	92	11	1	4
Month 4 (M4)	62	29	9	12
Month 6 (M6)	16	6	0	0
Month 12 (M12)	125	49	28	32
Month 24 (M24)	110	36	14	27
Suspected Rejection (SR)	12	4	34	28

Figure 1



BOS1_9 PRESENCE OF KIR2DL2/S2, KIR2DL5, AND KIR3DL1 MOLECULES IN LIVER RECIPIENTS WITH ALCOHOLIC CIRRHOSIS COULD BE IMPLICATED IN DEATH BY GRAFT FAILURE

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Background: Alcoholic liver disease is the second most common diagnosis among patients undergoing liver transplantation (LT). The innate immune system and the inflammatory cascade are essential to the multifactorial pathophysiology of alcoholic liver disease. Recent studies on killer-cell immunoglobulin-like receptors (KIR) receptors have suggested that these play a role in sepsis, liver rejection, and virus relapse. We aimed to study the influence of preclinical complications such as ascites and encephalopathy and KIR genetic characteristics on death due to sepsis, multiorgan (MF), and graft failure (GF) in AC patients undergoing LT.
Methods: 164 consecutive and deceased Caucasian AC patients who underwent LT were retrospectively reviewed. Pre-transplant complications, cause of death, and patient survival were analyzed. Genomic DNA was extracted from peripheral blood, and KIR genotyping was performed by PCR-SSO.
Results: A statistically significant increase in the presence of KIR2DL2+ in patients with MF compared to GF (75.8% vs. 51.2%; P=0.047). An increase was also observed in KIR2DS2+ in sepsis compared to GF (51.2% vs. 43.7%; P=0.018). Patients who died of MF, a decrease in KIR2DL5+ was observed in AC patients with and without encephalopathy (P=0.018). The presence of KIR3DL1+ in the AC patients significantly increased the mortality from sepsis (P=0.045), and this fact was confirmed by multivariate logistic regression. The presence of KIR3DL1+ in the AC patients significantly increased the mortality from sepsis (P=0.012) and was confirmed by multivariate logistic regression.KIR2DS1+ and KIR2DS4+ showed an increase in mortality due to GF compared to patients without these genes (P=0.011 and 0.012, respectively).However, this fact was confirmed only for KIR2DS1+ by multivariate logistic Cox regression.
Conclusions: Our results show that the presence of KIR2DL2/S2, KIR2DL5, and KIR3DL1 genes in the patient influences MF and GF after LT, according to our findings. Our findings highlight the AC patient's vulnerability to LT during hospitalization following the transplant and outside of it and the need to adopt critical preventive actions to build a healthcare routine screening to improve and modify treatments to increase survival.

BOS1_10 A NOVEL URINE-BASED LIQUID BIOPSY BIOMARKER FOR RENAL FIBROSIS IN KIDNEY TRANSPLANT

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Background: Kidney Fibrosis (KF) is a complex dynamic process that is the terminal stage of most progressive kidney transplant diseases. While traditional kidney allograft biopsy remains the gold standard for the diagnosis of KF, considerable progress has been made over the last years in the study of urinary proteomics as a diagnostic tool. Clear advantages over the traditional biopsy include accessibility, safety, serial sampling and the potential for non-invasive prognostic and diagnostic monitoring of the disease progression and an individual's response to treatment. A few years ago, our group identified urinary vitronectin (uVN) as a possible candidate to monitor KF; in this study, we aim to demonstrate whether this hypothesis is sustained in a clinical cohort.
Methods: Samples (blood/urine) from routine laboratory monitoring of 72 kidney transplanted patients with allograft biopsies were collected and classified according to their histopathological diagnoses to define two groups of patients: non-IFTA (<1) and IFTA (1 or >1); levels of uVN in corresponding urine samples were measured by enzyme-linked immunosorbent assay (ELISA).
Results: None of the clinical parameters, except for time after transplantation, could differentiate the two groups of patients (n=72). To analyse the correlation between routine follow-up laboratory tests and uVN with the histopathological fibrosis findings, a Spearman correlation test was performed. The highest value was found in the correlation between uVN and IFTA (r=0.22) compared to the other parameters (r<0.15) including proteinuria. Interestingly, in those patients with a follow-up of at least three years of functioning graft (n=47), both uVN and proteinuria had a significant p-value (p=0.022) for the correlation and were significantly (p=0.0092, uVN; p=0.0008, Proteinuria) able to differentiate between patients with and without IFTA. Yet, of note, uVN could identify about 20% of patients with non-pathological proteinuria. These results indicated that while the use of proteinuria alone would detect the 74% of patients with IFTA, the addition of uVN levels, we could identify up to 94% of KF non-invasively.
Conclusions: This study provides a novel potential for uVN as an add-on non-intrusive surveillance biomarker strategy of fibrosis in kidney transplant.

BOS1_11 NON-INVASIVE DETECTION OF REJECTION IN THE FIRST 2 WEEKS AFTER KIDNEY TRANSPLANTATION USING URINARY CHEMOKINES

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Background: Novel biomarker assays for the non- (or minimally) invasive detection of rejection, such as for example, donor-specific cell free DNA, are unable to diagnose rejection in the first 2 weeks after transplantation. The aim of this study was to examine if the urinary chemokines CXCL9 and CXCL10 can accurately detect biopsy-confirmed allograft rejection (BCAR) early after kidney transplantation.
Methods: Available urine samples collected at the time of a first biopsy performed within 14 days after transplantation (n=54, 50% deceased donors) were used from a cohort of 225 consecutive kidney transplant recipients. Biopsies were categorized into i. BCAR (n=16), ii. presumed rejection (n=16) or iii. no rejection (n=22). Urine samples collected at day 7 (no biopsy in the first 6 months after transplantation) served as controls (n=76, 54% deceased donors). Urinary CXCL9 and CXCL10 concentrations were determined with ELISA.
Results: Biopsies were performed at a median of 7 days (range: 2-14 days) after transplantation. Urinary CXCL9 concentrations were significantly higher at BCAR (368 pg/ml, range: 0-49619 pg/ml) compared to day 7 (4.5 pg/ml, range: 0-1577 pg/ml; p<0.001; ROC-AUC 0.82, 95%CI: 0.68 to 0.96), as well as compared to no rejection biopsies (0 pg/ml, range: 0-321 pg/ml; p<0.0001; ROC-AUC 0.86, 95%CI: 0.73 to 0.99). Similarly, CXCL10 concentrations were significantly higher at BCAR (238 pg/ml, range: 16-11949) compared to day 7 (28 pg/ml, range: 0-1320 pg/ml; p<0.001; ROC-AUC 0.83, 95%CI: 0.71 to 0.95), as well as compared to no rejection biopsies (35 pg/ml, range: 4-2037 pg/ml, p<0.05; ROC-AUC 0.77, 95%CI: 0.62 to 0.92). The positive predictive value for BCAR was 55% (day 7) and 62% (no rejection biopsies) for CXCL9 and 46% (day 7) and 35% (no rejection biopsies) for CXCL10. In contrast, the negative predictive value for BCAR was 94% (both day 7 and no rejection biopsies) for CXCL9 and 93% (day 7) and 92% (no rejection biopsies) for CXCL10. CXCL9 and CXCL10 concentrations were comparable between living donors and deceased donors.
Conclusions: Urinary chemokines CXCL9 and CXCL10 identify BCAR in the first 2 weeks after kidney transplantation. As a non-invasive measurement these markers have a high potential to augment clinical decision making in the early period after kidney transplantation.

BOS1_12 ACTIVE IMMUNOLOGICAL PARTICIPATION AND METABOLIC SHUTDOWN OF KIDNEY STRUCTURAL CELLS DURING KIDNEY TRANSPLANT REJECTION

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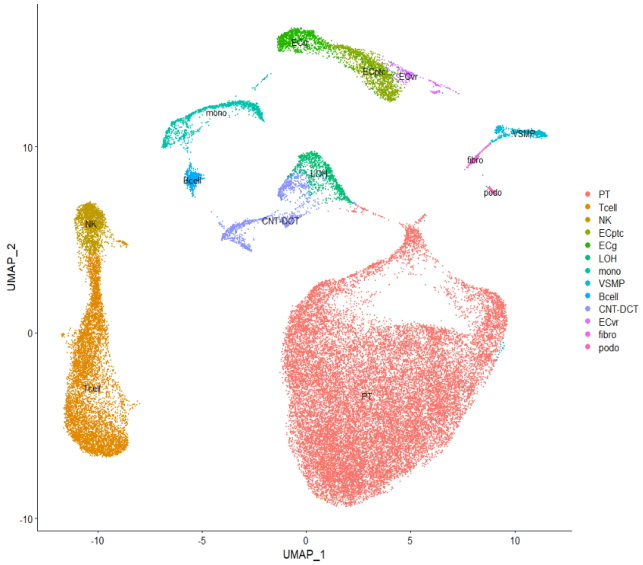
Background: The role of immune cells in rejection has been clearly established. However, immunosuppressive drugs directed against these cells appear insufficient to prevent and treat alloimmune damage. The response of kidney structural cells has been studied to a much lesser extent, but could provide new therapeutic opportunities.
Methods: We performed droplet-based single-cell RNA sequencing (10X Genomics) on 18 kidney transplant biopsies from 14 human recipients (13 allogenic and 1 syngeneic monozygotic twin transplant), yielding 39 948 single cell transcriptomes. We investigated structural cell expression changes in alloimmune inflammation and validated these signals in two large microarray cohorts of kidney transplant biopsies.
Results: Single-cell RNA sequencing identified cells from all structural compartments of the kidney, as well as infiltrated immune cells. Upon inflammation, endothelial cells of the glomerulus, peritubular capillaries, and vasa recta showed marked upregulation of immune-specific genes, e.g. HLA genes, adhesion molecules, and cytokines and chemokines, indicating active participation in the alloimmune process, with compartment-specific differences. Epithelial cells, including proximal tubular, loop of Henle and collecting duct cells, also showed upregulation of immune genes upon inflammation. Strikingly, in proximal tubule cells, a strong downregulation of aerobic metabolism and solute carriers was observed during inflammation. Cell-specific expression changes during rejection were validated in two large bulk transcriptomic biopsy datasets. Both upregulation of immune pathways and downregulation of metabolism were associated with poor survival of kidney allografts.
Conclusions: Kidney structural cells appear to be complicit in the alloimmune injury process, rather than mere passive targets. Through upregulation of HLA genes, adhesion molecules, and cytokines and chemokines, these cells potentially amplify the deleterious effects of the infiltrating immune cells. Strikingly, profound metabolic changes were observed in epithelial cells in rejection. These observations provide insight into the cellular origins of previous findings from bulk transcriptomic datasets and open avenues for newer therapies beyond the current focus on immune cells.



BOS1_13 DIRECT IMMUNOPHENOTYPING OF REGULATORY B CELLS AT 3 MONTHS HAVE A PROGNOSTIC VALUE OF IMPROVED GRAFT OUTCOME AND REJECTION RISK IN KIDNEY TRANSPLANT

Inés Perezpayá[*1], **Sergio G. Garcia[2], Maria Molina[1], Angela Casas[1], Rosana Gelpi[1], Omar Enrique Taco Sánchez[1], Monica Bolufer[1], Anna Vila-Santandreu[1], Jordi Bover[1], Francesc E. Borras[3], Laura Cañas[1], Marcella Franquesa[3]**

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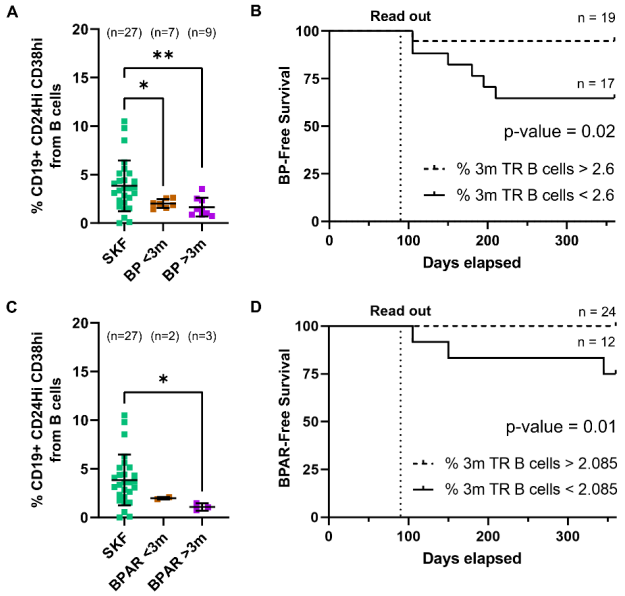
Background: Regulatory B cells (Bregs) have been postulated as major mediators of tolerance in kidney transplantation (KT) and have been associated with longer allograft survival and fewer rejection episodes
Methods: 51 kidney transplant recipients were followed up for 12 months (m) after transplantation. At pre- transplantation, 7 days and 3 ,6 and 12m post-transplantation, clinical and laboratory data were collected and peripheral blood lymphocyte populations were analysed by flow cytometry. We assessed total and relative counts of Bregs ($CD19^+$ $CD24^{hi}$ $CD38^{hi}$), Memory B cells ($CD27^+$ $CD19^+$), Naive B cells ($CD27^-$ IgD^+ $CD19^+$), Total B ($CD19^+$), and T cells ($CD3^+$, $CD4^+$ or $CD8^+$) and analysed their association with graft outcome.
Results: The median age was 60 years-old, most were male on dialysis. 51% were HLA-sensitized before transplantation,only one patient developed de novo HLA antibodies. 11.8% have had a previous KT and 80% had 4 or more HLA missmatches. Induction therapy received was basiliximab (47%), thymoglobulin (49%) or no induction.The most common maintenance immunosuppressive therapy was glucocorticoids, tacrolimus and mycophenolate mofetil.Only for-cause kidney allograft biopsies were performed in 22 patients and 6 of them had biopsy-proven acute rejection (BPAR). To analyse the association between Bregs and graft outcome, we stratified patients in stable kidney function (SKF) and biopsied patients (BP). At 3 months, %Bregs were higher in SKF (3.9% ± 2.6 vs 1.8% ± 0.78, p=0.001) predicting better graft outcome ($AUC_{Breg\%}$ = 0.78, SE: 0.07). Patients with BPAR had even lower Bregs % at 3m (1.4% ± 0.56) compared to patients with NO BPAR (1.9% ± 0.82). Other time points nor other subsets had a predictive value of allograft outcome. Our data allowed us to establish a cut-off value of 2.6% of Bregs at 3 months above which 95% of the patients remained with stable kidney function for up to 12 months and 100% free from rejection events (p=0.02). Patients with Bregs at 3 months below 2.085% presented 25% chances to present rejection episodes in the 12months follow-up (p=0.01).
Conclusions: Higher Bregs percentage at 3 months is a highly specific and sensitive predictive value of better graft outcome and lower rejection risk during the first year after transplantation, suggesting its potential as a biomarker



BOS1_14 Γ/Δ T CELLS IN ANTIBODY-MEDIATED REJECTION: RINGLEADER OR MERE EXECUTORS?

Xavier Charmetant[*1], **Guillaume Rigault[1], Chien-Chia Chen[2], Hannah Kaminski[3], Jonathan Visentin[3], Benjamin Taton[3], Gabriel Marsères[4], Jean-Paul Duong van Huyen[5], Alice Koenig[1], Thomas Barba[1], Pierre Merville[3], Emmanuel Morelon[1], Julie Déchanet-Merville[4], Valérie Dubois[6], Lionel Couzi[3], Olivier Thaunat[1]**

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Background: Antibody-Mediated Rejection (AMR) starts with the generation of donor-specific antibodies (DSA). The latter bind to the endothelial cells of the grafts, leading to the activation of the classical complement pathway and/or the recruitment of FcγR-expressing innate immune effectors.
The crucial role of T follicular helper cells (T_{FH}), which express an α/β TCR and provide help to allogeneic B cells for their differentiation into DSA-producing plasma cells is well known. In contrast, the role of γ/δ T cells in AMR pathophysiological cascade is unknown.
Methods and results: The role of γ/δ Tc in DSA generation was studied in a cohort of 331 kidney transplant patients with 10 years of follow-up. The incidence of de novo DSA was similar in recipients with low versus high γ/δ Tc count. *In vitro* experiments conducted on human cells confirmed that activated γ/δ Tc do not acquire CXCR5 and CD40L, two key molecules for T_{FH} function. Histological analysis reveals that γ/δ Tc mainly localize outside the B cell area of lymph nodes, prompting us to investigate whether γ/δ Tc could instead act like antigen presenting cells (APC) for the priming of T_{FH} cells. However, γ/δ Tc also fail to upregulate the expression of HLA II and costimulatory molecules upon stimulation. Finally, γ/δ Tc neither make B cells proliferate nor synergise with α/β Tc in proliferation assays. These results were confirmed in a murine *in vivo* model. After transplantation with an allogeneic Balb/c ($H\text{-}2^d$) heart, wild-type and TCRδKO (deficient in γ/δ Tc) B6 ($H\text{-}2^b$) mice develop similar DSA response, which rule out an APC-like function for γ/δ Tc. The fact that TCRαKO (deficient in α/β Tc) recipient mice do not develop any DSA confirm the lack of T_{FH}-like function for γ/δ Tc. While γ/δ Tc do not play a role in DSA generation, they can be detected in microvascular inflammation of patients' AMR biopsies, they express FcγR on their surface and efficiently damage allogeneic endothelial cells in coculture.
Conclusions: This translational study demonstrates that γ/δ Tc are not involved in the generation of DSA, but play a role during the effector phases of AMR.

BOS2_1 CLINICAL AND IMMUNOLOGICAL FACTORS ASSOCIATED WITH THYMIC FUNCTION AT THE TIME OF KIDNEY TRANSPLANTATION

Ioannis Katerinis*[1], Camille Kergaravat[2], Emmanuel Clave[2], Lise Morin[2], Christophe Legendre[1], Dany Anglicheau[3], Antoine Toubert[2], Julien Zuber[4]

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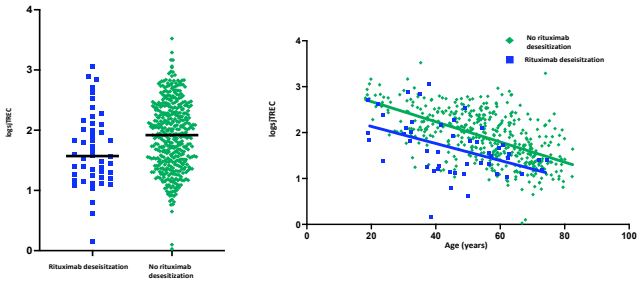
Background: End stage renal disease patients experience a hastened age-related decline of the immune system. The thymus is the unique source of naïve T cells generation. Our study aims to determine the main factors associated with the thymic function, as assessed by sjTREC measurement, at the time of transplantation
Methods: Four hundred-ninety-five consecutive patients, transplanted between January 2015 and March 2019, for whom stored peripheral blood leukocytes were available, were enrolled into the study. sjTREC quantification was performed in total PBMCs. Moreover, *TCRAD* gene was genotyped for the whole cohort, because its polymorphism was associated with thymic function in the general population.
Results: Different clinical factors (recipient age, gender, BMI > 30 kg/m^2, preexisting diabetes, dialysis vintage, positive CMV serology, past exposure to immunosuppressive drugs) and genetic variations (SNP rs2204985, rs10873018, rs12147006) were correlated to Log sjTREC. In univariate analysis, age, male gender, obesity, and rituximab-based desensitization regimen before ABO/HLA incompatible transplantation, were positively associated with worse thymic function. The best multivariate analysis model retained only age, male gender and pretransplant desensitization regimen. These results confirmed previous observation in the general population (age, gender), but also unveiled the negative impact of B-cell targeted therapies on thymic function. Ongoing analyses are investigating the impact of baseline thymic function on post-transplant clinical outcomes (including opportunistic infections, COVID19-related mortality, cancers) and on rates of immune reconstitution following T-cell depleting induction (post-transplant CD4+ T cell count trajectory).
Conclusions: Recipient age, gender, and rituximab therapy administered 1 month ahead of kidney transplantation are the three independent factors correlated with the baseline thymic function.

Variables	Univariate analysis		Multivariate analysis	
	Beta	P- value	Beta	P- value
Age at the transplantation	-0.0200	< 0.0001	-0.0212	< 0.0001
Female gender	0.2755	< 0.0001	0.2435	< 0.0001
BMI day 0	-0.0259	< 0.0001	-0.0106	0.057
Desensitization before transplantation	-0.2345	0.007	-0.5145	< 0.0001
Diabetes before transplantation	-0.1749	0.009	0.0454	0.44
Log CRP (day 0)	-0.0580	0.01	-0.0108	0.58
Time after ESRD	-0.0003	0.25		
CMV serology d0	-0.0499	0.37		
Range of transplantation	-0.0015	0.98		
rs10873019	-0.0364	0.53		
rs224985	-0.0288	0.62		
rs12147006	0.0264	0.64		



BOS2_2 DOES RECEPTOR-MEDIATED INTERNALISATION OF HYALURONAN (HA) MATRIX IN THE RENAL CORTEX EXPLAIN THE PROTECTION CONFERRED BY ISCHAEMIC PRE-CONDITIONING?

Aeliya Zaidi*[1;2], Irina Grigorieva[2], Charloette Brown[1], Gilda Pino-Chavez[2], Rafael Chavez[1;2], Robert Steadman[2], Soma Meran[2], Usman Khalid[1;2]

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Background: Ischaemia reperfusion injury (IRI) is a major cause of delayed graft function (DGF) and poor graft survival in transplanted kidneys. Ischaemic preconditioning (IPC) attenuates IRI via mechanisms that are not understood. Hyaluronan (HA) is a matrix polysaccharide normally undetectable in the renal cortex, but its accumulation is a hallmark of renal fibrosis. HA interacts with cells through its principal receptor, CD44. Our in vitro studies indicate that the variant HA isoform CD44v7/8 may be anti-fibrotic, as it promotes cytoplasmic internalisation and breakdown of HA. The aim of this study was to characterise CD44v7/8 in vivo expression in IRI and IPC to determine its potential role as a mediator of IPC protection.
Methods: Adult male-Lewis rats (n=24) underwent midline laparotomy and were grouped into Sham, bilateral 45min IRI or IPC+IRI (pulsatile IPC prior to IRI). Kidneys were retrieved at 28d and assessed histologically and transcriptomically for relevant markers of kidney injury/fibrosis. Blood was taken pre-op and 28d for serum creatinine measurement.
Results: IRI led to marked histological damage with key fibrotic markers significantly increased. IPC led to renoprotection with attenuation of fibrotic markers. IRI led to increased extracellular HA deposition within the renal cortex, particularly in the peri-tubular, peri-glomerular, and peri-vascular areas. In contrast, in IPC kidneys, HA was shown to be internalised into the renal tubular epithelial cells, with markedly less extracellular and interstitial deposition in the cortex. CD44v7/8 expression was attenuated in IRI kidneys, but markedly enhanced in IPC kidneys. These results were confirmed both at gene and protein level.
Conclusions: Extracellular HA deposition in the renal cortex promotes progressive renal fibrosis and damage following IRI. IPC enhances CD44v7/8 expression along the basolateral aspect of tubular epithelial cells and promotes HA internalisation from the pericellular matrix into the tubular cytoplasm thus reducing cortical HA deposition and thereby mediating protection in IPC. The exciting therapeutic potential of CD44v7/8 warrants further evaluation.

BOS2_3 DIFFERENTIAL KINETICS OF HLA CLASS II ANTIGENS EXPRESSION ON PRIMARY HUMAN GLOMERULAR ENDOTHELIAL CELLS

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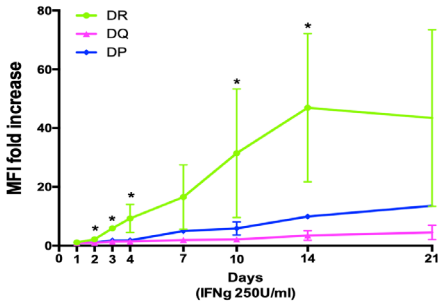
Background: *De novo* HLA-DQ donor specific antibodies are the most frequently detected and associated with adverse outcomes in allotransplantation. Yet, HLA-DR is expressed at higher levels and is considered the more antigenic molecule. Here we investigated the kinetics of HLA-DQ upregulation, compared with HLA-DR and HLA-DP, following IFNg stimulation in human primary glomerular endothelial cells (HPGEC; representing the target for antibody/T cell interactions in kidney transplantation).
Methods: HPGEC from different donors were cultured with increasing doses of IFNg (0, 250 or 2500U/ml) for up to 21 days (n=13). Surface expression of HLA-DR, DQ and DP was assessed by flow cytometry at different timepoints. Corresponding analysis ofmRNA gene expression (RT qPCR and Nanostring) and cytokines' secretion (Luminex) were performed.
Results: HPEGC did not express HLA class II at baseline, nor at any timepoint during culture, if not exposed to IFNg. As expected, HLA-DR demonstrated rapid increase in cell surface expression within 48 hours of IFNg treatment, reaching a plateau around day 14. On the other hand, HLA-DP followed by HLA-DQ showed significantly slower upregulation, with increasing expression continuing until day 21 (figure). Overall, average upregulation was about 40 fold higher than on day 1 for HLA-DR, compared with 13-fold and 4-fold for HLA-DP and DQ, respectively. Similar kinetics were observed for both IFNg concentrations, with greater intensity for the higher dose. mRNA studies demonstrated that the differential kinetics is also observed at the transcriptional level, with asynchronous dynamics (DR>DP>DQ) corresponding to the surface expression. CIITA was promptly upregulated by IFNg at 48h and remained stable throughout the 21 days F/U. Nanostring studies further demonstrated upregulation of the costimulation molecules PDL1, PDL2 and CD40 in response to IFNg stimulation. An induced transcription and secretion of the proinflammatory chemokines CXCl9 and CXCL10 was also noted (nanostring and cytokine luminex).
Conclusions: Differential kinetics of HLA-DQ to IFNg stimulation was demonstrated compared with other HLA class II molecules on HPGEC. Further studies are needed to explore whether this response is associated with the increased immunogenicity and pathogenicity of HLA-DQ.



BOS2_4 A PRO-INFLAMMATORY IMMUNE STATE IS INFLUENCED BY PERTURBATIONS OF MICROBIAL METABOLITES IN RENAL TRANSPLANTATION

Fernando Yuen Chang[*1], Amber Vaitkute[2], Meryl Attrill[2], Stephanie Chong[2], Hibo Mahdi[1], Paul Blair[2], Alan Salama[1], Simon Eaton[3], Mona Bajaj-Elliott[3], Anne Pesenacker[2], Reza Motallebzadeh[1]

[1]Royal Free Hospital, London, United Kingdom, [2]UCL, IIT, Pears Building, London, United Kingdom, [3]UCL Great Ormond Street Institute of Child Health, London, United Kingdom

Background: Long-term graft survival in renal transplantation remains a challenge. Emerging evidence suggests that the gastrointestinal microbiota-immune axis impacts on extra-intestinal health. Our study aims to identify the influence of microbial metabolites in recipient immunity, with our hypothesis that a pro-inflammatory state, promoted by reduced availability of bacterial-derived metabolites associated with immunoregulation e.g. short chain fatty acids (SCFAs) and tryptophan-derivatives is related to acute rejection (AR).

Methods: Ninety recipients and 21 live-donors were recruited with urine, stool and blood samples collected at baseline and up to 12-months after surgery. Flow cytometry was used to assess for circulating subpopulations of $CD19^+$ B-cells and $CD4^+$ T cells (cT_{FH} - $CD3^+CD4^+CD45RA^-CXCR5^+$ and cT_{FR} .$CD3^+CD4^+CXCR5^+FoxP3^+$) in a subcohort (n=54, figure 1). Faecal SCFAs and indole derivatives were identified by mass spectroscopy and high-performance liquid chromatography.

Results: Patients with AR had an almost 10-fold reduction of $FoxP3^+$ cT_{FR} cells after transplantation compared to baseline (p=0.03). Furthermore, there were lower frequencies of cT_{FR} cells at 3-months when compared to matched recipients without AR (0.009%±0.014% vs 0.10%±0.12%; p=0.01. Figure 1). There was a trend for higher frequencies of plasmablasts, resting memory B-cells and T_{FH} cells pre-transplantation in patients with AR, with fewer transitional B-cells (3.96%±1.14% vs 3.26%±1.23%; p=0.26) at 3-months. Although overall tryptophan availability increases after transplantation, patients with AR displayed reduced levels of SCFAs at 1-month, corresponding to the peak timepoint of AR occurrence (figure 2).

Conclusions: Our data has shown complex changes in microbial metabolites after transplantation that may influence balance of cT_{FH} vs cT_{FR} cells. The increase in dietary freedom after transplantation is reflected by increased tryptophan availability. Recipients with AR may harbour gut microbes that are unable to metabolise tryptophan into immune-regulatory metabolites, which predisposes a pro-inflammatory immune state. We postulate that there is decreased responsiveness or availability of AhR ligands, such as indoles and SCFAs, that contributes to a dysregulated immune milieu in AR.

Figure 1. Decreased levels of $FOXP3^+T_{FR}$ in recipients that develop BPAR

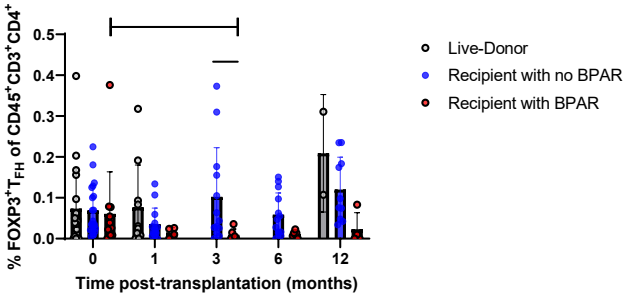


Figure 1. Levels of $FOXP3^+T_{FR}$ in peripheral blood of live-donors (n=20), recipients without biopsy-proven rejection (BPAR) (n=21) and recipients with BPAR (n=13). Recipients without BPAR subselected from cohort and matched with recipients with BPAR based on age, gender, level of sensitisation and HLA mismatch level. * - p<0.05

Recipients with BPAR have decreased proportion of circulating $CD3^+CD4^+CXCR5^+FOXP3^+$ T_{FR} at 3-month when compared to baseline (0.026% IQR[0.009-0.072] vs 0.003% IQR[0-0.020]; p=0.03) and compared to matched recipients without BPAR at 3-months (0.04% IQR[0.02-0.17] vs 0.003%[0.00-0.02]; p=0.01).

Figure 2. Snapshot of the faecal metabolome after live-donation and renal transplantation

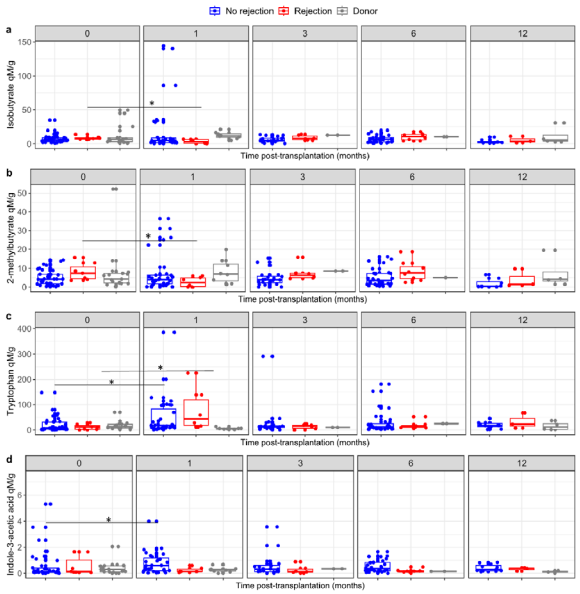


Figure 2. Faecal SCFA (Isobutyrate (*a*); 2-methylbutyrate (*b*) and Tryptophan (*c*) as well as a tryptophan derivative- Indole-3-acetic acid (*d*)) concentrations (μM/g) during transplantation in transplant donors (n=17) and transplant recipients with (n=7) and without (n=38) BPAR. * - p < 0.05.

BOS2_5 UNREPRESENTED HUMAN LEUKOCYTE ANTIGEN ALLELES ON SINGLE ANTIGEN BEAD ASSAYS: A COMPARISON AMONGST DIFFERENT TEST KITS

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Background: Human Leukocyte Antigen (HLA) alleles may generate antibodies that are undetectable by routine single antigen beads (SAB) assays if their unique epitopes are unrepresented. We compared the prevalence of unrepresented HLA alleles in available SAB kits in our cohort.

Methods: All individuals who had undergone two-field HLA typing (HLA-A, -B, -C, -DRB1, -DQA1, -DQB1, -DPA1, -DPB1) using sequence-based typing or sequence-specific primers from 2021 to 2022 were included. Two-field DRB3/4/5 typing was unavailable. HLA alleles detected were compared with alleles represented in the standard LABScreen (LS) kit (One Lambda) with and without the supplementary ExPlex (EP) kit (One Lambda), and the LIFECODES (LC) (Immuncor) SAB kit. Each unrepresented allele was compared with the most similar represented allele within each kit. Differences in amino acid sequences (IPD-IMGT Database v3.46) and eplet expression (HLAmatchmaker Class I v4.0, Class II v3.1) were identified (Figure 1). Differences in 3-dimensional molecular structures were visualised using generated models (SWISS-MODEL).

Results: Two-field HLA typing was performed for 80 individuals - all underwent HLA-A, -B, -C, -DRB1 typing, 78 underwent HLA-DQB1 typing and 42 underwent HLA-DQA1, -DPA1, -DPB1 typing. Overall, there was no difference in patients with unrepresented HLA alleles between the LS kit and the LC kit (72.5% vs 83.8%, p=0.09, Table 1). However, less patients had unrepresented HLA-B (26.3% vs 43.8%, p=0.02) and overall class I alleles (48.8% vs 65.0%, p=0.04) in the LS kit compared to the LC kit. Less patients had unrepresented HLA-A, -B, -C, -DRB1 alleles with the supplementary EP kit (LS+EP) compared to the LS or LC kit alone. In addition, less patients had unrepresented HLA-DQB1 alleles in the LS+EP kits compared to the LS kit. Less patients had unrepresented alleles with eplet mismatches, including those previously antibody-verified, in the LS+EP kits compared to the LS or LC kit alone.

Conclusions: Supplementary SAB kits may reduce the risk of undetected donor-specific antibodies. Less patients had unrepresented HLA-B alleles in the LS kit compared to the LC kit in our cohort. Further studies may be needed to compare the clinical performance of different SAB assays in detecting HLA antibodies.

Figure 1. Examples for Detection of Unpresented Human Leukocyte Antigen (HLA) Alleles and Eplet Mismatches with Most Similar Represented HLA allele in Single Antigen Bead Assays

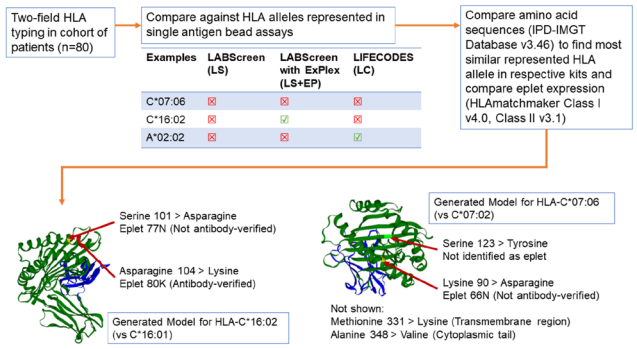

Table 1. Unrepresented Human Leukocyte Antigen (HLA) Alleles – A Comparison Amongst Different Single Antigen Bead Assays

	Total, n	Unrepresented in LS, n (%)	Unrepresented in LS+EP, n (%)	P value (LS vs LS+EP)	Unrepresented in LC, n (%)	P value (LS vs LC)	P value (LC vs LS+EP)
Any allele with antibody-verified eplet mismatch	80	17 (21.3%)	3 (3.8%)	<0.001	14 (17.5%)	0.55	0.005
Any allele with eplet mismatch	80	33 (41.3%)	17 (21.3%)	0.006	40 (50.0%)	0.27	<0.001
Any Allele	80	58 (72.5%)	33 (41.3%)	<0.001	67 (83.8%)	0.09	<0.001
Any Class I	80	39 (48.8%)	14 (17.5%)	<0.001	52 (65.0%)	0.04	<0.001
A	80	18 (22.5%)	8 (10.0%)	0.03	21 (26.3%)	0.58	0.008
B	80	21 (26.3%)	9 (11.3%)	0.02	35 (43.8%)	0.02	<0.001
C	80	18 (22.5%)	1 (1.3%)	<0.001	17 (21.3%)	0.85	<0.001
Any Class II	42	30 (71.4%)	20 (47.6%)	0.03	33 (78.6%)	0.45	0.003
DRB1	80	19 (23.8%)	5 (6.3%)	0.002	22 (27.5%)	0.59	<0.001
DQA1	78	8 (19.0%)	8 (19.0%)	1.00	10 (23.8%)	0.62	0.62
DQB1	42	8 (10.3%)	0 (0%)	0.003	3 (3.8%)	0.11	0.08
DPA1	42	1 (2.4%)	1 (2.4%)	1.00	1 (2.4%)	1.00	1.00
DPB1	42	18 (42.9%)	10 (23.8%)	0.06	18 (42.9%)	1.00	0.06

LS, LABScreen kit (One Lambda); LS+EP, LABScreen kit (One Lambda) with supplementary ExPlex kit (One Lambda); LC, LIFECODES (Immucor)

BOS2_6 EVALUATION OF METHODS FOR THE TISSUE-OF-ORIGIN DECONVOLUTION OF PLASMA AND URINARY CELL-FREE DNA IN ALLOGRAFT RECIPIENTS AND HEALTHY VOLUNTEERS

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Background: Donor-derived cell-free DNA (dd-cfDNA) has shown potential value in allograft surveillance to reduce the need for graft biopsies. However, limitations of dd-cfDNA-based allograft monitoring include multi-organ transplantation from the same donor, blood transfusions and the early transplantation phase. Analysis of graft tissue-specific methylation signatures in cfDNA could serve as an alternative approach, potentially with higher specificity to the relevant transplanted tissue.
Methods: We evaluated laboratory methods for the tissue-of-origin deconvolution of urinary (n=7) and plasma (n=9) cfDNA from organ transplant recipients (n=13) and healthy volunteers (n=3) using a novel enzymatic-based cytosine conversion method together with single- (ssLP) and double-stranded (dsLP) library preparation methods followed by low-coverage whole-genome bisulfite sequencing. The methods were adapted to preserve the cfDNA fragmentation patterns.
Results: The dsLP method showed a significantly reduced global methylation in urinary cfDNA of 56% compared to plasma-derived cfDNA with 75.8% ($p < 0.0001$). Conversely, no differences in the global methylation rate were observed between plasma and urinary cfDNA with the ssLP method (plasma: 80.2%; urine: 79.4%, $p > 0.05$). No significant differences were detectable between both library preparation methods for the tissue-of-origin proportions. However, there was a significantly higher proportion of sequences with undetermined tissue-of-origin with the dsLP method, which was more pronounced in urine (1.9% vs 32.6%, $p < 0.001$) than in plasma (0.2% vs 7.4%, $p < 0.001$).
Conclusions: This study outlines potential biases and pitfalls with methylome-based cfDNA tissue-of-origin deconvolution and detection of cfDNA from allograft tissues of interest. Based on these results, enzymatic conversion coupled with a single-stranded library preparation appears to be a robust and bias-free choice, especially for urinary-derived cfDNA, where DNase activity causes a reduction in intact double-stranded fragments.

BOS2_7 HUMAN REGULATORY B CELLS PREVENT EFFECTOR CD4+CD25- T CELL PROLIFERATION THROUGH A MECHANISM DEPENDENT FROM GRANZYME B AND LYMPHOTOXIN ALPHA

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Background: Granzyme B Regulatory B cells (GZMB+Bregs) have been described in humans in cancer, auto-immune diseases, HIV infection and transplantation. They have demonstrated suppressive properties on CD4+ effector T cells by inhibiting their proliferation and production of cytokines by a mechanism partially dependent on the granzyme B. Yet, their regulatory mechanisms remain unclear.
Methods: Single cell RNAseq (scRNAseq) experiments were carried on *in vitro* induced GZMB+Bregs (purity >95%), non-Breg cells and on $CD4^+CD25^-$ effector T cells cocultured with GZMB+Bregs or non-Breg cells. Functional analyses were performed to further investigate the role of these interactions with regards to the suppressive properties of GZMB+Breg.
Results: We report that the GZMB+Breg population exhibit a specific profile of 149 highly differentially expressed genes, mainly associated with cell proliferation, apoptosis, metabolism, and altered antigen presentation capacity consistent with their differentiated B cells profile. When cocultured with GZMB+Bregs, CD4+CD25- effector T cells are characterized by strong inhibition of genes for T cells proliferation, activation, IFN pathway, inflammation and apoptosis. Analysis of effector CD4+CD25- T cells / GZMB+Bregs interactions identifies Lymphotoxin alpha (LTA) as a key ligand expressed on GZMB+Bregs. Functional analysis using specific inhibitors was used to test their suppressive properties and we identified Lymphotoxin alpha (LTA) as a new and potent Breg ligand implicated in Breg induction, GZMB expression and suppressive properties.
Conclusions: We report for the first time for a role of LTA in the induction of GZMB+Bregs, and in its suppressive properties in human.

BOS2_8 THE INFLUENCE OF VIRUS-SPECIFIC IMMUNOGLOBULINES AS MODULATORS OF ANTIGEN-SPECIFIC T-CELL EXPANSION

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Background: Both cytomegalovirus-specific immunoglobulins (CMVIg) and varicella zoster virus-specific immunoglobulins (VZVIg) can contribute to viral control after transplantation. Apart from neutralizing activity towards the virus, little is known about their indirect effects on restoration of virus-specific T-cell immunity.
Methods: Therefore, we tested virus-specific T-cell activity in presence or absence of CMVIg and VZVIg in blood samples of 31 individuals (20 kidney transplant patients (KTX) and 11 immunocompetent controls). We performed a 6h stimulation assay using CMV or VZV lysate as stimuli. Staphylococcus aureus enterotoxin B (SEB) served as polyclonal stimulus. Activated T cells were flow-cytometrically identified based on co-expression of the activation marker CD69 and the cytokine interferon ɣ and further characterized regarding their expression of tumor necrosis factor α and interleukin 2. In addition, T-cell proliferation was analyzed by CFSE assay.
Results: After short-time stimulation, no differences were detectable for virus-specific T cells in presence or absence of Ig. Interestingly, however, proliferation of CMV-specific CD4 T cells was significantly higher in the presence of CMVIg ($p=0.007$) or VZVIg ($p=0.003$). The significant increase in T-cell proliferation in presence of CMVIg was also detectable after stimulation with lower CMV antigen concentrations (CD4 $p=0.022$; CD8 $p=0.012$). In contrast, both CMVIg and VZVIg led to a clear reduction of polyclonally activated CD4 and CD8 T cells both based on cytokine-induction after short-term stimulation (all $p<0.0001$) and on proliferation after long-term stimulation in the presence of CMVIg (CD4: $p<0.0001$; CD8: $p=0.0004$) and to a lesser extent of VZVIg (CD4: $p= 0.035$).
Conclusions: While immunoglobulins did not have any effect on immediate effector function, the presence of immunoglobulins increases the proliferative activity of specific T cells, which may have implications for the therapeutic use of immunoglobulins to restore antigen-specific T-cells in patients with active infections.

BOS2_9 GAMMA-DELTA T CELL THERAPY FOR POST-TRANSPLANT CYTOMEGALOVIRUS INFECTION: PROOF OF CONCEPT

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Background: Cytomegalovirus (CMV) disease remains a major challenge in solid organ transplant recipients (SOTRs), with a growing interest in developing anti-CMV adoptive cell therapies. Taking into account the current limitations of ab T cell therapies, our goal was to explore a complementary γδ T cell-based immunotherapy.
Methods: Healthy donors (both CMV-seropositive and CMV-seronegative) and kidney transplant recipients (KTRs) undergoing refractory CMV infection were enlisted in this preclinical study. γδ T cells were sorted from peripheral blood, then amplified and activated *in vitro,* using a T cell receptor (TCR) agonist combined to different cytokines, notably IL-4 and IL-15. The reactivity of expanded γδ T cells against CMV-infected target cells was then measured *in vitro*.
Results: γδ T cells amplification from both CMV-seropositive and CMV-seronegative healthy donors, as well as KTRs, was reproducible and compatible with a human cell-immunotherapy protocol. Amplified cells displayed an activated and differentiated phenotype, but low exhaustion, produced IFNγ in the presence of infected target fibroblasts, endothelial cells and macrophages, and were able to control viral dissemination *in vitro*. At the mechanistic level, anti-CMV reactivity was independent of the γδTCR but involved the co-stimulatory receptor lymphocyte function-associated antigen 1 (LFA-1). Finally, γδ T cell viability was preserved in the presence of immunosuppressive drugs used in transplant recipients. The efficacy of these amplified γδ T cells against CMV is now being evaluated in preclinical mouse models.
Conclusions: Altogether, these data provide a proof of concept for a future use of amplified γδ T cells, in the prevention and curative treatment of CMV disease in both CMV-seropositive and seronegative-SOTRs. These results pave the way for a future phase I clinical trial.

BOS2_10 THE DISTINCT INNATE IMMUNE RESPONSE OF DONATION AFTER CIRCULATORY DEATH LIVERS DURING NORMOTHERMIC MACHINE PERFUSION

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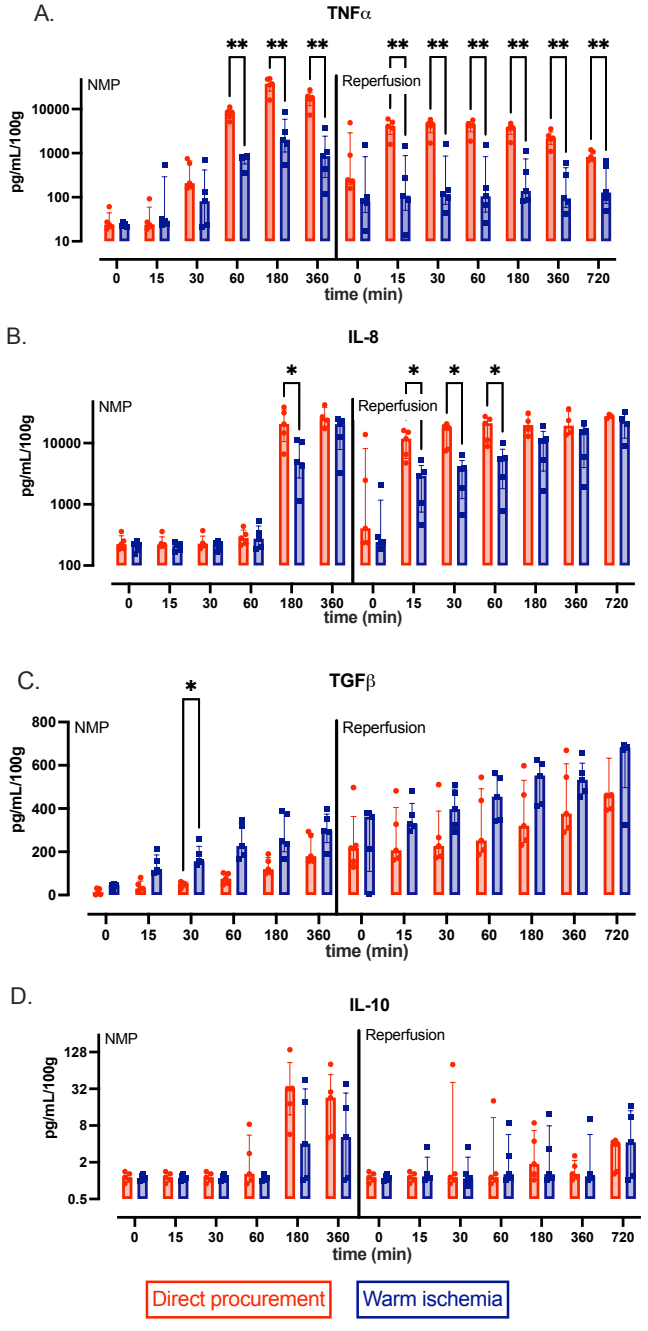
Introduction: Although normothermic machine perfusion (NMP) is increasingly used to clinically preserve and evaluate donor livers, little is known how NMP affects the immune compartment. We aimed to investigate the innate immune response during NMP of normal and warm ischemically damaged porcine livers.
Methods: Livers were either exposed to 60 min warm ischemia (WI60, n=5) or not (no WI n=5) before procurement, followed by NMP for 6 hours with a packed red blood cell based perfusate and subsequent 12 hours normothermic reperfusion with allogenic whole blood (to mimic transplantation). Perfusate levels of aspartate aminotransferase (AST), lactate, tumor necrosis factor-α (TNFα), interleukin 8 (IL8) and 10 (IL10) and transforming growth factor-β (TGFβ) were measured sequentially during NMP and reperfusion. On biopsies taken at different timepoints, expression of C/EBP homologous protein (CHOP), glucose regulated protein 78 (GRP78), B-cell lymphoma 2 (Bcl2) and Bcl2 associated X protein (Bax) were measured to reflect ER stress. Severity of histological injury after reperfusion was scored semi-quantitatively. Statistical analysis was done with two-way ANOVA.
Results: WI60 livers suffered more hepatic injury during NMP, as indicated by the elevated levels of AST (p=<0.001), and more severe histological damage (p=0.03 at 1h NMP). Lactate clearance during NMP (p=0.3) and reperfusion (p=0.3) were similar in both groups. TNFα and IL8 concentrations were lower in WI60 during NMP and reperfusion (all p<0.05) (figure). In contrast, TGFβ concentration was higher in WI60 only during NMP (p=0.003), whereas IL10 concentration was similar in both groups during NMP and reperfusion (p=0.3, p=0.8). We observed an increased expression of GRP78 in WI60, both during NMP (p<0.001) and reperfusion (p=0.03). CHOP expression was increased in WI60 during NMP (p=0.04) and reperfusion (p=0.07). There was no difference in expression of Bcl2 (NMP, p=0.9; reperfusion, p=0.4), whereas expression of the Bax was increased in WI60 during NMP (p=0.004), but not during reperfusion (p=0.3).
Conclusion: Warm ischemically injured livers exert a distinct innate immune response compared to healthy livers. The innate immune response seems to shift towards an anti-inflammatory and pro-apoptotic phenotype.

Figure



BOS2_11 EX SITU PORCINE LIVER MACHINE PERFUSION ACTIVATES THE COMPLEMENT SYSTEM AND INCREASES CYTOKINES INDEPENDENT OF PRE-INDUCED LIVER INJURY

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Background: Ischemia-reperfusion injury (IRI) is a key challenge in liver transplantation leading to short- and long-term failure of the transplanted liver. Machine perfusion (MP) has proven to limit the metabolic consequences of IRI and has the potential to rescue discarded livers. However, the effect of MP on the innate inflammatory response is unknown. We aimed to investigate complement activation and downstream effects that may be targeted to reduce IRI and inflammation during MP.
Methods: Porcine livers (n=24) were exposed to either biliary injury (n=8), global liver injury (n=8), or no liver injury (n=8). Ex situ liver MP was performed with 1h hypothermic, 1h rewarming, and 4h normothermic perfusion. Belzer preservation solution was used during the hypothermic phase. Thereafter, heparinized leukocyte- and platelet-depleted homologous blood was used as perfusate. Perfusate and tissue samples were collected at set time points and analysed for terminal complement complex (TCC) and cytokines (TNF, IL6, IL-1β, IL8 and IL10) using ELISA and Multiplex.
Results: During normothermic MP, TCC increased significantly from start (median 11 interquartile range [5.14-17]) to end MP (40 [15-60], p<0.0001). There was no statistical difference between the biliary injury, the global injury, and the no liver injury groups (p>0.5). During normothermic MP cytokines increased significantly in plasma (TNF, IL 6, IL10), in liver tissue (TNF, IL-1β, IL6, IL8) and bile tissue (TNF, IL-1β, IL6, IL8), all p<0.0001 Friedmann test/ Mann Whitney test.
Conclusions: Complement and downstream cytokines are strongly and persistently activated during normothermic MP independently of pre-induced liver injury. Cytokines increase significantly despite a leukocyte-depleted perfusate and are thus probably due to liver-derived cytokine production. Future studies should evaluate the source of cytokine production and if complement inhibition can suppress cytokine production during liver MP. Inhibition of complement activation might be a therapeutic option during MP.

BOS2_12 TETRAHYDRO-BENZOTHIOPHENE ROR GAMMA T INVERSE AGONISTS TO TARGET TH17 IN SENSITIZED SKIN ALLOGRAFT MOUSE MODEL

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Background: Th17 cells play a critical role in acute cellular as well as in chronic antibody mediated allograft rejection. We have recently designed tetrahydro-benzothiophene derivatives as novel inverse agonists of retinoic acid receptor-related orphan receptor gamma t (RORγt) and demonstrated in vitro activity in Th17 polarization assay from PBMCs. The objective of the current study is to determine the effect of tetrahydro-benzothiophene derivatives on the rejection of complete mismatch skin graft in a sensitized murine model.
Methods: C57BL/6 mice were sensitized by administration of 107 Balb/c splenocytes (IP) at day 0, 7 and 14 and transplanted with Balb/c skin grafts at day fifteen. Mice were injected daily with a tetrahydro-benzothiophene RORγt inverse agonist (TF-S14, 1mg/kg, IP), or tacrolimus (0.5mg/kg, IP) or combination. Graft survival was evaluated daily for rejection end point (100% necrosis). Skin grafts were sampled at day five for histology.
Results: Tetrahydro-benzothiophene RORγt inverse agonist prolonged median graft survival from 6 to 13.5 and from 7 to 23 days when combined with tacrolimus, Figure 1. Neutrophilic infiltration of skin-grafts decreased in RORγt inverse agonist, or combination therapy compared to vehicle or tacrolimus treated mice, Figure 2.
Conclusions: The novel tetrahydro-benzothiophene RORγt inhibitor offers a new therapeutic mechanism to treat rejection in highly sensitized patients regardless of degree of donor mismatch.

Figure 1. Sensitized allograft survival of Balb/c skin grafts in C57BL/6 recipient mice of vehicle treated (ctrl), TF-S14 1mg/kg treated (TF-S14), tacrolimus 0.5mg/kg treated (tacro) and TF-S14 1mg/kg + tacrolimus 0.5mg/kg treated (TF-S14+tacro). P-value <0.01, mantel-cox test; median survival for ctrl, tacro, TF-S14 and TF-S14 + tacro is 6, 7 ,13.5 and 23 days, respectively.

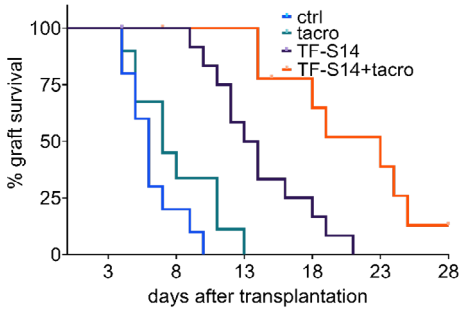
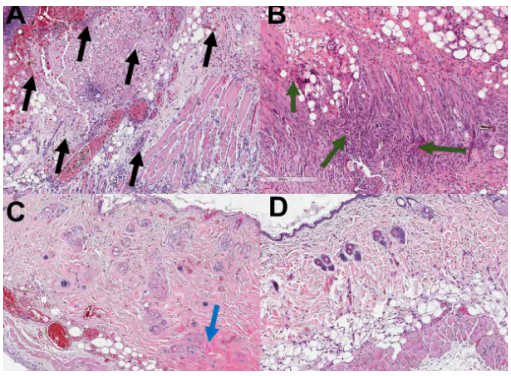


Figure 2. Histology images of skin grafts of at magnification x10; (A) control group showing diffuse inflammation and neutrophilic infiltration (black arrows), (B) tacro group showing neutrophilic infiltration (green arrows); (C) TF-S14 group showing localized inflammation (blue arrow), (D) TF-S14 + tacro group showing intact layers and no neutrophilic infiltration in the graft.



BOS2_13 CD8+CD3- CELLS ARE CRITICAL FOR TREG MEDIATED HUMORAL TOLERANCE

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Background: Recently, our group achieved significant extension of allograft survival in a murine model of skin transplantation by selective *in vivo* expansion and activation of Tregs using interleukin-2 (IL-2) coupled to a specific antibody against IL-2 (IL-2cplx). Here, we aimed to investigate the effect of alloreactive CD8+ cells in Treg-mediated skin graft survival.
Methods: Recipient C57BL/6 mice received IL-2cplx, rapamycin and a short-term treatment of anti-IL-6 mAb along with fully mismatched BALB/c or single MHCII mismatched BM12 (no CD8 T cell alloreactivity) skin grafts. Indicated groups were treated with different anti-CD8 mAbs, depleting either all CD8+ populations (anti-CD8a) or specifically CD8+ T cells (antiCD8b). To dissect the mechanisms of allograft rejection in this model, donor-specific antibody (DSA) development, *in vitro* T cell alloreactivity and graft infiltrating leucocytes were assessed.
Results: IL-2cplx therapy in combination with rapamycin and anti-IL-6 mAb led to prolonged survival of fully mismatched (BALB/c; MST = 30.5d) and MHCII mismatched (BM12; MST = 77.5d) skin allografts. Importantly, IL-2cplx based therapy prevented humoral rejection and development of DSAs. CD8 depletion did significantly extend skin graft survival, however CD8a (but not CD8b) depletion prevented humoral tolerance. Furthermore, CD8a depletion resulted in the increase of donor-responsive Th2 cells as well as graft infiltrating recipient CD4+ effector T cells by POD20. In addition, T follicular helper and T follicular regulatory cell levels were increased within the spleen in the absence of CD8 alloreactivity compared with non-depleted/fully mismatched recipients.
Conclusions: IL-2cplx therapy induces humoral tolerance and prevents the development of DSAs. Depletion of pan-CD8 cells using anti-CD8a mAb does not prolong skin graft survival but leads to donor-specific antibody formation whereas CD8b depletion did not restore humoral alloreactivity, suggesting a critical role of CD8+ non-T cells in the sustained prevention of recipient sensitization. Moreover, proinflammatory processes are thought to be a consequence of CD8a depletion, as increased migration of recipient CD4+ effector cells into skin grafts and elevated donor-responsive Th2 cells were observed.

BRIEF ORALS

Translational transplant immunology

BOS2_14 RESEARCH FOR NOVEL MECHANISM OF IMMUNO-SUPPRESSION THROUGH PD-1/PD-L1 PATHWAY

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Background: PD-1/PD-L1 pathway has begun to draw attention in cancer treatment as an immune checkpoint pathway, which is known to inhibit the activation of immune cells through PD-1 molecule. In the field of transplantation, it seems possible to inhibit immune response by activating these PD-1/PD-L1, as opposed to cancer treatment. We would like to check if the immune response after implantation can be suppressed, the rejection can be prevented, and the graft survival rate can be improved by using soluble PD-L1, a ligand capable of activating PD-1 on the surface of T lymphocytes.
Methods: Using BALB/c mouse and C57BL/6 mouse, the mouse heart transplant model is constructed, and CNI (tacrolimus) and soluble PD-L1 Fc are applied to this model to compare the immune response and transplant performance after implantation. Group 1 : FK group (n=15). Group 2 : soluble PD-L1 Fc group (n=15). Group 3 : FK + soluble PD-L1 Fc group (n=15). The survival rate of the three groups, histologic properties of the transplant, and the subsets of immune cells through mouse blood FACS, and indirectly predict the incidence of inflammatory reactions by comparing quantities of inflammatory cytokine in the blood.
Results: The group using sPD-L1 Fc alone showed a similar degree of graft survival to the group without immunosuppressants, and the FK group identified a graft survival of less than 45 days. The group, which used FK and sPD-L1 Fc together, identified between 60% and 45 days of graft survival.
This increase in graft survival in FK + sPD-L1 Fc group was also reflected in biopsy results, which showed that inflammatory cell infiltration was the mildest in the heart tissue of FK + sPD-L1 Fc group. Lymphocyte, macrophage, and FOXP3 + cell are increased in allograft heart tissue in combination of FK and sPD-L1 group. Perivascular inflammation is reduced in combination of FK and sPD-L1 group.
Conclusions: sPD-L1 alone is not sufficient to prevent allograft rejection. Combination of FK and sPD-L1 induce long-term graft survival. Systemic cell count change or inflammatory cytokine level is not clear to explain this results. Further assessment focused on localized change occurring in cardiac allograft is necessary.

Transplant Plus: Regenerative therapies and Xenotransplantation

BOS3_1 THE (PRO)RENIN RECEPTOR IS INVOLVED IN KIDNEY ORGANOID DEVELOPMENT

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Background: The (pro)renin receptor [(P)RR], a receptor for prorenin and renin, is widely distributed in the body, including the kidneys. Studies in (P)RR knockout mouse models indicate that (P)RR ablation can be detrimental to renal development and function. However, the lack of human models hinders investigation into the role of (P)RR in human kidney development. The advent of human induced pluripotent stem cell (iPSC) – derived kidney organoids provides a tool to study the role of (P)RR in human kidney development.
Methods: To investigate the effects of (P)RR knockdown on kidney organoid development, human iPSC – derived kidney organoids were generated according to a previously described protocol. We silenced the (P)RR by introducing (P)RR antisense oligonucleotides (ASOs) by electroporation at the stage of iPSCs and nephron progenitor cells induction, respectively. The development of kidney organoids was monitored morphologically and through protein expression analysis of nephron markers by immunohistochemistry staining which was quantified by Image J.
Results: After silencing the (P)RR at the initial stage of differentiation, the size of iPSCs-derived organoids was substantially smaller, but the size of tubular structures was bigger. We observed a decrease by 50% in both WT1 (glomerular cell marker) and PDGFRα (stromal cell marker) expressions in (P)RR-knockdown organoids, a 4-fold and 2-fold increase in expressions of fibrogenic cell markers α-SMA and COL1A1 respectively, and no change in Villin1 (proximal tubular cell marker) and Cadherin-1 (distal tubular cell marker) expression. Additionally, (P)RR knockdown at the stage of nephron progenitor cells induction decreased the expressions of Villin1 and Cadherin-1 in organoids by 50% and 60% separately, while it induced a 4-, 3-, 2- and 2-fold increase in the expressions of CD31 (endothelial cell marker), PDGFRα, α-SMA and COL1A1 respectively.
Conclusions: This study shows that (P)RR silencing at the initial stage of differentiation or at the stage of nephron progenitor cells induction impaired normal development of kidney organoids. Its absence caused a shift into the direction of fibrogenic cells. This study provides new insights into the understanding the role of (P)RR in human kidney development.

BOS3_2 ENGINEERING VASCULARIZED ENDOCRINE PANCREAS TO CURE TYPE 1 DIABETES

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Background: The aim of this study was to engineer functional, vascularized endocrine pancreas utilizing decellularized human placental cotyledons (hPLCs), human blood outgrowth endothelial cells (BOECs) and pancreatic islets. BOECs can be obtained from the recipients and can be used for construct revascularization.
Methods: hPLCs were decellularized using 1% SDS and 0.1% Triton. The acellular hPLCs were first repopulated with BOECs and then seeded with 1500 human islet eqvivalents (IEQ). Recellularization was confirmed by hystological and immunohistochemical methods, and endocrine function by glucose stimulated insulin secretion tests. The assembled vascularized endocrine constructs were transplanted in the subcutaneous (SC) space of STZ diabetic NSG mice (PLCs+Islets+BOECs). Control mice has been transplanted with non-endothelialized scaffolds (PLCs+Islets) seeded with the same number of islets and free islets into the prevascularized subcutaneous space (SC) and under the kidney capsule (KC).
Results: Engineered vascularized endocrine constructs displayed a continuous CD31+ endothelial cell network throughout the hPLC with islets embedded in the vascular bed. Furthermore, constructs demonstrated physiologic insulin release in response to glucose stimulation. Transplantation of the PLCs+Islets+BOECs led to normalization of blood glucose levels within first week in 80% of animals, in comparison with 60% in PLCs+Islets group. None of the mice transplated with islets into the prevascularized subcutaneous space returned to normoglycemic state. Removal of graft-bearing constructs led to recurrence of hyperglycemia in all mice within 24 h. Immunohistochemical staining showed larger β-cell mass, as assessed by the insulin-positive area per field in the PLCs+Islets+BOECs group compared with that of the PLCs+Islets group at 90 days posttransplant. Explanted grafts stained for CD31 showed that vessel density was significantly higher in the PLCs+Islets+BOECs samples compared to PLCs+Islet samples.

Conclusions: The engineered vascularized endocrine pancreas offers a fully biocompatible construct, restoring a matrix environment to the graft near-identical to that of native islets and provides mechanical protection which allows transplanted islets to engraft and function long-term.

BOS3_3 GENERATION OF VASCULARIZED ENDOCRINE CONSTRUCTS FOR TYPE 1 DIABETES

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Background: Disruption of islet extracellular matrix (ECM), poor vascularization, inflammatory reaction and immune destruction lead to a significant islet loss following intraportal islet transplantation. Human amniotic membrane (HAM) is known for its rich ECM, immunomodulatory, anti-inflammatory and anti-fibrotic properties. Blood outgrowth endothelial cells (BOECs) constitute an ideal source of autologous endothelial cells. The aim of this work was to investigate whether incorporation of pre-vascularized insulin-secreting organoids (PVO) into a pre-vascularized HAM-derived hydrogel will provide an optimal micro-environment and support engraftment and function of the insulin-secreting endocrine constructs.
Methods: PVOs composed of different ratios of dissociated insulin-secreting cells (EndoC-βH1/rat islet cells), human amniotic epithelial cells (hAECs) and BOECs (1000 cells/organoid) were generated on microwells. Hydrogels were obtained by acidic-digestion of decellularized, lyophilized HAMs collected from C-section-procured placentae. PVOs along with additional BOECs were loaded in the hydrogel (5 mg/ml) and cultured in a vasculogenic media. Cell distribution, migration and proliferation in hydrogel was assessed *in vitro* by immunohistochemical staining. Insulin-secreting cells function was also assessed. To evaluate *in vivo* function, the best performing PVOs were admixed with BOECs ($2x10^6$BOECs/ml), loaded in hydrogel and cultured in vasculogenic media for 2 days to enhance endothelial cell assembly into tubular, vascular-like structures. Vascularized constructs were then transplanted under the skin of diabetic NSG mice.
Results: *In vitro* studies showed that the best performing PVO ratio was composed of 50% insulin-secreting cells, 25% hAECs and 25% BOECs. Generated PVOs displayed a good function *in vitro* when loaded in HAM-derived hydrogel alone and with the additional BOECs. In addition, engineered HAM-hydrogel supported the development of the vascular-like structures, with a strong positive staining for CD31.
Conclusions: Our findings suggest that insulin-secreting constructs composed of PVOs and BOECs-vascularized HAM-derived hydrogel could be a promising strategy of β cell replacement therapies in alternative sites other than the liver.

BOS3_4 ALLOGENEIC MESENCHYMAL STROMAL CELL THERAPY IN KIDNEY TRANSPLANTATION: SHOULD REPEATED HLA MISMATCHES BE AVOIDED?

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Background: While most studies have investigated autologous mesenchymal stromal cells (MSC) MSC in kidney transplantation (KTx), 2 recent trials studied allogeneic MSC, as an off-the-shelf product is more feasible in clinical settings. Trial A investigated MSC therapy in KTx by selecting MSC to avoid repeated HLA antigen mismatches (MM) between kidney and MSC donors (Figure 1A), while Trial B did not perform MSC selection. We performed in-depth analysis to determine whether repeated HLA MM should be avoided to prevent donor-specific antibody (DSA) formation.
Methods: Trial B patients (n=10) received 1 infusion of MSC at day 3 post-KTx, while Trial A patients (n=10) received 2 infusions at week 25 and 25 post-KTx. Patients and donors were HLA typed for 11 loci at the second field. Two Trial B patients were excluded because no material for high resolution typing was available. Amino acid mismatch (AAMM) analysis with HLA-EMMA was performed between kidney donor and recipient and MSC donor and recipient, and repeated AAMM were identified (Figure 1B). Single antigen bead (SAB) data up to 5 years post-Tx were analyzed.
Results: Previously, DSA were reported in 2 out of 8 Trial B patients within 1 year post-Tx. Re-analysis of the SAB data in the light of high resolution typing revealed that 1 previously DSA detected at 1 month post-Tx was misclassified. In the same patient, DSA were detected at a later timepoint, directed against a shared AAMM (55R). As this DSA was detected 16 months post-KTx, it is unlikely that it was induced by the MSC. In another patient, previously assigned DSA were dismissed due to high background signal in the SAB assay. There was no DSA formation in Trial A. In Trial B, 4 out of 8 patients had repeated antigen MM, while in Trial A, 1 repeated antigen MM occurred. Total repeated AAMM were higher in Trial B, but this was not statistically significant (median 16 versus 8, p = 0.056). Importantly, although 1 Trial A patient did not have any repeated antigen MM for HLA-DQB1, there was a high number of AAMM (14).
Conclusions: Selection of MSC to avoid repeated HLA MM at the split antigen level is not sufficient to prevent repeated MM at the amino acid level. As the clinical relevance of repeated AAMM seems limited for the risk of DSA, our study suggests that it is not necessary to prevent repeated HLA MM in allogeneic MSC therapy in KTx to prevent DSA.

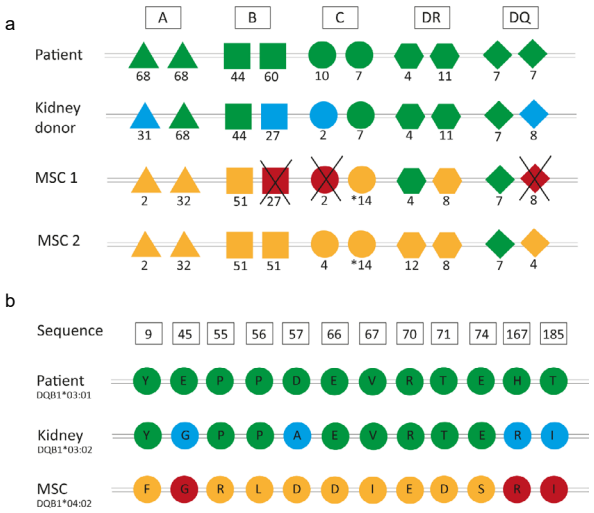

Figure 1 Principle of repeated HLA antigen and amino acid mismatches. (a) In Trial A, MSC donors were selected in such as fashion that HLA mismatches on the split antigen level that occurred between recipient and kidney donor were not present between the recipient and MSC donor. (b) Example from a patient that does not have a repeated HLA-DQB1 antigen mismatch (patient: DQ7, kidney: DQ8, MSC: DQ4), but still has three repeated amino acid mismatches.
Color legend: green, typing of the recipient; blue, mismatches between recipient and kidney donor; yellow, mismatches between recipient and MSC donor; red, repeated mismatches. MSC, mesenchymal stromal cell.

BOS3_5 DEVELOPMENT OF AN ADVANCED PLATFORM FOR RAT LIVER NORMOTHERMIC MACHINE PERFUSION EQUIPPED WITH A BIOREACTOR SEEDED WITH MESENCHYMAL STEM CELLS

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Background: Mesenchymal stem cells (MSCs) exert immunomodulatory and regenerative effects in hepatic ischemia reperfusion injury (IRI). Coupling MSCs-based therapy with Normothermic-Machine-Perfusion (NMP) could enable to more efficiently mitigate the detrimental consequences of IRI in higher-risk livers. We aimed at developing an advanced perfusion system for rat liver NMP equipped with a bioreactor seeded with viable MSCs.
Methods: The study includes 2 work packages (n=5 each group): 1) Development: bioreactors with 2x107 human MSCs were connected to the NMP circuit and subjected to 4 h-liverless perfusion (Liverless-NMP). Perfusate samples were serially collected, MSCs were harvested at the end of perfusion; 2) Bioreactor-based liver NMP: rat livers underwent 30 min-cold storage and were perfused for 4 h on the MSCs-bioreactor-based NMP circuit (Liver-NMP+bioreactor) or the standard NMP platform (Liver-NMP). Perfusates and biopsies were collected throughout and after NMP.
Results: During Liverless-NMP, MSCs remained viable and released mediators and extracellular vesicles (EVs). Flow cytometry of cells harvested after the procedure revealed a preserved expression of stemness markers, indicating that MSCs were not affected by the perfusion itself. Perfusates collected over bioreactor-based liver NMP showed higher concentrations of MSCs-related mediators and EVs compared to Liverless-NMP. Livers of the Liver-NMP+bioreactor group produced more bile, released less damage biomarkers, and secreted higher amount of acute phase proteins relative to standard NMP. Bioreactor-based liver-NMP was likewise associated with higher ATP production and reduced tissue succinate accumulation, as well as with lower perfusate concentration of inflammatory mediators, coupled with higher amount of protective factors.
Conclusions: We provide a novel MSCs-based protocol for liver NMP, thereby creating a modern perfusion platform. The integration of a bioreactor seeded with viable MSCs enables to induce a liver-tailored response, thus allowing a more efficient utilization of MSCs benefits during NMP. Compared to standard NMP, livers exposed to MSCs-derived secretome showed improved mitochondrial function, sustained cell viability, reduced inflammation, and activation of healing processes.

BOS3_6 THE CYTOPROTECTIVE EFFECTS OF EXTRACELLULAR VESICLES DERIVED FROM HUMAN AMNIOTIC EPITHELIAL CELLS ON PANCREATIC ISLETS

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Background: A considerable islet loss is observed following islet transplantation in type 1 diabetes patients due to hypoxia, inflammation and poor vascularization. Human amniotic epithelial cells (hAECs) have been shown to have cytoprotective effects on pancreatic islets under stressful conditions, due to their anti-inflammatory, immunomodulatory and regenerative properties. The aim of this study is to investigate whether extracellular vesicles derived from these cells (hAECs-EVs) would be able to exert similar properties.
Methods: hAEC-EVs were isolated from conditioned culture media of hAECs by sequential ultracentrifugation and characterized by nanoparticle tracking analysis, transmission electron microscopy, western blot and mass spectrometry. To test their cytoprotective effects, islets subjected to hypoxia in vitro were either treated or not with hAEC-EVs. The islet function was assessed by glucose-stimulated insulin secretion assay and viability by TUNEL staining.
Results: Characterization of hAEC-EVs showed the successful isolation of these vesicles. hAEC-EVs had a mean diameter of 160 nm and expressed EV markers such as CD9, CD63 and TSG101. Human islets exposed to hAEC-EVs, when compared to control, had an increased insulin secretion. In the future, we plan to better understand the mechanisms underlying the observed effects.
Conclusions: These preliminary results suggest that hAEC-EVs might become an interesting tool for protecting pancreatic islets from hypoxia.

BOS3_7 INSULIN-INDEPENDENCE IN LARGE ANIMAL MODELS AFTER PANCREATECTOMY ANDAUTOTRANSPLANTATION OF 3D-BIOPRINTED BIONIC PANCREATIC PETALS

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Background: The first milestone of a new therapy for the treatment of T1D is the development of 3D bioprinted petals consisting of: pancreatic islets and biomaterials. The aim of the study was to demonstrate the functionality of pancreatic islets in in vivo studies on large animals.
Methods: Domestic pigs were the research model. The animals were divided into 4 groups:(1)healthy pigs (Control; n=3);(2) animals with T1D after pancreatectomy, treated with insulin (T1D;n=3);(3) animals after pancreatectomy and autotransplantation of pancreatic islets to the liver (LIVER; n=3);(4) animals with T1D after pancreatectomy, which were autotransplanted with bionic petals (3D-PETALS; n=3).The effectiveness of the transplantation (TX) was assessed by the concentration of glucose, insulin intake and C-peptide. The observation lasted 1 month.
Results: The results showed that in the LIVER group, insulin intake within 3 weeks decreased by 71% compared to the demand before TX. Whereas 1 month after TX, the demand was lower by 62%. The 3D-PETALS group showed that the insulin intake in 3 weeks after TX decreased by 65%, and within a month decreased by 84%. In the 4th week after TX, the insulin intake average in the T1D group was 8.17U, while in the LIVER group=2.44U and in the 3D-PETALS group=1.06U. Islet TX significantly reduced insulin intake (T1D vs LIVER; p=0.0001 and T1D vs 3D-PETALS; p<0.0001). Glucose measurement showed significant changes. After 1 month of follow-up, glucose levels were significantly lower in the LIVER vs T1D (265.8mg% vs 310.2mg%; p<0.0001) and 3D-PETALS & T1D (198.3mg% vs 310.2mg%; p=0.0354). Most importantly, glycemic levels were also significantly lower between the LIVER & 3D PETALS groups (265.8mg% vs 198.3mg%; p=0.0021). The concentration of C-peptide during the study was 0.14ng/ml.
Conclusions: Bioprinted petals with dECM-based bioink significantly reduces diabetic parameters. Thus, it seems to be an effective therapy for people with T1D.

BOS3_8 A MICROFLUIDIC BILE-DUCT-ON-A-CHIP PLATFORM FOR STUDYING BILIARY EPITHELIUM IN A DISH

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Background: Damaged biliary epithelium after transplantation can result in loss of graft function due to impaired regeneration of. Accurate *in vitro* models for studying the effects of different organ preservation strategies (e.g. machine perfusion), prolonged ischemia times and reperfusion injury on the integrity of the biliary epithelium are lacking. LGR5$^+$ intrahepatic cholangiocyte organoids (ICO) do allow for the *in vitro* expansion of healthy cholangiocytes. However, access to the organoids lumen, which represents the luminal side of a bile duct, is limited and can only be accessed by disrupting the three-dimensional organoid structure. Therefore, we aimed to establish a bile-duct-on-chip (BDOC) platform using ICO with an accessible lumen to study the biliary epithelium *in vitro*.
Methods: Four-channel BDOC (dimensions;L:1cm, WH:500µm) were prepared using polydimethylsiloxane (PDMS). All channels were filled with collagen type-I or a hydrogel derived from decellularized liver extracellular matrix, and viscous finger patterning was used to create a lumen (Ø:300µm) inside the hydrogel. ICO were initiated from human donor liver biopsies (n=5) and added to the channels (10^5cells/channel) to grow for 21 days at 37˚C. Integrity of the biliary epithelium was monitored using confocal microscopy and histology.
Results: The ICO cells self-organized into a columnar monolayer within 21-days. They expressed cholangiocyte markers cytokeratin-7 and 19. Zonula occludens-I and anion exchange protein 2 staining revealed that the cells were polarized similar to biliary epithelium. After 21 days, the cell layer formed an impermeable barrier against 70kDa FITC-Dextran. Glycocalyx components, like sialiated carbohydrates, could be removed using neuraminidase. The cells were able to restore the glycocalyx, as shown by intact apical sialic acid staining.
Conclusions: This BDOC platform can simulate small diameter intrahepatic bile ducts *in vitro* and allows for assessment or treatment of the biliary epithelium from the luminal side. ICO-derived cells formed a polarized, cholangiocyte barrier and were able to restore the glycocalyx after enzymatic treatment. This platform is ready to assess the effect of organ preservation strategies and biliary regeneration.

BRIEF ORALS

Transplant Plus: Regenerative therapies and Xenotransplantation

BOS3_10 TACROLIMUS-LOADED MIXED THERMOSENSITIVE HYDROGEL FOR IMPROVING THE OUTCOME OF SKIN AND VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

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Background: The previous study showed the mixed hydrogel, consisting of P-Lys-Ala-PLX and Pluronic® F127, had high drug encapsulation efficiency and appropriate drug release rates, making it a promising option for drug delivery. The study aims to evaluate the effectiveness of using this mixed thermosensitive hydrogel as a controlled drug delivery system for immunosuppressant drug, such as tacrolimus to prevent rejection and maintain allograft function with minimal systemic side effects.
Methods: Skin or vascularized composite allografts from Brown-Norway were transplanted to Lewis rats. The recipients were divided into three groups and received either daily systemic injections of 2mg/kg tacrolimus, a single mixed thermosensitive hydrogel injection, or a single mixed thermosensitive hydrogel injection loaded with 10mg tacrolimus. The mixed hydrogel formulation was used as the injectable carrier for tacrolimus. Tacrolimus concentration, kidney function, peripheral immune response, allograft survival, histopathological changes, chimerism, and nerve regeneration were observed.
Results: Recipients that received a single mixed thermosensitive hydrogel injection loaded with tacrolimus showed an initial burst release of tacrolimus in the blood during the first 15 days after transplantation, followed by a subsequent decrease to subtherapeutic levels that remained detectable for at least 90 days. The levels of creatinine and blood urea nitrogen among groups were comparable. The single mixed thermosensitive hydrogel injection loaded with tacrolimus had a local effect, with less infiltration of $CD3^+$ T cells in the allograft but no significant changes in the levels of regulatory and effector T cells in blood circulation. This resulted in long-term graft survival for skin and vascularized composite allotransplantation. Improved outcomes were also indicated by the presence of chimerism and nerve regeneration.
Conclusions: The mixed hydrogel formulation is a safe and reliable drug delivery system with potential advantages for skin and vascularized composite allotransplantation. It is a promising system for the delivery of immunosuppressive drugs in the field of transplantation.

BOS3_11 SINGLE CELL RNA SEQUENCING ANALYSIS OF HUMAN AMNIOTIC EPITHELIAL CELLS TO DECIPHER THE MECHANISMS OF IMMUNOMODULATION CONFERED TO PANCREATIC ISLETS

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Background: Long-term function of islet graft remains a challenge due to inflammatory, ischemic, allogenic and autoimmune aggression responsible for damages to the transplanted islets. Incorporation of human amniotic epithelial cells (hAECs) into islet organoids has proven to be a valuable strategy to inhibit inflammation- and hypoxia-mediated islet destruction, improve their engraftment and enhance islet survival after transplantation. However, mechanisms of the regenerative, immunomodulatory and anti-inflammatory properties of those cells remain elusive and need to be investigated. This work aims at identifying these mechanisms using single-cell RNA sequencing (scRNA-seq).
Methods: hAECs were isolated from 3 amnions obtained from C-section-procured placentae, and frozen immediately after isolation. Cells were thawed and dead cells were sorted out by fluorescence-activated cell sorting. To identify genes and cell subpopulations with regenerative, immunomodulatory and anti-inflammatory properties that may play a role into strengthening islet engraftment, function and viability, libraries were generated on a Chromium controller (10x Genomics) and scRNA-seq was carried out on an Illumina NovaSeq 6000 generating 100-250 bp pair-end reads. Expression data were normalized, filtered, and clustered using the Seurat V4 version through the open access Cellenics online platform. The identification was followed by validation on flow-sorted cells using qPCR and immunofluorescence.
Results: We identified 4 distinct cell types expressing established markers for epithelial, stromal and rare populations, showing hAECs comprise different cells subpopulations. Most of the clusters included cells from each group. Homogeneity in clusters, genes and pathways were found between the 3 samples of hAECs. We expect to identify upregulation of pathways related to immunomodulation in one of those clusters.
Conclusions: Our study revealed the shared regulation of genes and pathways in the 3 samples of hAECs for the first time at single-cell resolution, and demonstrated their relevance to islet engraftment and for the protection of the islet graft. A better understanding of immunomodulatory properties of hAECs will be of outmost importance for the development of cell-based therapies for type 1 diabetes.

BRIEF ORALS

Transplant Plus: Regenerative therapies and Xenotransplantation

BOS3_12 FEASIBILITY OF MANUFACTURE OF CHIMERIC ANTIGEN RECEPTOR (CAR)-REGULATORY T CELLS (TREGS) FROM PATIENTS WITH END-STAGE RENAL DISEASE (ESRD)

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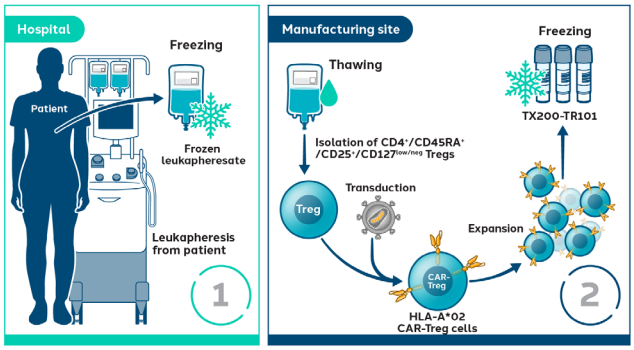
Background: Gene-modified cell therapy with Tregs is a promising approach to prevent graft rejection and induce immunological tolerance in organ transplantation. We are developing a cell therapy comprising autologous naïve Tregs that are isolated from leukapheresate, transduced with lentiviral vector encoding a CAR recognising human leukocyte antigen class I molecule A*02 (HLA-A*02) and expanded *ex vivo* before cryopreservation as resultant drug product (TX200-TR101) (see figure). In an ongoing first in human study (NCT04817774), kidney transplant recipients will receive a single infusion of TX200-TR101 2-3 months after transplantation. The Phase 0 study described here evaluated the feasibility of manufacture of TX200-TR101 for the target population, ie, ESRD necessitating kidney transplantation. Participants in this study did not receive an infusion of drug product.
Methods: Four patients with ESRD and HLA-A*02 negative typing underwent leukapheresis to collect starting material for manufacture of TX200-TR101. Manufacturing success criteria were predefined as cell quantity in each batch of ≥10^4 cells/kg body weight, cell viability of ≥70% and transduction efficiency of ≥20%. Other variables included Treg identity and maturation by phenotyping, residual bead count, vector copy number, level of endotoxin, sterility and presence of mycoplasma. The characteristics of leukapheresate starting material and resultant drug product from ESRD patients were compared with those of commercially purchased leukapheresate and resultant drug product from 10 healthy donors.
Results: No safety issues were identified during leukapheresis collections. Batches of drug product were manufactured from all 4 patients with ESRD and met the predefined manufacturing success criteria. White blood cell populations in leukapheresate, and quality, quantity and functional activity of manufactured CAR-Tregs were comparable between patients with ESRD and healthy donors. CAR-Treg drug product from 1 patient with pre-existing lymphopenia had similar high quality but reduced cell quantity compared with batches from the other ESRD patients, although yield was still above the predefined target minimum number of cells.
Conclusions: Manufacture of high-quality naïve CAR-Tregs from patients with ESRD is safe and feasible.



Leukapheresate is collected from the patient (**panel 1**), frozen and shipped to the manufacturing site (**panel 2**). After thawing, naïve Tregs ($CD4^+/CD45RA^+/CD25^+/CD127^{low/neg}$) are isolated, transduced with lentiviral vector encoding chimeric antigen receptor (CAR) recognising HLA-A*02, expanded and frozen as resultant drug product (TX200-TR101).

BOS3_13 AUXILIARY LIVER XENOTRANSPLANTATION TECHNIQUE IN A TRANSGENIC PIG TO A NON-HUMAN PRIMATE MODEL

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Background: Xenotransplantation using pigs' liver has long been proposed as an alternative method to overcome this donor shortage issue or more importantly as a bridge to allotransplantation. However, xenotransplantation in a pig to primate model has been challenged by profound thrombocytopenia and coagulation disorders, leading to uncontrollable hemorrhage and early mortality. Here we suggest that the left auxiliary technique using left lateral lobe graft can potentially be a useful model to help broaden knowledge on liver xenotransplantation (XLT).
Methods: Fifteen consecutive (XLT) was carried out using male cynomolgus monkeys of specific pathogen-free health status as recipients. All experiments were approved by the Institutional Animal Care and Use Committee in Seoul National University Hospital (SNUH-IACUC). Right auxiliary XLT was performed in two cases, orthotopic XLT was performed in eight cases, and left auxiliary XLT was performed in five cases.
Results: Right auxiliary XLT cases were not survived after surgery from the massive bleeding during the recipient right liver hepatectomy. Right liver of primate encircle the inferior vena cava (IVC) and dissection between the right liver and IVC was the main cause of bleeding. Orthtopic XLT cases survived less than seven days which was resulted from the profound thrombocytopenia and coagulation disorder. Among the five left auxiliary XLT cases, two cases survived more than three weeks without profound thrombocytopenia and anemia. One of that two animals survived 34 days after XLT which was reported longest survival after XLT performed in primate.
Conclusions: Left auxiliary XLT is suitable operational technique for XLT experiment using non-human primate. With this technique, risk of thrombocytopenia and coagulation disorder can be minimized and long term survival after XLT can be obtained which was essential to assess the graft condition such as rejection after XLT.

BRIEF ORALS

Transplant Plus: Regenerative therapies and Xenotransplantation

BOS3_14 LONG-TERM (2 YEARS) SURVIVAL OF PORCINE TO NONHUMAN PRIMATE LIFE-SUSTAINING KIDNEY XENOTRANSPLANTATION

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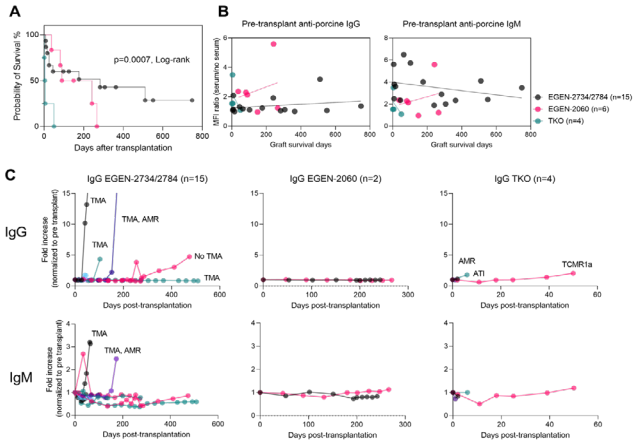
Background: Xenotransplantation holds immense potential as replacement therapy for end stage renal disease. Development of porcine xenografts with triple knock-out of xenoantigens (TKO) and knockin of human transgenes have improved xenograft survival considerably.
Methods: TKO donors, and TKO donors also expressing various human transgenes (*CD46*, *CD55*, *THBD*, *PROCR*, *CD47*, *TNFAIP3*, and *HMOX1*) were produced by eGenesis (EGEN-2734, n=10; EGEN-2784, n=5; EGEN-2060, n=2) on a Yucatan minipig background. EGEN-2784 expresses the same human transgenes with additional deletion of porcine endogenous retrovirus. Life-sustaining kidney transplantation was performed in cynomolgus macaques using these genetically modified porcine grafts. T and B cell depletion was followed by a short course of corticosteroid and tacrolimus. Immunosuppression was maintained with anti-CD154 monoclonal antibody w/wo mycophenolate mofetil. IgG/IgM antibodies binding to donor porcine endothelial cells were surveyed by flow cytometry.
Results: Overall recipient survival is significantly superior with donor organs expressing human transgenes compared to TKO only grafts (median, 283 vs. 5 days, p=0.0018, Log-rank, figure 1A). *De novo* donor-specific antibodies (DSA) were detected in serum from some recipients but did not correlate with clinical outcome and pathological findings of antibody mediated rejection in all cases (figure 1B). Similarly, pre-transplant anti-porcine antibody titers showed no correlation to survival, where the longest surviving animal (>740 days) showed higher comparative pre-transplant IgM binding. Post-transplant DSA was generally associated with antibody mediated rejection but not thrombotic microangiopathy, which were the most common causes for rejection (figure 1C).
Conclusions: Life-sustaining renal xenograft survival exceeding two years was achieved in cynomolgus macaques using TKO porcine kidneys expressing multiple human transgenes. Although the outcome is heterogenous, pre-transplant anti-porcine antibody titer binding do not correlate with clinical outcome. Post-transplant *de novo* DSA was generally associated with antibody mediated rejection but not with thrombotic microangiopathy. These long-term findings solidify the potential of kidney xenotransplantation.



Looking through the glass – fresh perspectives on ethicolegal and psychosocial aspects of donation and transplantation

BOS4_1 CLINICAL TRANSLATION AND IMPLEMENTATION OF A BIO-ARTIFICIAL PANCREAS: A QUALITATIVE STUDY EXPLORING THE PERSPECTIVES OF PATIENTS WITH TYPE 1 DIABETES

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Background: In preclinical research settings the bio-artificial pancreas is being developed that can be implanted in patients with diabetes type 1 to produce and secrete insulin. First-in-human clinical trials are expected in a few years. In this interview study, the perspectives of patients with type 1 diabetes on the clinical translation and implementation of the bio-artificial pancreas were explored to elucidate their perspectives, needs, and preferences.
Methods: An interview guide was developed and pilot-tested. Semi-structured interviews were carried out with 20 type 1 diabetes patients. Inclusion was stopped once data saturation was reached. The interviews were audio-taped, and transcribed verbatim. A qualitative content analysis with an inductive approach was conducted to categorize the data, and develop themes within a coding frame.
Results: Most patients reported a range of expected advantages of the bio-artificial pancreas as a potential treatment that could be divided into four themes: the ethical value beneficence (e.g. better health and psychosocial outcomes), autonomy (e.g. more freedom and flexibility in their daily lives), privacy (e.g. a therapy invisible to others to avoid stigmatization and without the risk of sharing personal health data) and justice (e.g. suitable for patients without self-management skills required for device-based treatment). Further, preferences regarding informed consent procedures, the implantation site and follow-up care were mentioned. Patients also shared their views on rescinding control of their treatment, and their concerns regarding the irreversibility of the surgical procedure, cell sources used and accessibility of the therapy.
Conclusions: Insights from this interview study allow researchers, policy makers and clinicians to align the clinical translation and implementation of the bio-artificial pancreas with patients' needs and preferences. Alignment is likely to improve chance of successful implementation.

BOS4_2 PSYCHOLOGICAL SCREENING AND FOLLOW-UP CARE FOR LIVING LIVER DONORS: 5-YEAR PROSPECTIVE COHORT DATA FROM A SINGLE ACADEMIC CENTRE

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Background: Transplantation with a living donor has proved to be an effective solution for patients on the waiting list for a liver transplantation. To maximise the benefits that living donor liver transplantation offers, careful donor screening is an absolute prerequisite. In our centre, this screening also involves standard psychological screening by a licensed health care psychologist, and if indicated psychological treatment.
Methods: We report on the psychological screening and care for all potential living donor candidates who entered the program since 2018. Donors were screened using the ELPAT Psychosocial Assessment Tool (EPAT), both the interviews and the questionnaires. Data on additional psychological care was retrieved from the medical records.
Results: One hundred an two donors (54 female, mean age 35,4 (SD 9,7)) underwent psychology screening for living liver donation. Intended recipients were first-degree relative (52), partners (10), other family members (17), friends (9) and unrelated (14, of which 6 undirected and 8 directed). Ambivalence was present in 9 cases. Pressure from others to donate was reported in 3 donor candidates, and 10 experienced some type of moral obligation to donate. All potential donors were given the possibility to opt out from donation during the whole process until surgery was started. Fifty-eight donor candidates had sought professional mental health support and/or used psychotropic drugs in the past. However, the average scores for current anxiety and depression, as measured by validated screening questions (PHQ-2 and GAD-2) were low. Of all candidates, 2 were rejected for psychological reasons. From this cohort, 38 eventually donated part of their liver. Of these, 12 received additional psychological care, for various reasons. In addition 3 donor candidates who were medically unfit to donate received counselling to improve coping.
Conclusions: The EPAT is a useful tool for living liver donor screening, covering all important psychological domains. Providing psychological treatment on indication proved to be a feasible way for this group to deal with potential psychological complaints. Donors appreciate knowing from the start that it was possible to receive additional psychological care, and 12 out of 38 living liver donors made use of this offer.

BRIEF ORALS

Looking through the glass – fresh perspectives on ethicolegal and psychosocial aspects of donation and transplantation

BOS4_3 PSYCHOSOCIAL EVALUATION OF LIVING KIDNEY DONORS IN QATAR – PROCESS AND OUTCOMES OF THE COMMITTEE FOR OVERSIGHT OF LIVING DONATION

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Background: Transplants from living donors comprise 38% of global kidney transplant activity. They offer better outcomes for many recipients, but several socioeconomic and psychological factors must be addressed in evaluation of prospective living kidney donors (PLKD), to optimize care in local contexts. The Committee for Oversight of Living Donation (COLD) was established in Qatar in 2014 to provide standardized multidisciplinary psychosocial evaluation of all PLKD, to ensure adherence to legal and ethical standards, and to enable appropriate care provision throughout the evaluation and donation processes.
This study describes the COLD protocol for PLKD evaluation and reports outcomes of eight years' experience evaluating PLKD.
Methods: This retrospective, observational cross-sectional study used data manually extracted from the COLD database of all PLKD who presented Sep 2014 – Dec 2022 inclusive. Donors' demographic data, asserted relationships with intended recipients, and outcomes of psychosocial evaluation (acceptance/decline as potential donor) were reviewed and analyzed using descriptive statistics. Reasons for decline were thematically coded.
Results: 898 PLKDs (54% M) were evaluated by the COLD; 50% were Qatari citizens and 50% non-citizens from 43 different countries. 96% declared a relationship with intended recipients (76% genetic; 20% emotional). Of those unrelated, 22 claimed to be directed altruistic donors and 19 non-directed altruistic. 788 (88%) were accepted by the COLD, 44 dropped out, and 66 were declined. Of those declined, 17 were genetically related, 7 emotionally related, and 42 unrelated ("altruistic"); 12 were citizens and 54 non-citizen residents. Main reasons for decline were psychological unfitness, insufficient socioeconomic supports, coercion (by employer or family), and medical contraindication.
Conclusions: The COLD's multidisciplinary structured approach to psychosocial evaluation of PLKD has been effective in identifying and assessing the severity of risk factors, which are notably present across a range of demographics. This demonstrates the need for comprehensive evaluation of all PLKD, not just expatriates or those non-genetically related. The COLD protocol may be a useful tool for psychosocial evaluation of PLKD in other countries.

BOS4_4 TRANSPLANT EXPERIENCES AND QUALITY OF LIFE IN PATIENTS WHO UNDERWENT AN INCOMPATIBLE KIDNEY TRANSPLANT: A CROSS-SECTIONAL PILOT SURVEY

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Background: Desensitization programs for ABO and HLA-incompatible kidney transplantation has enabled end-stage kidney patients to undergo transplantation with a living donor. Studies to date have focused on medical feasibility and outcomes. We aimed to explore the emotional response, medication adherence and the health-related quality of life (HRQoL) among incompatible kidney transplant (KT-i) recipients and to compare HRQoL with Dutch patients with a chronic illness and Canadian compatible transplant recipients.
Methods: In this cross-sectional study, the Transplant Effects Questionnaire (TxEQ) was used to measure emotional response and medication adherence, and the Patient Reported Outcomes Measurement Information System (PROMIS-29) to measure HRQoL (9 subscales). Questionnaires were sent to all consecutive patients who underwent desensitization for either ABO or HLA incompatibility in the past five years in the Erasmus MC. Dutch data from Elsman et al. 2022 and Canadian data from Tang et al. 2019 were used for comparison.
Results: Twenty-eight patients participated (response rate 85%) on average three years after transplantation. Average age at transplantation was 49 years (SD=15); 19 (68%) were male. Twenty had undergone ABOi, 5 HLAi and 3 combined ABOi/HLAi. There were no significant differences between groups on outcomes but group size was small. All patients reported being adherent to immunosuppressive medication. Three patients (11%) experienced high guilt and 15 (43%) high levels of worrying. Compared to the Dutch patients, KT-i recipients had significantly lower physical functioning, however, pain was significantly less intense. There were no significant differences on HRQoL between KT-i recipients and stable Canadian compatible kidney recipients. Higher worry was related to higher depression and fatigue.
Conclusions: This study emphasizes the importance of psychosocial outcomes after incompatible transplantation. Future studies should be prospective and include a matched control group of compatible recipients to allow investigation of the impact of desensitization on psychosocial outcomes.

BOS4_5 ANXIETY AND DEPRESSIVE SYMPTOMS AMONG PATIENTS ON DIALYSIS, KIDNEY AND KIDNEY-PANCREAS TRANSPLANT RECIPIENTS

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Background: Many patients on dialysis have significant anxiety and depression, which are associated with poor medication adherence and outcomes. Kidney (KT) and kidney-pancreas (KP) transplant improves quality of life compared to dialysis. We compare anxiety and depressive symptoms of KP and KT recipients with patients on dialysis using Patient Reported Outcome Measurement Information System (PROMIS) scores.
Methods: Secondary analysis of data from our research database, which include cross-sectional convenience sample of adult patients on dialysis, KT and KP recipients. Demographic data are self-reported, clinical data are from health records. Patients completed the PROMIS-29 profile domains, which include the anxiety and depression domains. Higher scores correspond to more severe symptoms; a score >= 60 indicates clinically potentially significant anxiety or depression. Scores were compared using ANOVA and linear regression adjusted for age, sex, ethnicity, comorbidity and time since starting current treatment modality.
Results: Of 717 participants (87 KP, 347 KT and 283 dialysis), 423(59%) were male, mean(SD) age was 62(14) years. Sex distribution was similar between treatment groups; patients on dialysis were significantly older than transplant recipients (mean[SD] age 64[14] vs 53[9] vs 52[16] years for dialysis vs KP vs KT, respectively; p<0.001). Mean(SD) anxiety 52(12) vs 54(10) vs 52(9) (p>0.05) was similar between all three groups. However, depression 51(11) vs 52(9) vs 48(9) (p<0.01) was lower among KT recipients compared to both KP and patients on dialysis. The proportion of patients with clinically potentially significant distress (either anxiety or depression) was the highest among patient on dialysis and lowest for KT (36% vs 30% vs 22% for dialysis vs KP vs KT, P<0.001). The results remained similar in multivariable adjusted regression models.
Conclusions: These results suggest that KP recipients have higher level of anxiety and depressive symptoms compared to KT recipients; their symptom severity is similar to patients on dialysis. Further studies need to assess if mental health support improves these symptoms and quality of life for KP recipients.

BOS4_6 LONG TERM OUTCOMES OF CHILDREN OF FEMALE KIDNEY TRANSPLANT RECIPIENTS – A RETROSPECTIVE REGISTRY STUDY

Goni Katz-Greenberg[*1], **Lisa Coscia[2], Serban Constantinescu[2;3], Michael Moritz[2]**

[1]*Duke University School of Medicine, Medicine, Durham, United States,* [2]*Transplant Pregnancy Registry international; Gift of Life Institute, Philadelphia, United States,* [3]*Lewis Katz School of Medicine, Temple University, Medicine, Philadelphia, United States*

Background: Pregnancy and short-term outcomes of kidney transplant recipients (KTRs) and their offspring (OS) have been previously described, but long-term data regarding health and development of KTRs' OS are lacking. We sought to describe these using data from the Transplant Pregnancy Registry International (TPRI).
Methods: Since 1991, the TPRI has enrolled pregnant KTRs. Data are collected via questionnaires, periodic phone interviews and medical record review.
We extracted basic data of KTRs and their pregnancies, and all available data on their OS. Each live birth was treated as a separate episode. Each disease/disorder was extracted individually as an OS could have more than one. Severity of disease was not included.
Descriptive statistics were expressed as absolute numbers (%) for categorical data and as median with interquartile range (IQR) for skewed distribution.
Results: There were 1747 distinct live births in the TPRI, and 1546 OS with>1 year of follow-up (f/u) were included in the analysis (Figure 1). A vast majority [1508 (97.5%)] were from North America, and 805 (52%) of OS were male. Median f/u was 15.32 years (6.80-23.51), with 1142 (73.8%) of OS reported as healthy and developing well at last f/u. Most common diagnoses were allergies, asthma, and renal disease (2.8%), most commonly due to anatomical malformation. There were 144 reported behavioral and psychiatric disorders (Table 1).
Conclusions: This is the largest cohort of OS of female KTRs to date. While there is apprehension among clinicians regarding outcomes of pregnancy and OS of KTRs, our study shows that 74% of OS were healthy at last f/u. Despite high rate of prematurity and low birthweight, the majority of OS seem to have normal long-term development. The proportion of reported neurological or psychiatric disorders in the OS is overall similar to the general population. Whereas previous data have shown association between a chronically ill parent to a child's wellbeing, further studies are needed to assess causation in this study population. Lastly, etiologies of renal disease were mainly anatomical or genetic disorders and may impact early child development and/or manifest in early adulthood. Despite its retrospective design, our study demonstrates most OS are healthy which should be included in counseling KTRs contemplating parenthood.

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Figure 1. Study Flow Diagram

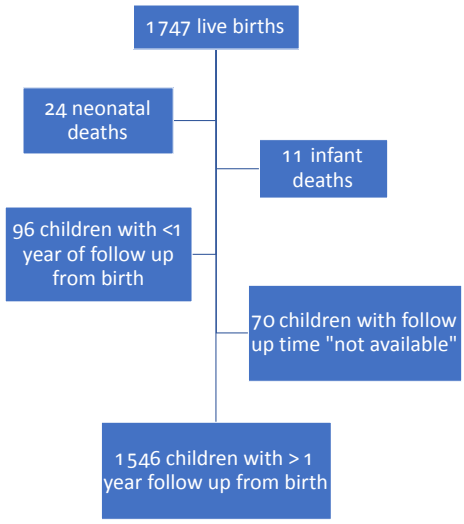

Table 1: Baseline characteristics and outcomes

	n=1546
Mother's race, n (%)	
Black/African American	88 (5.7)
White/Caucasian	1088 (70.3)
Asian	96 (6.2)
Other	131 (8.5)
Not available	143 (9.3)
Mother's age at conception, years, median (IQR)	30.2 (26.4-33.7)
Time between last KT to conception, years, median (IQR)	4.4 (2.3-7.8)
Gestational age, weeks, median (IQR)	36.9 (34.5-38)
Birth complications, n (%)	
Yes	668 (43.2)
No	873 (56.5)
Not available	5 (0.3)
Birth defects, n (%)	
Yes	97 (6.3)
No	1442 (93.3)
Not available	7 (0.4)
Birth weight, grams, median (IQR)	2,693 (2,126-3,090)
Child's health, n (%) *	
Health and developing well	1142 (73.8)
Asthma	50 (3.2)
Allergies	55 (3.5)
Diabetes	7 (0.4)
Hypertension	9 (0.6)
GI	
Gastroesophageal reflux disease (GERD	18 (1.2)
Other	9 (0.58)
Renal	
Alport syndrome	5 (0.32)
FSGS	4 (0.26)
PCKD	2 (0.13)
Anatomic (e.g. – hypoplasia)	12 (0.78)
Other	20 (1.3)
Neuro/psych	
Attention-deficit/hyperactivity disorder (ADHD)	61 (3.94)
Autism spectrum disorder	18 (1.2)
Anxiety/Depression	31 (2.0)
Developmental delay	7 (0.4)
Seizure disorder	11 (0.71)
Other	16 (1.03)

*Number/percentages will not add to 1546 children and 100%, as individuals can have more than 1 aliment

BOS4_10 PROFESSIONALS' PERSPECTIVES ON REPORTING OF TRAVEL FOR ORGAN TRANSPLANTATION: AN INTERNATIONAL CROSS SECTIONAL STUDY

Georgina Irish[*1;2], Riadh A. S. Fadhil[3;3], Eric Rondeau[4], Sanjay Nagral[5], Mohammad Ali Ahmadipour[6], P.Toby Coates[2], Dominique Martin[6]

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Background: International travel for organ transplantation (ITOT) may involve ethically legitimate activities as well as organ trafficking or "transplant tourism". Little information is available on the prevalence of ITOT, limiting efforts to investigate, monitor, and respond to trends. Longstanding calls to address this data gap include recommendations to establish an international registry for clinician case reporting. However, transplant professionals' willingness to be involved in reporting is unknown. This study aimed to assess the feasibility of an ITOT registry by exploring clinician attitudes towards reporting ITOT.

Methods: With the support of the Declaration of Istanbul Custodian Group, the Transplantation Society and the International Society of Nephrology, an online anonymous survey was conducted [Oct-Dec 2022]. The English language questionnaire items addressed: respondent demographics, recent experiences of cases involving ITOT, and reporting of ITOT cases to national or international registries (preferences, attitudes, and influential factors). Data were analysed using descriptive statistics.

Results: 335 transplant professionals from 73 countries (42% European) completed the survey. Of respondents with experience of ITOT patients, 210 (84%) had cared for people who had donated/received an organ transplant since 2017. Their most recent case experiences involved travel to/from 109 countries (31 European). 54% of respondents indicated they were likely/very likely to submit ITOT cases to an international registry (30.7% unsure; 15.5% unlikely/very unlikely), compared with 76.3% to a national registry (14.8% unsure; 9% unlikely/very unlikely). Several factors influencing willingness to report were identified, with privacy concerns and risk of harm paramount (Table 1); 53.1% preferred to report anonymously.

Conclusions: Collection of data regarding ITOT activities should be a concern for all countries. An international ITOT registry may complement national registries and support ethical practice in ITOT. Effective collection of ITOT data will depend on international collaboration and systems addressing ethical reporting concerns of transplant professionals.

Table 1: Transplant professionals' attitudes on ITOT registry reporting

Top 3 factors encouraging reporting of ITOT	**n, %**
Confidence that the data would be securely stored and protected	170, 69.4%
Confidence that data will be used for the benefit of patients	167, 68.2%
Ability to preserve patient anonymity	162, 66.1%
Top 3 factors discouraging reporting of ITOT	
Risk of data being used in ways that may cause harm to patients	164, 69.5%
Risk of the patient being identified	157, 66.5%
Risk of data being used in ways that may cause harm to you or professional colleagues or institutions	138, 58.5%

BRIEF ORALS

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BOS4_11 THE ORGANIZATION OF THE HUMAN ORGAN TRADE: A COMPARATIVE SCRIPT ANALYSIS BETWEEN LEGAL AND ILLEGAL KIDNEY TRANSPLANTS

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Background: It is unknown what the similarities and differences are between legal and illegal kidney transplants. The aim of our study is to explore the similarities and differences in activities, actors and locations between legal and illegal kidney transplants, utilizing crime script analysis.
Methods: Data was gathered pertaining to the Netcare –and Medicus case, in South Africa, Kosovo, United Kingdom and Israel. The collected materials consisted of law enforcement data and 36 interviews with 45 respondents, most of whom were involved in the investigation and prosecution of these cases. The data was analysed using qualitative content analysis.
Results: Our analysis reveals the extensive preparations and high degree of organization that are needed to execute illegal transplants. Offenders in the illegal transplant schemes utilized the same opportunity structures that facilitate legal transplants, such as transplant units, hospitals and blood banks. When compared to legal transplants, the studied illegal transplant scripts reveal a wider diversity in recruitment tactics and concealment strategies and a higher diversity in locations for the pre-operative work-up of donors and recipients.
Conclusions: Our analysis helps guide state -and non-state actors into how and where they can recognize, report and disrupt dubious transplant activity.

BOS4_12 IMPLEMENTING A VALUES-DRIVEN POLICY IN A COMPLEX SYSTEM: WHAT HAPPENED WHEN THE SOFT OPT-OUT SYSTEM OF ORGAN DONATION WAS IMPLEMENTED IN ENGLAND?

Leah Mc Laughlin[*1], **Jane Noyes**[1], **Paul Boadu**[2], **Mustafa Al-Haboubi**[2], **Stephen O Neill**[2], **Lorraine Williams**[2], **Jennifer Bostock**[2], **Nick Mays**[2]

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Background: In May 2020 England implemented a 'soft' opt-out system of consent to organ donation on the assumption that switching the default to one more closely aligned with the preferences of citizens would make organ donation easier.
Methods: A mixed-methods evaluation comprising: review of Parliamentary debates and feedback from legislators; surveys and interviews with healthcare professionals; analyses of representative public attitude surveys and public responses to media campaigns; interviews with family members approached about organ donation and the public; and analysis of donor audit data (e.g. consent rates), informed by input from a lay (public) perspective.
Results: Implementing a 'soft' opt-out system into a well-established and complex opt-in system has been challenging. Consent forms, procedures and audits have become more complicated. Professionals frequently have to move between scenarios with families where opt-out applies, and others where family consent (opt-in) is still required. Bereaved families have no idea when this is required and continue to believe they are the decision makers. There is an (increasing) mismatch between establishing one's wishes on the organ donor register and what the family are asked after death by staff. Support for organ donation continues to vary between subgroups of the population. The opt-out system appears to have had little impact so far on these differences. Nonetheless, implementation created a context for mis/disinformation to spread, especially among minority ethnic and faith groups. Disruptions from COVID-19 mean any impact of the law change on consent rates remain unclear.
Conclusions: COVID-19 has hampered the ability to identify the effectiveness of the law change. At the same time, the legacy of informed consent has made it difficult to adapt fully to the opt-out system. This has prevented the principle behind the Act that everybody is a potential donor being realised in practice. Rather than presuming that the opt-out system will work as intended, it is likely to be more effective to improve the organ donation system in other ways.

BOS4_13 ANALYSIS OF JUDICIAL LITIGATION CONCERNING ORGAN TRANSPLANTATION IN ONE OF THE LARGEST EUROPEAN UNIVERSITY HOSPITALS

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Background: Given both intrinsic complexity and proof of collective solidarity, it is commonly believed that solid organ transplantation (SOT) has remained relatively spared from increased judicialization of medical activity. Present study aims to assess judicial procedures after SOT in a large French university hospital.
Methods: All judicial litigations about SOT, occurring in the 29 SOT units of Assistance Publique-Hôpitaux de Paris, with judicial verdict from 2015-2022 were reviewed. Causes of complaints, verdicts and awards were analyzed.
Results: Within study period, 47 litigations about adults SOT were registered, representing 1.1% of total ligations. Within seven years, litigations increased from 0.71% to 1.34%. No pediatric SOT complaint was registered. SOTs concerned were as follows: 24 (51%) kidney transplantations, 16 (34%) liver transplantations, 4 (8%) cardiac transplantations and 3 (6%) pulmonary transplantations. Among kidney transplantations, 10 (42%) involved living donor kidney transplantations including 6 (60%) from the living donor. Causes of complaints were 30 (64%) early postoperative complications including 8 inadequate graft/recipient matching or error in the procedure, 5 (10%) iatrogenic complications requiring SOT and 3 (6%) delayed registration. Lack of information about the occurrence of delayed complications was alleged in 18 (38%). Recipient's mortality was 63% (n=26). Verdicts were in favor of the institution in 37 (78%) cases.
Conclusions: SOT is increasingly affected by judicialization of the medical society. Although no liability was held against the medical institution in nearly 80% of cases, this study is strongly in favor of an extension of both patients and family information using standardized documents regarding with precision all specific risk of SOT but also concerning grafts/donors medical and economical specific risks.

BRIEF ORALS

Looking through the glass – fresh perspectives on ethicolegal and psychosocial aspects of donation and transplantation

BOS4_14 NATIONAL HEALTH INSURANCE COVERAGE OF ORGAN PERFUSION MACHINES (PM) IMPROVES ACCESS TO TRANSPLANTATION

Helene Logerot[*1], **Selda Salman**[1], **Emilie Savoye**[1], **Carine Jasseron**[1], **Richard Dorent**[1], **François Kerbaul**[1], **Michel Tsimaratos**[1], **Corinne Antoine**[1]

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Background: At the level of the national health care system, the insurance cost of managing chronic kidney, liver and lung diseases is significantly in favour of transplantation. Perfusion of harvested organs significantly increases the number of quality grafts available. Although activity is increasing, the overall cost for the healthcare system is offset by the savings in the patients care pathway.
Methods: France is a government-managed health care system where organ transplantation is funded both by Diagnosis Related Groups-like system and by specific lump sum for transversal activities related to organ transplantation (OT). Several criteria have been gathered to reach right level of funding: (1) evidence of efficacy, quality and safety of PM, (2) perfusion indications endorsed by transplant societies of each discipline (3), organization model, (4), European conformity marked technology (5), costs studies. For each organ lump sum, specific costs studies were considering based on cost effectiveness analysis and simulation; integrating identified additional costs of expenditure items as human resources (additional operating time), purchase of PM, consumable, amortization, maintenance and storage.
Results: The French National Transplantation Organisation (ABM) has evaluated PM's additional costs. The Ministry of Health has validated the amounts. Thus, since 2012 for kidneys, 2019 for lungs and 2023 for liver perfusion, the specific lump sums are:

Organ perfusion	Lump sum (€)	Transplantation (2022 activity)
Kidneys (every 3 procedures, 2 kidneys/procedure)	9577	1312
Lungs (1 ex-vivo perfusion and rehabilitation)	34057	49
Liver (1 hypothermic oxygenated perfusion)	4840	90

In 2022, PM were used in 88.5% of kidney transplants with expanded criteria donors, 15% of lung transplants, and 7% of liver transplants. In addition, 1,451 receivers had improved access to transplants at an average cost of €2,894 per transplant. The final presentation will show comparative results over several years and the share of the PM in the overall funding of OT.
Conclusions: France is the first European country to have implemented incentives national funding for the use of PM. The aim is to ensure equity of access to optimal graft preservation for all patients and to improve extended criteria donors graft outcome without extra cost for the transplant centers. The evaluation of this policy confirms its medical and scientific relevance as evidenced by the increase in transplant activity.

Contemporary heart transplantation: scores, pumps, cells and much more

BOS5_1 IMAGING AND FUNCTIONAL EVALUATION OF THE EFFECT OF TRANSPLANTATION OF MESENCHYMAL STEM CELLS IN EXPERIMENTAL MODEL OF MYOCARDIAL INFARCTION

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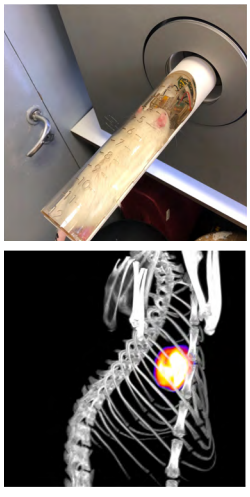
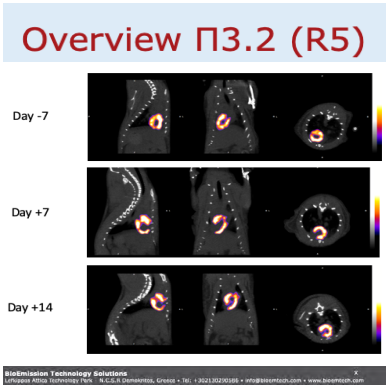
Background: Myocardial infarction remains worldwide with high mortality beside the extended researches for pharmaceutical therapies. Isolation of mesenchymal stem cells (ADSCs) from adipose tissue created a new spectrum of research. ADSCs are now known to be able to differentiate to myocardial cells and create cardiac tissue. In our protocol we use the genetic factors GATA-4 and nkx2,5 which are associated with the regeneration and differentiation of the myocardium respectively.
Methods: We used 34 adult Wistar rats (30 females – receivers and 4 males - donors) weighting 200-250gr. The female-receivers were randomly allocated in 3 groups (sham operated,control and experimental group). On Day -7 (7 days pre-operatively) we performed a SPECT–CT with injection of 99mTc-sestamibi to all female animals. On Day 0 (operation day) all groups underwent left thoracotomy and - besides sham operated - ligation of LAD for 45min with ECG monitoring confirming ischemia. *Control :* injection of N/S intramyocardially. *Sham:* no ligation. *Experimental :* injection of ADSCs intramyocardially without removal of ligation. On Day +7 and Day +14 (7 and 14 days post-operatively) the animals that survived underwent new SPECT-CT followed by euthanasia on Day +16 (16 days postoperatively) together with blood sampling and heart harvesting for histological and immunohistochemical evaluation.
Results: ADSCs were successfully engrafted into the myocardium and had beneficial effect on the ischemic myocardial area of the experimental groups with regeneration and increase of contractility especially in the 14th postoperative day compared with the control groups. Specifically imaging with SPECT-CT revealed significant absorption of 99Tc and viability of the myocardium on postoperative Day 14 in the experimental groups. The expression of GATA-4 and nkx2,5 was significantly upregulated compared with the control groups.
Conclusions: ADSCs are definitely the therapeutic approach of the future and GATA-4 as nkx2,5 are the genetic factors that are leading to an extended regeneration of the ischemic myocardium. The promising results in our protocol lead to further evaluate the clinical significance of ADSCs transplantation in cases of acute myocardial infarction.





BRIEF ORALS

Contemporary heart transplantation: scores, pumps, cells and much more

BOS5_2 TRANSPLANTING PATIENTS WITH AMYLOIDOTIC CARDIOMYOPATHY: A DREAM FOR FEW

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Background: Amyloidotic cardiomyopathy (AC) is a rare indication for heart transplantatic data about post-HT outcome. In this single center retrospective study, we re across different eras and etiologies.
Methods: We included all patients (pts) receiving HT for AC (1998-2022), collecting data about demography, clinical characteristics and hemodynamics (by right heart cath) before, one month and one year after HT. The endpoints were overall survival and freedom from cardiovascular death at 1, 5, 10 years (y); analysis was stratified by er as (availability of drugs for transthyretin, TTR, in 2018), and etiologies (TTR vs AL).
Results: Among 25 pts (19 TTR, 6 ALL 13 received HIT-liver transplantation, 7 HT, 4 HT- autologous stem cell transplantation (ASCT), one heart liver kidney transplant. Patients transplanted in the more recent era were less frequently affected by TTR (83% vs 50%) and had better survival at all time points (p<0.05). Pts with AIL vs TTR had lower protidemia at HT, and were transplanted more frequently in urgency (50% vs 5.6%, p<0.05) due to worse conditions (higher right and left filling pressures, lower cardiac index). lln 3/4 pts with ASCT, hematological disease relapsed after 10-14 months; chemotherapy was safelytolerated. Overall survival was 90.9±6.1%, 62.8%±10.5%, 36.2±10.8% at 1, 5, 10 yrespectively. Despite similar one year .survival, AL pts had a worse o utcome than TTR at Sy (26.7±22.6% vs 76.6±10.3%, p=0.06) and l0y (0% vs 36.5+12.5%) and died more frequently for CV causes at Sy (53.3+24.8% vs 85.5±9.5%, AIL vs TTR, p=0.03); sepsis was the leading cause of death in TTR pts. AL were more frequently on steroids at one year (100% vs 59%, p<0.05) due to more frequent rejection episodes (50% vs 5.9%, p=0.02); no pts with heart-liver transplant had rejection. Pre-HT low protidemia was the only predictor of death at Sy in TTIR pts.
Conclusions: Outcomes of pts with AC after HT are worse than in the other etiologies. TTR has become frequent indication for HT, with good outcomes and low rejection risk in heart-liver trans allowing steroid reduction. AL pts are commonly transplanted in urgency, with a frequent re of hematologic disease even in HT-ASCT and a poorer prognosis. Transplant benefit needs carefully evaluated in AL pts.

BOS5_3 THE FIRST IMPLANT OF A BIOARTIFICIAL TOTAL ARTIFICIAL HEART IMPLANTATION IN A PATIENT WITH SEVERE PULMONARY HYPERTENSION

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Background: The improvement of the outcomes of medical therapy using the 4 pillars of heart failure medications and device therapy has shifted the indication to mechanical circulatory support in a later phase of the clinical trajectory in which the burden of right ventricular failure is higher. Since the onset of biventricular failure is often followed by acute cardiogenic shock, heart transplantation is rarely the timely answer to the patient decompensation and LVAD implantation is frequently the bedside available solution when the right ventricular is already ongoing.
Methods: The Aeson® Total Artificial Heart (TAH) is intended to provide physiologic heart replacement therapy for patients suffering from end-stage biventricular heart failure with a minimal antithrombotic medication based on low-molecular-weight heparin and aspirin. Another unique feature of the Aeson® TAH is that it autoregulates pump outputs in response to changes in preload detected by pressure sensors located inside the device ventricles. This feature potentially improves the functional capacity of the recipients allowing to perform more significant exercise respect to the reduced functional capacity of LVAD recipients. Blood flow variations are achieved by alterations to the beat rate and systolic time intervals. Early clinical experience suggests that a successful bridging to heart transplantation with the Aeson® TAH is feasible.
Results: We implanted the first Aeson® Carmat TAH in a patient with biventricular failure with a severe Pulmonary Hypertension (PH), the implantation was made as bridge to transplantation also if the preoperative investigations showed only a partial reversibility of PH due to the complexity and the risks associated with alternative surgical solutions. We report this case report to focus on the usefulness of the insightful data addressing the reversibility of pulmonary hypertension as a tool to catch the right timing to bring the patient to transplant if implanting the device as a bridge to candidacy.
Conclusions: Our first experience with the Aeson TAH was positive. The device pressure sensor's information may be helpful to monitor the evolution of patients with pulmonary hypertension and help assess the proper timing of transplant listing especially in a bridge to candidacy policy.

BOS5_4 MULTIDRUG-RESISTANT ORGANISMS IN CRITICAL CARE AND 30-DAY OUTCOMES OF HEART TRANSPLANT PATIENTS

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Background: Nosocomial infections are known to predominate during the first month after solid organ transplantation. Moreover, transplant recipients invariably share recognized risk factors for acquisition of multidrug-resistant organisms (MDRO), namely previous hospital admissions and increased exposure to antimicrobials and invasive procedures. MDRO carriage increases the complexity of patient management in the Intensive Care Unit (ICU), and is causally associated with infections by MDROs, including septicemia. We investigated the impact of MDRO acquisition on 30-day patient outcomes post heart transplantation (HT) in a heart and lung transplantation center in Athens, Greece.
Methods: Patients admitted in the ICU post HT between 1/1/2019 and 31/12/2022 (4 years) were retrospectively analyzed. Data was collected regarding MDROs commonly encountered in critical care, for which a national mandatory reporting requirement is in place. These include carbapenem-resistant organisms (CROs), specifically *Acinetobacter*, *Klebsiella* and *Pseudomonas*, as well as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin- resistant *Enterococcus* (VRE) strains. Outcomes of interest were continued ICU stay, as well as mortality at 28-days post transplantation.
Results: MDROs were isolated in 6 out of 48 HT recipients (12.5%), of whom 2 (33.3%) were already MDRO carriers on admission to the ICU. The time interval from ICU admission to first MDRO acquisition ranged from 3 to 18 days. *Acinetobacter* and *Klebsiella* were the most prevalent MDROs, followed by *Pseudomonas*, while *MRSA* and *VRE* lagged behind. Septicemia episodes occurred in 2 out of 6 HT patients with MDROs (33.6%). Mortality at 28 days was 0/6 HT patients with MRDOs, while 5/42 (11.9%) in HT patients without MDROs. Extended ICU stay (post 30 days) was 3/6 (50%) for HT with MDROs, versus 5/32 (15.6%) in the absence of MDROs.
Conclusions: MDROs are mainly ICU acquired rather than already present at transplantation. CROs are the most prevalent MDROs. MDRO acquisition is strongly related to septicemia episodes, and, while it does not seem to be related to early post transplantation mortality, it seems to entail a prolonged ICU stay.

BOS5_5 OUTCOME OF HEART TRANSPLANT BRIDGED WITH VENO-ARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION: A SINGLE CENTER EXPERIENCE

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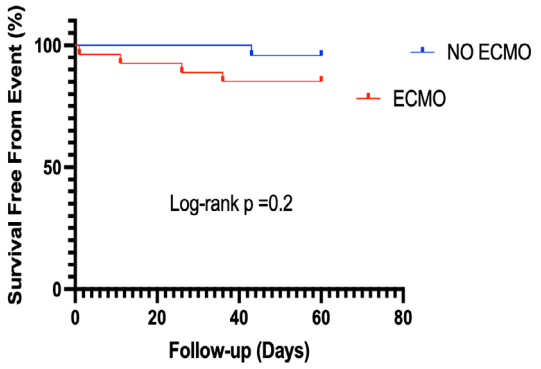
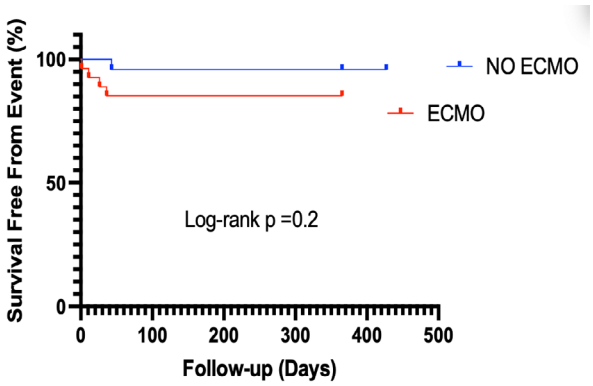
Background: despite advances in medical therapy, heart transplantation (HT) remains the gold standard for severe heart failure (HF). Patients admitted for acute decompensated HF develop cardiogenic shock (CS) in about 1% of cases, requiring prompt intervention to reverse hypoperfusion and end-organ damage. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) as bridge to transplant gives the highest priority to the patient, reducing waiting list time. Reported data about post-transplant outcome after VA-ECMO bridging is controversial.
Methods: we evaluated the follow-up of both patients bridged to transplant with VA-ECMO and patients transplanted electively between 2014 and 2019 at our institution. Of 181 patients who underwent heart transplantation in that period,

we compared the outcome of 27 (15%) transplanted on VA-ECMO support to the outcome of 24 (13%, matched for sex, age and anthropometric characteristics) transplanted without support in the same period.
Results: VA-ECMO bridged patients were less likely to be women, had more frequently previous cardiac surgery and had higher bilirubin levels. There were no significant differences in age, creatinine levels, mean pulmonary arterial pressure (mPAP) and donor characteristics between the two groups. We found a statistically significant difference in VA-ECMO patients regarding fewer days on waiting list (Table). The Kaplan-Mayer curves showed no statistically significant differences in event-free survival (Figure).
Conclusions: data from our study suggests that, despite being on worse clinical condition with more hepatic damage at transplant, there are no significant differences in early and medium-term survival between patients on VA-ECMO support and the other group. The shorter time on waiting list in VA-ECMO population may have a protective role in these patients preventing further organ damage and complication related to the mechanical support itself. Larger case series and more in-depth statistical analyses should be carried out in future studies to confirm this result.





	ECMO	No-ECMO	p value
Age at HT, *median (Q1-Q3)*	48 (32 - 56)	50 (36- 50)	0.4
Female, *n (%)*	8 (29.6)	16 (66.6)	**0.01**
BMI, *median (Q1-Q3)*	22 (21 - 25)	22 (21 -25)	0.67
Aetiology			
***Ischemic** n (%)*	4	6	0.4
***Non-ischemic** n (%)*	23	18	0.5
***Previous Cardiac-Surgery** n (%)*	9 (33)	0 (0)	**0.002**
Creatinine, *median (Q1-Q3)*	1 (0.69 – 1.69)	0,9 (0.75-1.19)	0.5
Bilirubin, *median (Q1-Q3)*	1,3 (0.79 – 2.4)	0.6 (0.42 – 0.96)	**0.001**
mPAP, *median (Q1-Q3)*	22.5 (15.5 – 26.7)	21 (15.2 – 30)	0.77
CI, *median (Q1-Q3)*	2.2 (1.6 – 2.5)	1,7 (1.5 -1.9)	**0.03**
Days on waiting list, *median (Q1-Q3)*	8 (3 – 41)	151 (49 - 309)	**< 0.0001**
Days on ECMO, *median (Q1-Q3)*	4 (8 - 10)	-	-
Age of donor, *median (Q1-Q3)*	47(36.5 – 51.5)	42.5 (23.5 – 54.7)	0.6
BMI of donor, *median (Q1-Q3)*	24.7 (22.9- 27.4)	23.9 (21 – 27.3)	0.7
Time of ischaemia, *min, median (Q1 – Q3)*	195 (163 – 231)	176.5 (157.8 – 209.5)	0.22

Legend: HT = Heart Transplantation; CI = Cardiac Index; BMI = Body Mass Index;

BOS5_6 HEART TRANSPLANT AFTER VENO-ARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT: MID-TO LONG TERM OUTCOMES FROM A THREE-CENTERS REGISTRY

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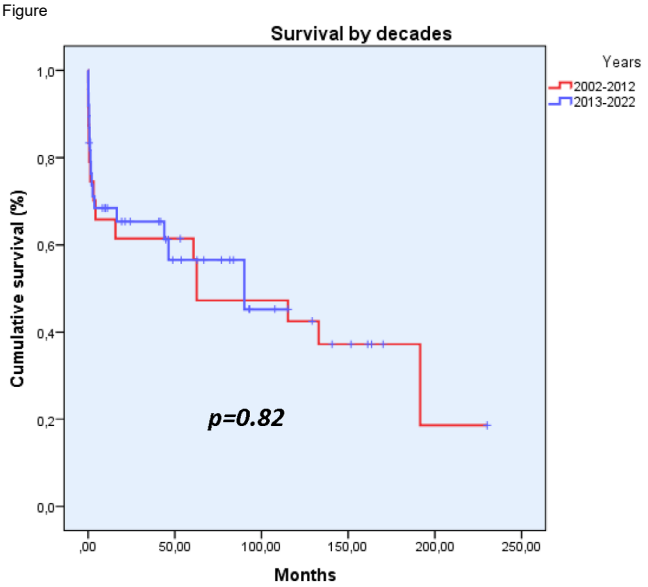
Background: The use of Veno-Arterial ExtraCorporeal Membrane Oxygenation (VA-ECMO) as Bridge-to-Transplant (BTT), although increasing, is controversial. In the past decade, early studies reported VA-ECMO support as an independent risk factor for mortality after heart transplant (HT). However, recently investigations showed improving results at short-term follow-up and to date, long term survival has been poorly investigated. Therefore, it is the aim of this study to analyse short and long term outcomes of VA-ECMO BTT, also stratifying by decades.
Methods: From 2002 to 2022, data of all consecutive VA-ECMO BTT patients were retrospectively collected at three Italian Heart Transplant Centres. Short-to-long term outcomes were explored. Multivariate analysis was performed to assess preoperative independent factors for hospital mortality. Kaplan-Meier curve was estimated for long-term survival after HT. A subanalysis by decades (2002-2012 vs 2013-2022) was also performed.
Results: A total of 63 consecutive patients undergoing HT were bridged by VA-ECMO over 20 years. Most patients were males (74.6%). Mean age was 45.6±15.7 years old. Mean time on VA-ECMO until HT was 10.2±8.5 days. Primary graft dysfunction was 20.6%, and 14.3% of patients needed post-operative VA-ECMO support. Acute kidney injury requiring dialysis and post-operative infections occurred in 35% and 24%, respectively. Bleeding complications were 27%. Sepsis and multi-organ failure resulted as the main causes of death (77%). Hospital mortality was 25.4%. Recipient age at transplant (OR 1.09 [95%CI:1.017-1.17]; p=.034), preoperative systolic pulmonary arterial pressure >50 mmHg (OR 6.3 [1.23- 32.84]; p=.027), and platelets number (OR 0.98 [0.96-0.99]; p=.034) independently predicted hospital mortality. Cumulative survival was 67.4%, 56.7% and 48.2% at 1, 5 and 8 years of follow-up. Stratification by decades showed no differences in terms of post-transplant survival (2002-2012: 65.8% and 56.7% vs 2013-2022: 68.4% and 56.5% at 1 and 5 years, respectively; p=0.8) (Figure).
Conclusions: HT after VA-ECMO still maintains suboptimal results. Better stratification tools according to preoperative risk factors can implement these results. Outcomes after HT post- VA-ECMO support don't seem to be improved during the last 20 years.

Figure



BRIEF ORALS

Contemporary heart transplantation: scores, pumps, cells and much more

BOS5_7 HEART TRANSPLANT SURVIVAL OUTCOMES: ROLE OF DONOR-TRANSMITTED ATHEROSCLEROSIS

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Background: An increasing number of potential heart recipients with UNOS1 status forces to find solutions for the shortage of donor organs by expanding the criteria for selecting optimal donors. Coronary assessment of a cardiac graft is inaccessible in the pre-transplant period; therefore there exists a risk of transmission of the coronary atherosclerotic from a donor to a recipient.
Methods: We retrospectively reviewed the medical records of 1155 recipients who underwent Heart transplantation in the Shumakov Center from 2009 to 2018; 985 were men, and 170 women, aged 10 to 74 years. All patients underwent coronary angiography in the early postoperative period and were divided into 3 groups: I - recipients with hemodynamically significant lesions of the coronary arteries (CA), II – pts. with signs of CA atheromatosis (rough contours or stenoses up to 50%), and III – pts. without signs of CA. The analysis included the following criteria: sex, age, cause of donor's brain death, UNOS status.
Results: In 332 pts. (groups I and II) signs of donor-transmitted atherosclerosis were found. In 130 cases the lesion was assessed as hemodynamically significant and percutaneous coronary intervention was performed. In 823 cases there were no signs of atherosclerosis. In recipients with UNOS status 1A (n=355) and 1B (n=436), transmission of atherosclerosis was detected more often than in recipients with UNOS 2 (60% and 40%, respectively). The age of donors in groups I and II was significantly higher than in groups III (p = 0.0001). No association was found between the frequency of donor-transmitted atherosclerosis and the gender of the donor. Acute cerebrovascular accident as a cause of donor's brain death in groups was: 90% in I, 84% in II, and 80% in III. Five-year survival in I group was 75.6%, II - 72.5%, and III - 74.6%, no significant difference between groups (I/II p=0,849, I/III p=0,389, II/III p=0,421).
Conclusions: Donor-transmitted atherosclerosis, including hemodynamically significant lesions of the CA, is associated with the age of the donor. Early endovascular correction of hemodynamically significant lesions neutralizes the potentially negative impact of coronary stenosis on the survival of heart transplant recipients.

BOS5_8 POST-OPERATIVE INFECTIONS AND KIDNEY DYSFUNCTION IN HEART TRANSPLANT RECIPIENTS: A DEADLY BOND

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Background: Post-operative infections (POI) are a frequent complication after heart transplantation (HT). Limited data exist on their incidence, risk factors and influence on subsequent outcome. In this study we aimed to analyze epidemiology, risk factors and clinical impact of POI in a cohort of consecutive HT recipients receiving transplant between 2016 and 2021.
Methods: Clinical charts of adult recipients were reviewed. For study purposes we considered as POI events cases with clinical/laboratory signs of infection with identified microbial isolate or imaging diagnostic for infection, occurring within the first 6 weeks after surgery. Recipients who died in the first month after HT were excluded. Study endpoint was all-cause mortality at three years after transplant.
Results: Study cohort included 116 patients (27 (23%) females, age 53±10y), of these 27 (23,3%) had diabetes, 12 (10,3%) COPD and 28 (24%) had GFR< 45 ml/min/1.75m2 before HT (>stage 3B CKD). 18 (15%) patients experienced at least one POI at 23±19 d after surgery. Three patients had multiple microbial isolates. K. Pneumoniae was the most frequent isolated pathogen (22%), followed by E. Coli (16,7%) and Candida spp (16,7%). POI accounted for a lower 3 year survival (59±12 vs 90±3%; P<0.01), and for a 6.5 times (2.3-17.5) increased risk of death (P<0.01). Patients with pre-HT CKD and COPD were more likely to develop POI, and need for post-operative continuous veno-venous hemofiltration was associated with high odds ratio of POI (15.9 (4.7-52.6); P<0.01). Patients with POI surviving to hospital discharge showed a significant drop from pre-HT GFR (58±24 to 42±16ml/min/1.75m2; P=0.03), while GFR remained stable in those without POI. Recipient age, active pre-transplant infection, urgency status and mechanical circulatory support were not associated with POI.
Conclusions: POI occur in a meaningful proportion of HT recipients and significantly impact mid-term outcomes. Renal function is a crucial factor in identifying patients at risk for POI, and renal replacement therapy exposes these patients to an extremely high risk for POI and death. POI may favor loss of renal function in surviving patients. Specific and customized interventions are needed to protect peri-operative renal function and prevent POI in this vulnerable population.

BOS5_9 VALIDATION OF THE CLINICAL UTILITY OF MICRORNA AS NON-INVASIVE BIOMARKERS OF CARDIAC REJECTION: A PROSPECTIVE LONGITUDINAL MULTICENTER STUDY

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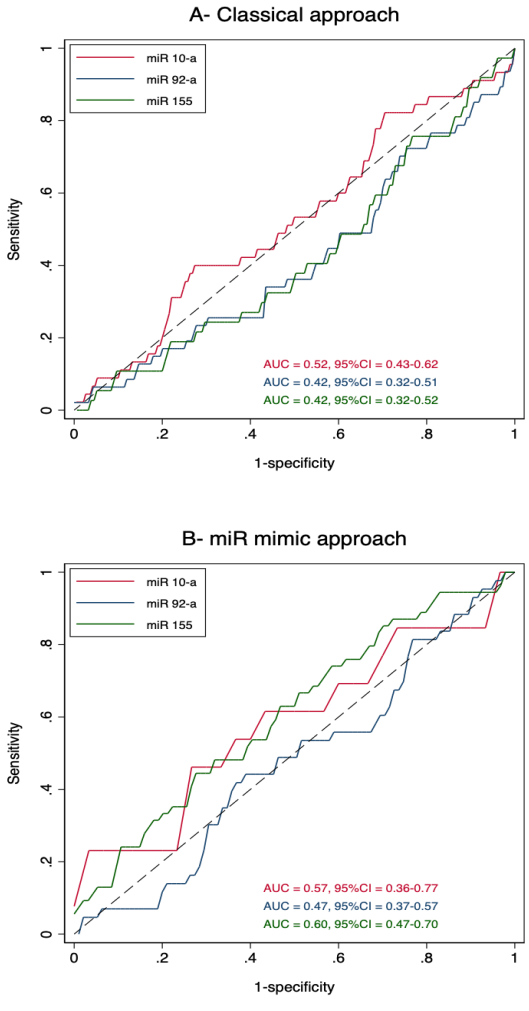
Background: Circulating microRNAs (miRNA) have been identified as non-invasive biomarkers of cardiac allograft rejection in retrospective studies but their clinical utility to detect rejection has not yet been evaluated in large prospective and unselected cohorts of patients.
Methods: We designed a longitudinal prospective study (NCT02672683) including 11 heart transplant referral centers. Patients were included from August 2016 to March 2018. Either de-novo HTx recipients or patients transplanted ≥ 1 year were included at the time of an endomyocardial biopsy (EMB, protocol or for-cause). The primary endpoint was to validate the association between the peripheral expression of 3 previously identified circulating miRNA (miR-10a, miR-92a, and miR-155) with allograft rejection on concomitant EMB. Relative miRNA measurements were performed by normalizing miRNA PCR copy numbers by an endogenous control. A sensitivity analysis was performed by applying an absolute quantification method of microRNA using standard dilution curves of microRNA mimics. The association between miRNA and rejection was tested using mixed effect logistic regression.
Results: A total of 461 patients were included representing 831 EMB. Overall, 79 rejection episodes occured, including 25 ACR ≥ 2 R and/or 56 AMR ≥ pAMR 1. In a first pre-specified interim analysis based on 258 EMB from 184 patients including 49 rejection episodes (62% of overall rejections, ACR ≥ 2R = 17, pAMR1(H+) = 14, pAMR1(I+) = 9, pAMR2 = 11), no association between any of circulating miRNA and rejection was found (Figure 1-A). A sensitivity analysis performed with the absolute quantification method on 191 EMB from 134 patients including 94% of overall rejections confirmed those results (Figure 1-B). The analysis of remaining sera was stopped for futility.
Conclusions: In this prospective longitudinal multicenter study of unselected patients, the clinical utility of 3 circulating miRNA as non-invasive biomarkers of cardiac rejection was not confirmed.

Figure 1



BOS5_10 THE DIAGNOSTIC VALUE OF MIR-339 FOR CORONARY STENOSIS OF CARDIAC ALLOGRAFT

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Background: Cardiac allograft vasculopathy is one of the main factors negatively affecting the long-term results after heart transplantation (HTx), which is characterized by the coronary arteries stenosis and causes the graft loss. MicroRNAs (miRs) are a new class of regulatory molecules that affect various cellular functions and have potential value for diagnostic of post-transplant complications. MiR-339 was shown as a promising biomarker of chronic graft rejection. This can potentially reduce the frequency of invasive diagnostic interventions or partially replace them, which will expand the possibilities of a personalized approach to the early diagnosis of post-transplant complications and postoperative management. The aim is to determine the diagnostic value of miR-339 levels for the coronary arteries stenosis of cardiac allograft.
Methods: The study enrolled 53 heart transplant recipients, aged 16 to 70 (48.6 ± 10.9) years. Expression levels of miR-339 were measured in blood plasma by PCR and expressed in relative units. The coronary artery stenosis of cardiac allograft was verified by the results of coronary angiography.
Results: 16 heart recipients (30%) had the stenotic lesion of the coronary arteries of the transplanted heart: 6 of them had the progression of initial stenotic lesion of the coronary arteries of donor heart, and 10 – the coronary arteries stenosis developed after HTx (62.5% of cases). The levels of miR-339 in heart transplant recipients with stenotic coronary arteries are significantly lower than in recipients without ones (p=0.03). When the miR-339 expression level is below -7.9 fold change the relative risk of coronary arteries stenosis is RR=6.0±0.91 [95% CI 1.003–35.909], p=0.04. The sensitivity and specificity were sufficient for use in clinical practice: Se=85.7% and Sp=100.0%. We found significantly poorer Kaplan-Meier survival (log-rank p=0.03) in heart transplant recipients who had miR-339 expression above threshold level (fig.).
Conclusions: Decreasing miR-339 expression level after HTx is associated with the coronary arteries stenosis in heart graft and lower survival rate, which allows us to evaluate miR-339 as a potential biomarker of chronic graft rejection.

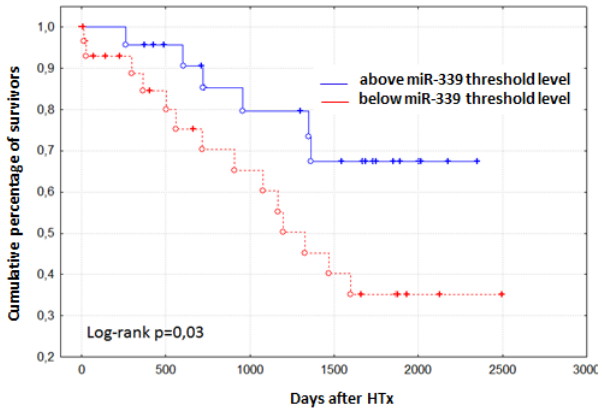

Fig. Kaplan-Meier survival curves of heart recipients with miR-339 above and below threshold level

BOS5_11 THE IMPACT OF EXERCISE TRAININGS ON PHYSICAL CAPACITY AND QUALITY OF LIFE AFTER HEART TRANSPLANTATION

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Objective: to estimate the dynamic of physical capacity (PC) and quality of life depending of exercise trainings in recipients after heart transplantation (HTx).
Methods: From 2010 to 2022 HTx was performed in 205 patients (46±14 year-old; 149 – male) who completed cardiopulmonary exercise test before, 3 months, 1 year and 5 years after HTx. Dynamics of VO_{2peak} and V_E/VCO_2slope were measured. Physical activity was defined by questionnaire – IPAQ. Exercise trainings were prescribed to all recipients but less than one third of patients followed recommendations and were physically active (3 months – n=67; 1 year – n=66, 5 years – n=36). We estimated the dynamic of physical (PCS) and mental component summary (MCS) by SF-36 questionnaire.
Results: PC had significantly increased in 3 months (VO_{2peak} – 15.4±3.4 ml/min/kg, p<0.001; VO_{2pred} – 52.5±10.5, p<0.001; V_E/VCO_2slope – 38.5±6.9, p<0.001) and then continued to improve (1 year, p<0.001; 5 years, p<0.05). After HTx PCS increased (3 months – 41.8±8.5, p<0.001; 1 year – 46.9±9.3, p<0.001; 5 years – 48.1±7.6, p=0.414). In 3 months MCS improved (48.0±8.3, p<0.001) but then started to slowly decrease (p<0.001). One year after HTx 55% of patients reached normal values, 38 (73%) of them were physically active. Physically active recipients achieved better results of VO_{2peak} (3 months, p=0.019; 1 year, p=0.006) and PCS: 1 year (p=0.086) and 5 years after HTx (p=0.030). The levels of PCS correlated with VO_{2peak} (3 months - r=0.417, p<0.001; 1 year – r=0.414, p<0.001; 5 years – r=0.458, p=0.002) and V_E/VCO_2slope (3 months – r=-0.302, p=0.007; 1 year – r=-0.461, p<0.001; 5 years – r=-0.324, p=0.037). In 5 years there were correlations between VO_{2peak} and resting heart rate (p<0.001) and active heart rate (p<0.001) but no difference depending on post-transplant TTE results and the number of allograft rejections (p>0.05).
Conclusions: After HTx there was an improvement of PC and PCS that continued to increase in long-term but only half of transplant recipients (55%) reached normal values of VO_{2peak} and most of them were physically active (73%). Physically active patients also achieved higher PCS but no matter of VO_{2peak} raise their MCS started to slowly decrease long-term after HTx. There was no difference depending on post-transplant TTE results and the number of allograft rejections after HTx.

BOS5_12 MICRORNA-101 PLASMA LEVEL: DIAGNOSTIC AND PROGNOSTIC VALUE FOR CARDIAC GRAFT ACUTE CELLULAR REJECTION

Olga Gichkun*[1], Sergey Gautier[1], Olga Shevchenko[1], Sofya Sharapchenko[1], Dmitriy Velikiy[1], Natalya Mozheiko[1], Alex Shevchenko[1]

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Background: Acute cellular rejection (ACR) causes graft dysfunction after heart transplantation (HTx). Endomyocardial biopsy is «gold» standard for its in vivo diagnosis. The search for new minimally invasive laboratory technologies for its early detection is extremely relevant. MiRNAs (miR) are a new class of regulatory molecules that have potential value for diagnostic and prediction of post-transplant complications. The aim is to determine the value of miR-101 plasma level for detection the patients with the risk of ACR after HTx.
Methods: The study enrolled 79 heart transplant recipients, aged 16 to 70 years. The miR-101 expression level was measured by PCR in blood plasma before and after the HTx and presented in relative units. The plasma levels of ST2 (proteomic biomarker of cardiac graft acute rejection and cumulative cardiovascular events) was measured by ELISA. The diagnostic and prognostic value of miR-101 was evaluated by the receiver operating characteristic analysis.
Results: According to the ISHLT classifications, 36 recipients with ACR (R1G – R3G degree) after HTx were identified. The comparison group consisted of 43 recipients without rejection. MiR-101 level was significantly lower in heart transplant recipients with ACR than in heart recipients without it (p=0.01). When miR-101 level below –8.36 relative units the relative risk is RR=1.92±0.16 [95% CI 1.39 – 2.63], p=0.0001 with Se=39.5% and Sp=96.0%. The risk of ACR with ST2 level above 36.84 ng/ml was RR=2.56±0.26 [95% CI 1.53 – 4.26], p=0.0003.The diagnostic characteristics of miR-101 and ST2 combination

were analyzed. The Se and Sp of the duplex test have increased to 69.2% and 100% respectively, RR=4.00±0.43 [95% CI 1.71 – 9.35], p=0.001. Moreover, miR-101 pre-transplant level in heart recipients with ACR was significantly lower compared to recipients without rejection (p=0.02). The prognostic relative risk of ACR in recipients with miR-101 pre-transplant value below –9.73 relative units was RR=3.00±0.47 [95% CI 1.19 - 7.56], Se=62.5%; Sp=100% (p=0.02).
Conclusions: The measurement of miR-101 plasma level before and after HTx can be helpful for identifying the recipients with the risk of ACR, and optimize the appointment of biopsy and therapy correction. The combination with ST2 improves the diagnostic characteristics of the test.

BOS5_13 DEVELOPMENT AND VALIDATION OF SPECIFIC POST-TRANSPLANT RISK SCORES ACCORDING TO THE TRANSPLANT ERA: A UNOS COHORT ANALYSIS

Guillaume Coutance[*1], **Mickael Lescroart[2], Evan Kransdorf[3], Jignesh Patel[3], Alexandre Loupy[1]**
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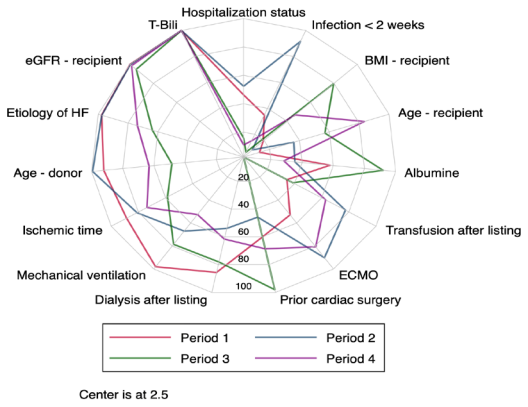
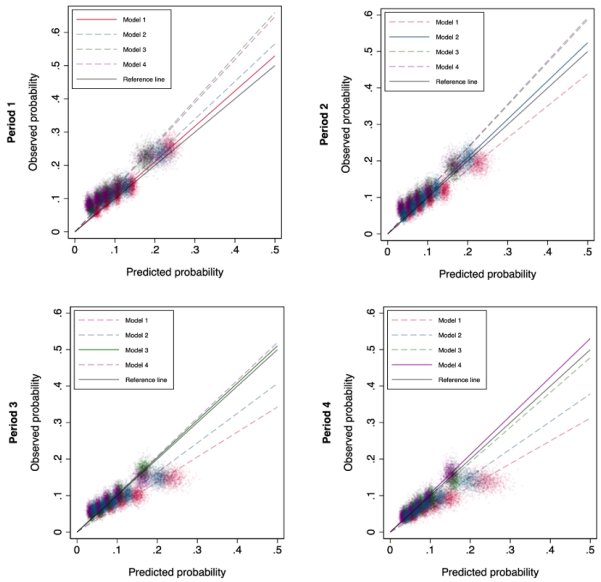
Background: The clinical use of post-transplant risk scores is limited by their poor statistical performance. Neglecting the dynamic evolution of demographics and risk factors over time may be a key issue. We hypothesized that developing specific prognostic models for each transplant era may improve risk stratification.
Methods: We analyzed the UNOS database including first, non-combined heart transplantations with a common allocation scheme (2003-2018). The endpoint was death or retransplantation during the first year post-transplant. We analyzed the evolution of post-transplant outcomes, demographics, and odds ratios of major predictive variables over time. Then, we build (logistic regression, derivation cohort 2/3) and compared (validation cohort 1/3) the statistical performance (discrimination, calibration, reclassification indices) of era-specific models and non-era-specific models (2001-2005, 2006-2010, 2011-2015, 2016-2018). In a sensitivity analysis, we randomly generated 1,000 bootstrap samples to analyze the variability of specific predictive models and compare era and non-era-specific models.
Results: A total of 34,747 patients were included; 3,674 patients (10.6%) met the composite endpoint. We observed a significant improvement in post-transplant outcomes (p < 0.001) and an important evolution in baseline characteristics over time. We found a significant interaction between time and the effect of the following variables: bilirubin, recipient age and prior cardiac surgery (p<0.01). Era-specific models differed from each other, both in terms of variables and odds ratios (Figure 1A). Era-specific models outperformed the statistical performance of non-era-specific models in a majority of samples, both in terms of discrimination, calibration (Figure 1B) and reclassification indices.
Conclusions: We found important evolution in post-transplant outcomes, baseline characteristics and predictive models over time. Era-specific models outperformed the statistical performance of non-era-specific models in a majority of samples. This finding suggests the need for a regular update of post-transplant predictive models to account for the evolving demography of candidates and medical practices.

Figure 1
A



B



BOS5_14 GRAFT REMODELING AFTER THORACIC TRANSPLANTATION: MIR-339 AND GALECTIN-3 IN THE DIAGNOSIS OF STRUCTURAL CHANGES

Olga Gichkun[*1;2], **Sergey Gautier[1;2], Olga Shevchenko[1;2], Olga Tsiroulnikova[1;2], Sofya Sharapchenko[1;1], Dmitriy Velikiy[1], Ivan Pashkov[1], Maksat Bekov[1], Natalya Mozheiko[1], Alex Shevchenko[1;2;3]**
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Background: Graft remodeling after heart (HTx) and lung (LTx) transplantation, caused by ACR, AMR and fibrosis leads to its dysfunction. Timely and minimally invasive diagnostic methods for graft structural changes detection are required. MicroRNAs (miRs) are small non-coding regulatory molecules; miR-339 inhibits proliferation of pulmonary artery smooth muscle cell by targeting fibroblast growth factor signaling. Galectin-3 (gal-3) is known as a proteomic biomarker of the inflammatory processes, immune response, and fibrosis. The aim is to evaluate the miR-339 and gal-3 plasma levels in patients with graft remodeling – myocardial fibrosis after HTx and airway obstruction after LTx.
Methods: The study enrolled 83 patients after HTx, aged 16 to 70 years, and 57 patients after LTx, aged 10 to 74 years. MiR-339 plasma levels were measured by PCR (Qiagen, USA) and are expressed in relative units. Gal-3 levels were determined by ELISA (Bender MedSystems GmbH, Austria). The diagnostic value of biomarkers was evaluated by the ROC analysis.
Results: According to the ISHLT classifications, 48 recipients with myocardial fibrosis, 36 – with ACR, and 2 – with AMR after HTx were detected. MiR-339 and gal-3 levels were significantly higher in heart recipients with fibrosis than without it (p=0.018, p=0.043, resp.). During follow-up 12 lung recipients with non-infectious airway obstruction and 16 – with infections, and 2 – with ACR after LTx were identified. MiR-339 and gal-3 levels in lung recipients with airway obstruction were significantly higher compared to recipients without it (p=0.036 and p=0.014, resp.). MiR-339 and gal-3 threshold levels and diagnostic characteristics for myocardial fibrosis and airway obstruction detection were determined.
Conclusions: MiR-339 and gal-3 have been shown to be promising profibrotic biomarkers whose increasing in duplex tests identifies recipients with graft remodeling after HTx and LTx.

Diagnostic characteristics of miR-339 and gal-3 for graft remodeling

Biomarker	Myocardial fibrosis after HTx				Airway obstruction after LTx			
	RR	95% CI	Se	Sp	RR	95% CI	Se	Sp
miR-339	1.31	[1.02–1.70]	36.2%	87.5%	2.63	[1.14–6.02]	60.0%	75.9%
gal-3	1.46	[1.07–1.98]	60.9%	78.6%	3.62	[1.16–11.24]	72.7%	72.7%
miR-339 + gal-3	2.00	[1.08–3.72]	54.5%	100.0%	7.14	[1.05–48.60]	83.3%	81.8%

BRIEF ORALS

Treatable traits lead the way towards better outcomes in lung transplantation

BOS6_3 INCREASED TOTAL CELL-FREE DNA EARLY AFTER LUNG TRANSPLANTATION IS ASSOCIATED WITH BASELINE LUNG ALLOGRAFT DYSFUNCTION

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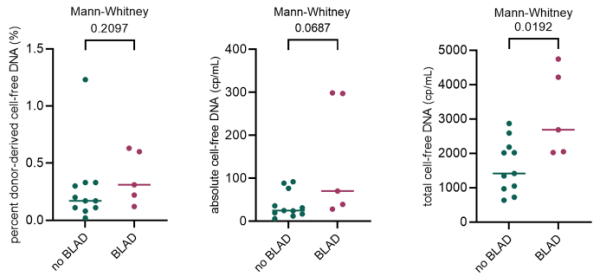
Background: Baseline lung allograft dysfunction (BLAD) is the inability to achieve the expected peak lung function within the first year after lung transplantation (LuTx). The underlying cause of BLAD is not yet fully understood, but early graft alteration has been identified as a risk factor. We hypothesized that early levels of absolute and percent plasma donor derived cell-free DNA (ddcfDNA and %ddcfDNA, respectively), which are biomarkers of graft damage, as well as total cell-free DNA (cfDNA) levels, may have predictive value for the incidence of BLAD.
Methods: A total of 16 patients who underwent bilateral LuTx between May 2021 and March 2022 (women 50%), followed-up in a single center were included, with a median age at the time of LuTx of 50.2 years (IQR 37.8 - 63.8). Blood samples were collected monthly from 3 up to 6 months post-LuTx. Samples obtained during rejection or infection were excluded. %ddcfDNA, ddcfDNA (cp/mL) and cfDNA (cp/mL) levels were obtained by the Prospera test. BLAD was defined as the inability to achieve forced expiratory volume in 1 second and forced vital capacity of 80% predicted on two consecutive measurements within the first year post LuTx. Analyses were performed by Mann-Whitney test.
Results: 46 samples were analyzed (median 2.9 per patient). 5 of 16 patients had BLAD (31.3%). Median %ddcfDNA value for the non-BLAD group was 0.17% (IQR 0.11 - 0.31) and for the BLAD group 0.31% (IQR 0.22 - 0.60), p=0.21. In absolute values, median ddcfDNA for the non-BLAD group was 24.92 cp/mL (IQR 18.17 - 56.18) and for the BLAD group 70.29 cp/mL (IQR 39.17 - 297.26), p=0.069. Median cfDNA for the non-BLAD group was 1413.46 cp/mL (IQR 1009.63 - 2101.32) and 2685.63 cp/mL (IQR 2046.48 - 4215.17) for the BLAD group, p=0.019. Figure 1.
Conclusions: Increased total cfDNA levels obtained between 3rd-6th month after LuTx were associated with a higher risk of BLAD. Due to the fact that 90% of cfDNA originates in white blood cells, we hypothesize that a proinflammatory state might be a risk factor for BLAD incidence but further investigation is required. Although a trend for elevated ddcfDNA and %ddcfDNA was observed for BLAD, this was not statistically significant.

Figure 1: Comparison of 3rd-6th month median of percent donor-derived cell-free DNA, absolute donor-derived cell-free DNA and total cell-free DNA between lung transplant recipients with and without baseline lung allograft dysfunction (BLAD).



BOS6_4 CLINICAL RELEVANCE OF CELL-FREE DNA QUANTIFICATION AND QUALIFICATION DURING THE FIRST MONTH AFTER LUNG TRANSPLANTATION

Pascal Pedini[1;2], **Benjamin Coiffard[3], Silvia CASAS*[4], Audrey Boutonnet[5], Coralie Frassati[1;2], Jacques Chiaroni[1;2], Martine Reynaud-Gaubert[3], Christophe Picard[1;2]**

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Background: Many studies have reported the relevance of donor-derived cfDNA (dd-cfDNA) after lung transplantation (LT) to diagnose and monitor acute (AR) or chronic rejection or infection (INF), analysis of cfDNA fragment size is not sudied. The aim of this study was to determine the clinical relevance of dd-cfDNA and cfDNA size profiles in events (AR and INF) during the first month after LT.
Methods: This is a prospective, single-center study including 62 LT patients at the Marseille Nord Hospital (LARA project). Total cfDNA quantification was performed by fluorimetry and digital PCR, dd-cfDNA by NGS (AlloSeq cfDNA-CareDX®) and the size profile by BIABooster (Adelis®). A biopsy at D30 allowed establishing the following groups: stable, nonstable (AR, INF and AR+INF).
Results: Quantification of total cfDNA, for all methods, was not correlated with the patient's status at D30, percentage of dd-cfDNA was significantly higher for nonstable patients at D30 (p=0.0004). A threshold of 1.72% of dd-cfDNA determined the nonstable patients (NPV: 91.4%). The analysis of small sizes (80-120 bp) identified the INF with a threshold of 3.7% (PPV: 100%). An algorithm combining the two analyses allows to significantly differentiate the type of lesions due to allografts.
Conclusions: Our algorithm aims at guiding the performing of biopsies, which are invasive and risky for the patient. This combined noninvasive biomarker of allograft injury requires to be confirmed. For this purpose, a control cohort is being included and a multicenter study is planned.

BRIEF ORALS

Treatable traits lead the way towards better outcomes in lung transplantation

BOS6_5 COMPARISON OF PLASMA DONOR-DERIVED CELL-FREE DNA WITH LASHA SCORING SYSTEM IN LUNG TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Background: Donor-derived cell-free DNA (dd-cfDNA) has been investigated as a non-invasive alternative approach to transbronchial biopsies (TBBs) to evaluate lung allograft injury (LAI) following transplantation. The aim of the study was to compare the diagnostic yield of dd-cfDNA to scheduled TBBs systematically evaluated according to the LASHA template.
Methods: Twenty-one recipients were prospectively enrolled between October and November 2022. TBBs were scored according to LASHA template. Alveolar macrophages, oedema, and mild capillary dilation with score <2 were considered nonspecific and classified as unremarkable if not associated with altered microbiological or immunological findings. A comprehensive immunological and microbiological/cytological evaluation was carried out on blood and bronchoalveolar lavage (BAL), respectively. dd-cfDNA was measured (%) by NGS on plasma collected at the same time of TBBs.
Results: dd-cfDNA was under the threshold of 0.85% in 10 patients. In 8 patients, TBB was negative or unremarkable. None showed immunological complications. The negative predictive value was 80%. dd-cfDNA was over the threshold in 11 patients. The positive predictive value was 82%.
Conclusions: Plasma dd-cfDNA is highly predictive of LAI, even after a granular histological evaluation. Further studies are needed to confirm the clinical validity of cfDNA, especially for the detection of specific or concomitant pathological lesions of LAI.

Sex	Age (years)	Months From Ltx	CLAD	DSA	Altered Histological Parameters In LASHA Template	Infections in BAL	dd-cfDNA (%)	Lung Allograft Injury
M	66	26	0	-	Unremarkable	-	0,08	No
M	34	4	0	-	Negative	+	0,11	Yes
M	58	17	0	-	Unremarkable	-	0,13	No
M	66	3	0	-	Negative	-	0,22	No
F	61	21	0	-	Negative	-	0,24	No
M	55	8	1	-	Negative	-	0,26	No
F	33	2	0	-	Organizing pneumonia (I/R injury?)	-	0,26	No
F	26	94	0	-	Negative	-	0,35	No
F	34	52	0	-	Unremarkable	-	0,50	No
M	64	15	0	-	Neutrophilic/cellular debris in alveolar septa	-	0,58	Yes
F	24	7	0	-	Unremarkable	-	0,86	No
M	61	3	0	-	Neutrophils in alveolar septa	+	0,90	Yes
M	65	53	0	+	Unremarkable	-	1,27	Yes
F	40	5	0	-	Organizing pneumonia	+	1,28	Yes
F	26	181	1	-	Negative	-	1,68	Yes
F	21	17	0	-	A1B0	-	2,03	Yes
M	56	4	0	-	A3B0	+	3,54	Yes
M	65	5	0	-	Negative	+	4,67	Yes
M	46	128	0	-	Unremarkable	-	4,75	No
M	36	61	0	+	Unremarkable	+	5,40	Yes
F	41	63	2	+	Neutrophilic/cellular debris in alveolar septa	-	6,85	Yes

BOS6_6 DIAGNOSTIC YELD AND SAFETY OF CRYOBIOPSY VERSUS FORCEPS BIOPSY IN LUNG ALLOGRAFT RECIPIENTS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Background: Endoscopic surveillance with transbronchial biopsy in lung transplant (LTx) is crucial, since an early diagnosis of acute cellular rejection (AR) can affect long term survival. Histological diagnosis of AR is usually obtained using transbronchial forceps biopsy (FB). In recent years, transbronchial cryobiopsy (CB) has been increasingly used, as it obtains larger samples than FB, without crush artefacts. Few studies have compared the two methods in terms of diagnostic accuracy and safety. The aim of this study is to assess the diagnostic yield and safety of CB in comparison with FB, for sampling lung tissue in transplant recipients.
Methods: We analyzed through a retrospective study our case series of the two procedures. From January 2013 to December 2017, 251 FBs were performed in 110 patients, 223 for surveillance purposes and 28 on clinical indication. From January 2018 to October 2022, 218 consecutive CBs were performed in 137 patients, 159 for surveillance purposes and 59 on clinical indication. All biopsies were scored according to the ISHLT criteria. Clinical and functional data, complications, and histologic results were collected.
Results: Diagnostic yield was higher in the CB group for all parameters: grade of AR was detected in 95.0% vs 84.5% in the FB group (p<0.001). Diagnostic rate of airway inflammation was 65.1% vs 51.8% (p=0.005), for chronic rejection 89.0% vs 64.9% (p<0.001). Pneumothorax requiring chest drainage occurred in 3.6% in the CB group and in 4% of patients in the FB group (p non-significant). Moderate and severe bleeding complicated CB and FB procedures in 7 (3.2%) and 3 cases (1.3%), respectively (p=0.178).
Conclusions: Transbronchial cryobiopsies improved the diagnostic yield in the monitoring of the lung allograft. The risk of bleeding and pneumothorax has not increased significantly. Prospective studies will better define the role of CB after LTx.

BOS6_7 INFLUENCE OF THE RESPIRATORY TRACT'S MICROBIOLOGICAL SPECTRUM ON THE OUTCOME AFTER LUNG TRANSPLANTATION

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Background: Lung transplantation (LuTX) is the standard of care for patients with chronic progressive, end stage lung diseases. Adherence to prescribed immunosuppressive medication is crucial to prevent graft failure, but it also makes lung-allograft-recipients more susceptible to infections. Years of chronic disease and prior hospitalizations on one side, along with intensive-care stay and airway intubation prior to organ donation on the other, facilitate the spread of pathogenic germs in the respiratory tract. This retrospective cohort study aimed to investigate the relationship between the respiratory tract's germ spectrum and its impact on post-LuTX survival.
Methods: Only patients that received a single or double LuTX from 2014 onwards were considered for this study. In addition to a valid and complete follow-up after TX, inclusion criteria were pre- and postoperative sputum samples, as well as intraoperatively performed smear-tests of donor and recipient bronchus. Microbiological findings were categorized into bacteria and fungi. Bacteria were again grouped into gram-positive and gram-negative (aerobic/anaerobic) germs.
Results: Up to this point, 200 patients with valid data on pre-, intra- and postoperative microbiological testing have been included. The most common bacteria found were Staphylococcus aureus and Streptococcus pneumoniae, while the predominant fungi were Candida albicans and species. Positive microbiological findings in intraoperative and postoperative samples showed a trend towards a decreased five-year survival. Furthermore, preoperative sputum samples with positive fungal findings were significantly associated with a negative outcome.
Conclusions: This study suggests that the respiratory tract's microbiological composition can influence post-LuTX outcome and survival. As sepsis and multi organ failure, themselves often due to an infectious cause, have gradually replaced graft failure as the leading cause of death in LuTX-patients over the last decades, understanding the role of microbiological colonization is important for improving the outcome and long-term survival after LuTX.

BRIEF ORALS

Treatable traits lead the way towards better outcomes in lung transplantation

BOS6_8 FUNGAL INFECTION WITHIN THE FIRST YEAR AFTER LUNG TRANSPLANTATION DOES NOT AFFECT LONG TERM SURVIVAL

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Background: Lung transplantation is the only definitive treatment for end-stage lung diseases. However, lung transplantation has the poorest survival rate among all solid organ transplantations. The poor long-term survival after lung transplantation is mainly due to chronic lung allograft dysfunction (CLAD), while one of the most common causes of death within the first year post transplantation is infection caused by microorganisms such as viruses, bacteria and fungi. The majority of fungal infections appear within 3 – 12 months after transplantation. Invasive fungal infections are feared and affect up to approximately 10 % of all transplanted patients during the first year after the transplantation. The invasive fungal infections are most commonly caused by Aspergillus species, which create a hypoxic environment in the small airways of the lung allograft, which is believed to increase the risk of rejection. Previous studies state that lung transplant patients with a fungal infection have increased risks of both morbidity and mortality compared to patients without fungal infections.
Methods: In the current study we investigated how fungal infections during the first year after lung transplantation impacts the overall survival. A total of 88 lung transplant recipients, transplanted between the years 2011 and 2018 were included. Patient charts were reviewed for collection of data. Out of the 88 patients included, 68 had a fungal infection during the first year after lung transplantation, and 20 did not (table 1).
Results: In the group with fungus, there were 33 men and 35 women (age 19 – 68 years). In this group there were 33 patients with aspergillus species, 20 with candida species, four with both, two with pneumocystis species and nine with other fungal infections. In the group with no fungal infection there were 10 men and 10 women (age 16 – 65 years). Analysis comparing the survival between recipients with and without fungal infection during the first-year post lung transplantation, showed no statistically significant difference between the groups (p = 0.57) (hazard ratio; 1.2 (95% CI: 0.6 – 2.3) (figure 1).
Conclusions: In this study, long term survival following lung transplantation was not affected by fungal infections within the first 12 months post transplantation reflecting an equal survival between the groups.

	Age, mean (range)	Male sex, n (%)
No fungal infection	52 (19 – 68)	10 (50)
Fungal infection	49 (16 – 65)	33 (49)

Table 1: descriptive statistics

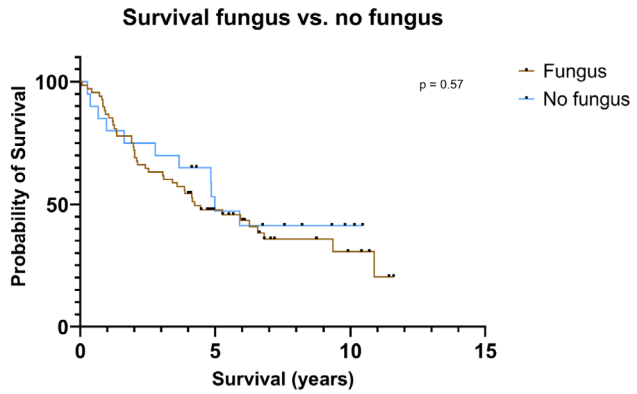

Figure 1: Kaplan Meier curve, showing no significant effect on overall survival of patients with fungal infection during the first 12 months post lung transplantation compared to patients without fungal infection.

BOS6_9 POLIOMAVIRUS BK REPLICATION IN URINE DETERMINES A RAPID DECLINE IN KIDNEY FUNCTION AFTER LUNG TRANSPLANTATION

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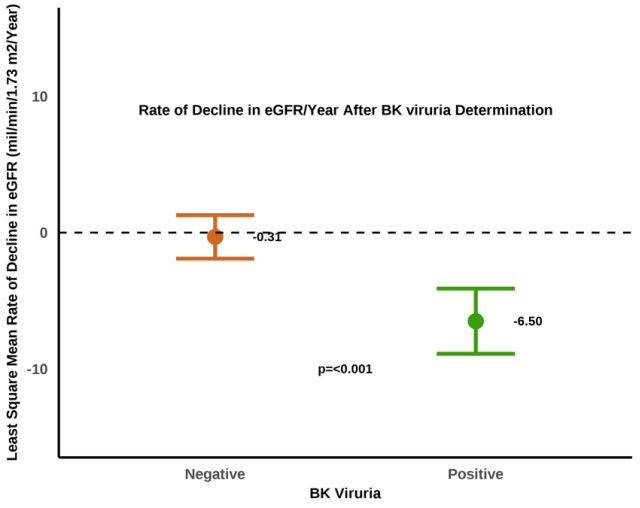
Background: Different modalities of non-renal solid organ transplantation can develop chronic kidney disease (CKD) as a long-term complication. After lung transplantation (LT), the prevalence of CKD rounds 5-15% depending on the time of evaluation of renal function (RF) after LT. BK polyomavirus replication has recently gained interest as a cause of CKD. Thus, the present study aimed to assess whether the replication of polyomavirus BK in the urine of lung transplant recipients is associated with an increase in the rate of decline of the eGFR slope during follow-up.
Methods: We determined BK viruria in 56 LT recipients. Further, they were categorized according to viruria as positive or negative. Demographic and clinical variables were analyzed. The eGFR slope was calculated considering the estimated glomerular filtration rate (GFR) from 2 years before the determination of BK viruria and up to 2 years later. A total of 7 eGFR measurements were used (-2 years, -1-year, baseline, +6 months, +1 years, and +2 years). Linear regression was used to determine the variables associated with the decrease in the eGFR slope. Logistic regression allowed identifying the variables associated with rapid progression (eGFR slope >5 mil/min/1.73 m2/year).
Results: 38 out of the 56 TP showed negative viruria, whereas 18 were positive. The least squares mean decrease in the eGFR slope was greater in subjects with positive viruria (-6.50 mil/min/1.73 m2/year vs. -0.31 mil/min/1.73 m2/year, p<0.001). Positive BK viruria was independently associated with a decrease of -6.2 mil/min/1.73 m2/year (p<0.001, Figure 1) in multivariable linear regression. Likewise, these subjects showed a 26.3-fold increase in the risk of being rapid progressors with a sustained decline in the eGFR of > 5 mil/min/1.73 m2/year (p=0.002). Age, the use of calcineurin inhibitors as immunosuppressors, nor albuminuria attenuated the effect of viruria on the rate of eGFR decline.
Conclusions: In our study, subjects with BK viruria showed a greater rate of decline of eGFR slope. In addition, subjects with BK viruria showed a rapid progression pattern to advanced stages of CKD.

Figure 1. Least squares mean yearly rate of decline in eGFR according to BK viruria. Model adjusted for age, transplantation vintage, ICN through levels, and albuminuria.



BRIEF ORALS

Treatable traits lead the way towards better outcomes in lung transplantation

BOS6_10 EVALUATION OF LONG-LASTING LUNG INFLAMMATION IN CIRCULATORY DEATH RAT DONORS USING TISSUE CULTURE AND NORMOTHERMIC REGIONAL PERFUSION

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Background: Lung transplantation after circulatory death (DCD) is an option to treat end-stage diseases. Lungs are highly affected organs and present a long transplantation waiting list, moreover, they have a considerable chance of developing primary graft dysfunction(PGD). In order to expand the donor pool, normothermic regional (*in-situ*) perfusion is an alternative to *ex-vivo* lung perfusion. Lung tissue culture can be a tool to evaluate the long-lasting release of inflammatory mediators. This aimed to study the late inflammatory profile of DCD donor lungs, after warm ischemia, using normothermic regional perfusion and tissue culture.
Methods: Male Wistar rats were submitted to circulatory death (19.1% KCl solution, i.v.) followed by 30 minutes of ventilated warm ischemia. Afterwards, the lungs were placed in cold storage (CS; at 4ºC for 2 hours); or perfused *in situ* for 2h with Perfadex® in an open circuit (P; at 37ºC via the pulmonary artery). The perfusate was collected at 15 and 120 minutes of perfusion period. Lungs were harvested for cellular infiltrate on histopathological analysis. Lung fragments were placed in culture (24 hours - explant), and medium was used to measure IL-6, TNF-α and IL-10 concentration.
Results: CS lungs homogenates presented lower concentration of TNF-α than P lungs (CS:10.75±3.41; P:58.65±20.48 pg/mg; p=0.0576). There were no differences in IL-10 and IL-6. In the perfusate, the inflammatory mediators concentration increased with time in both groups. Conversely, in the lung tissue culture (24 hours later), IL-6 (CS: 15.99±1.20; P: 7.52±1.86 pg/ml/mg; p= 0.0032) and IL-10 (CS: 35.35±8.33; P:20.22±6.46 pg/ml/mg; p= 0.4772) were higher in CS indicating a time and preservation dependent inflammatory response. Nonetheless, TNF- α was not altered in the explant quantification, but it is important to consider that it is an early mediator.
Conclusions: Comparing the immediate tissue analysis and the 24h tissue response, the normothermic regional perfusion of the lungs seems to reduce the inflammatory cytokines production and that could indicate a worse scenario in the recipient of cold-stored organs.
Financial support: grant 88887.511368/2020-00, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES

BOS6_11 EFFECT OF DONOR AGE ON LUNG TRANSPLANT SURVIVAL: A MULTICENTER RETROSPECTIVE STUDY FROM THE COLT DATABASE

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Background: Shortage of organ requires lung transplantation (LT) teams to consider older donors. The effects of donor age in LT are not clearly established and data are needed to enable an adequate choice of lung donor.
Methods: We retrieved data from a French and Belgian multicenter lung transplantation cohort. Recipients who underwent heart and lung transplantation, single LT and those who benefited from a retransplantation were excluded. The objective was to determine a correlation between donor age and post-transplant survival.
Results: The analysis was performed on 1191 recipients. Donors over 60 years of age are more frequently female and have a less frequent history of smoking. Lung grafts from donor over 60 years of age are more frequently allocated to recipients of older age, female gender, chronic obstructive pulmonary disease as underlying disease and with cardiovascular comorbidities. The 5-year survival of recipients of lung grafts from donor over 60 years of age was lower than that of recipients of lung grafts from younger donors (62.1% versus 69.3%, respectively, p < 0.001). In multivariate analysis, donor age over 60 years was a risk factor for mortality (HR = 1.28, 95% CI [1.01 - 1.63], p = 0.039). Other predictors of survival in multivariate analysis were for recipients female gender (HR = 0.74, 95% CI [0.60 – 0.92], p = 0.006), cystic fibrosis underlying disease (HR = 0.45, 95% CI [0.35 – 0.58], p < 0.001), and a history of ischemic heart disease (HR = 1.67, 95% CI [1.12 – 2.48], p = 0.011).
Conclusions: Donor age greater than 60 years is an independent risk factor for survival after transplantation. The age criterion must be considered in the acceptance decision for a lung transplant.

BOS6_12 IDENTIFYING TREATABLE TRAITS IN RESTRICTIVE ALLOGRAFT SYNDROME: A NESTED CASE-CONTROL STUDY

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Background: Chronic lung allograft dysfunction (CLAD), with its main phenotypes bronchiolitis obliterans syndrome (BOS) and restrictive allograft syndrome (RAS), remains a major cause of mortality after lung transplantation. Several risk factors for CLAD development have been identified. However, most studies hitherto did not assess RAS as a separate phenotype or pooled all phenotypes of CLAD together, making it difficult to distinguish between RAS and BOS. Therefore our aim was to identify (and confirm) risk factors for RAS.
Methods: In this retrospective nested case-control study, all patients transplanted at our center from 2010 till 2021 (n=789) were evaluated for inclusion. CLAD patients were phenotyped according to the 2019 ISHLT consensus. 69 patients with RAS or mixed phenotype were included, and 1 non-CLAD control per case, matched for age, sex, transplant indication and era of transplantation was selected based on incidence density sampling. (Time-dependent) Cox regression was used to assess the occurrence of acute cellular rejection, anti-HLA antibodies, donor-specific antibodies (DSA), primary graft dysfunction (PGD), bacterial and fungal infection and blood lymphocytosis and monocytosis with respect to RAS/Mixed onset.

Treatable traits lead the way towards better outcomes in lung transplantation

Results: Univariate analysis demonstrated that post-transplant pseudomonas isolation, transient anti-HLA antibodies, DSA, invasive pulmonary aspergillosis (IPA) and fungal isolation (with clinical symptoms impeding diagnosis of colonization, but insufficient endoscopic/radiologic features for invasive fungal disease) were associated with increased RAS/Mixed phenotype occurrence. Multivariate analysis confirmed the association for pseudomonas isolation, transient HLA, DSA and IPA.
Conclusions: We have identified a set of risk factors associated with RAS that could be therapeutic targets in lung transplant follow-up.

Covariates		Hazard ratio	Standard error	P
PGD at 72h post-LTx				0.4364
	Grade 1	0.6498	0.2434	
	Grade 2	0.6501	0.2195	
	Grade 3	0.9993	0.3513	
Acute rejection		1.0502	0.1280	0.6915
HLA-antibodies				
	Transient	**1.5734**	**0.1861**	**0.0006**
	Perisistent	**1.4975**	**0.2296**	**0.0165**
Donor-specific-antibodies		**1.8452**	**1.8452**	**0.0070**
Pseudomonas isolation		**1.1573**	**0.0551**	**0.0068**
Non-pseudomonas isolation		1.0801	0.0392	0.0506
Invasive fungal disease				
	Invasive pulmonary aspergillosis	**1.4649**	**0.1065**	**0.0000**
	Fungal trancheobronchitis or bronchial anastomotic infection	1.3278	0.2160	0.1063
Non-invasive fungal disease				
	Colonization	1.0788	0.2241	0.7193
	No colonization	**1.2286**	**0.0664**	**0.0003**
Peripheral blood lymphocytes (10^9/L)		1.0178	0.1336	0.8936
Peripheral blood monocytes (109/L)		1.3465	0.5533	0.4749

BOS6_13 EXTRACORPOREAL PHOTOPHORESIS IN CHRONIC LUNG ALLOGRAFT DYSFUNCTION. SINGLE CENTER EXPERIENCE

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Background: Extracorporeal photopheresis (ECP) is a procedure that involves the apheresis and collection of the leukocyte-enriched blood, which is exposed to ultraviolet light in the presence of 8-methoxypsoralen and then, reinfused to the patient. This results in lymphocyte apoptosis and induction of regulatory T-cells. ECP is an accepted therapy in lung transplant recipients (LT) for treatment of chronic lung allograft rejection (CLAD).
Methods: We performed a retrospective study of all lung transplant recipients who were treated with ECP for CLAD at Hospital la Fe, Valencia (Spain) from July 2017 to January 2022. ECP treatment was performed with off-line methods and processing one volemia. Treatments were performed weekly (1st mo.), quarterly (till 6 mo.) and then, monthly (6-12 mo.). A positive response to ECP was considered change in the mean decrease of FEV1 6 months after ECP, compared with 6 months prior to ECP. A small group of patients receive ECP due to recurrent acute rejection (RAR) (n=03). Means (paired Student's t-test) and mortality (Kaplan-meier) were analysed with SPSS 20.0 software.
Results: Thirty-eight patients received ECP for CLAD (28 bilateral LT, 9 single-LT, 1 heart-lung transplant; 27 male & 11 female), with median age of 47 years (range 19-71). CLAD stage at ECP initiation was CLAD 1-2 52'6%, CLAD 3-4 28%. CLAD subtype obstructive 32'3%, restrictive 23'1%, mixed 35'9%. Immunosuppression at ECP start consisted of tacrolimus and everolimus in most patients (60.5%). Median 6-month decline of FEV1 prior and after to ECP was 386mL and 165mL, respectively (P= 0.028). The slope decreased more when the underlying disease was an interstitial lung disease (ILD) (309mL and 35mL, respectively (P= 0.001). At the time of this evaluation, 10 (26.3%) patients have died (3/17 ILD, 2/8 COPD and 4/10 cystic fibrosis) and 2 (5.3%) have received re-transplant. Of this group, 45.5% had CLAD 3 or 4 prior to ECP. Patients who receive ECP due to RAR did not relapse. There were no major adverse events related to ECP.
Conclusions: ECP treatment is associated with a decrease in the mean decline in FEV1 in progressive CLAD patients. ILD-LT recipients might respond more than others. Advanced stage of CLAD at the start of ECP implied more mortality. RAR patients responded. ECP was proved as a safety alternative for LT recipients.

BOS6_14 EVEROLIMUS IN LUNG TRANSPLANT RECIPIENTS FOR CLAD PREVENTION: A REAL LIFE EXPERIENCE

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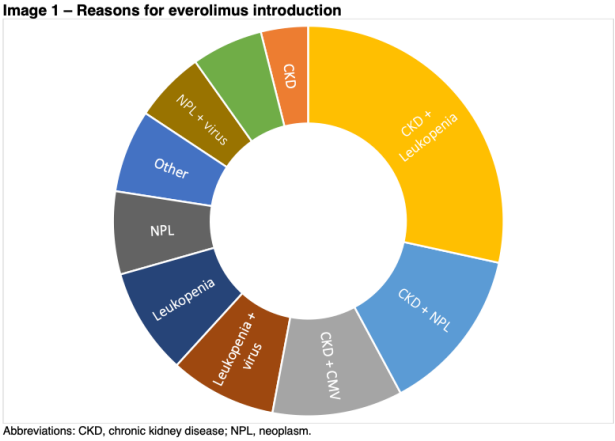
Background: We hereby report our real – life experience with everolimus (EVE) in lung transplant (LuTx) recipients as a means to prevent chronic lung allograft dysfunction (CLAD); we also aimed to evaluate the safety of this drug in this setting.
Methods: This was a retrospective study including all adult patients who underwent LuTx from January 2015 to December 2022, received regular outpatient follow up for at least 12 months from LuTx and were administered a triple combination immunosuppressive regimen, consisting of corticosteroids, tacrolimus and an antiproliferative agent. Exclusion criteria were: retransplant and administration of everolimus as treatment for CLAD. Patients were divided into two groups: those receiving everolimus and the others (thus receiving azathioprine or mycophenolate).
Results: 139 patients were considered, 46 receiving EVE. Details on baseline characteristics of our population and comparisons between the two groups can be found in table 1; of note, no significant difference was found. With regard to the reasons for EVE administration, details can be found on image 1; it should be noted that three quarters of these patients (35, 76%) simultaneously presented more than one indication for this treatment. Median time for EVE introduction was 14 (9, 24) months from LuTx. As for relevant side effects related to EVE, we observed: proteinuria in 4 (9%) patients, thrombotic events in 2 (4%), edema in 4 (9%), organizing pneumonia (OP) in 1 (2%), major infections in 12 (26%) and stomatitis in 1 (2%). After 6 months of treatment with EVE, 4 (9%) patients presented a worsening e-GFR of at least 10 mL/min (median Delta eGFR 2 (-2; 10) mL/min), whilst 11 (24%) patients experienced a FEV1 decline of at least 200 mL (median Delta FEV1 0 (-200; +180) mL). Finally, everolimus was discontinued in 5 (11%) patients: 3 for recurrent infections; 1 for pulmonary toxicity (OP) and 1 for edema, proteinuria and worsening kidney disease.
Conclusions: In light of currently available scientific evidence and based on our data, everolimus seems as effective as other antiproliferative agents in preventing CLAD in LuTx recipients, especially in those who may need a strategy to minimize nephrotoxicity and/or myelotoxicity without compromising immunosuppressive efficacy. Safety profile proved to be acceptable.

Table 1

		General population (139 pts)	Everolimus (46 pts)	Other IST regimens (96 pts)	p value
Sex (females)		72 (52%)	24 (52%)	48 (52%)	0,76
Age at LuTx (years)		40 (28; 55)	36 (28; 52)	42 (28; 58)	0,47
Bilateral LuTx		134 (96%)	43 (94%)	91 (98%)	0,20
Indication for LuTx	CF	76 (55%)	29 (68%)	47 (51%)	0,10
	ILD	40 (29%)	7 (15%)	33 (36%)	
	COPD	13 (9%)	6 (13%)	7 (8%)	
	Other	10 (7%)	4 (9%)	6 (7%)	
CLAD (incidence of)		37 (27%)	13 (28%)	24 (26%)	0,45
	BOS	22 (16%)	8 (17%)	14 (15%)	
	RAS	5 (4%)	2 (4%)	3 (4%)	
	Mista	10 (7%)	3 (7%)	7 (8%)	
CLAD-free survival (months)		45 (41; 49)	44 (38; 49)	46 (41; 50)	0,46
Survival (months)		76 (71; 81)	77 (71; 84)	74 (68; 81)	0,27

Abbreviations: CF, cystic fibrosis; CLAD, chronic lung allograft dysfunction; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; LuTx, lung transplantation; pts, patients.

Image 1 – Reasons for everolimus introduction



Abbreviations: CKD, chronic kidney disease; NPL, neoplasm.

BRIEF ORALS

Complications and infections after kidney transplant

BOS7_1 PREDICTION OF KIDNEY GRAFT SURVIVAL AMONG DECEASED TRANSPLANT RECIPIENTS IN THE UK: AN ARTIFICIAL INTELLIGENCE APPROACH

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Background: Predicting kidney allograft outcome can direct clinical care and resource allocation. The aim of our study was to develop a prediction tool for death censored graft survival using artificial intelligence.
Methods: All deceased kidney transplant patients registered in the UK Transplant Registry database from 2007 till 2020 were retrospectively reviewed. Exclusion criteria: age<18 years old, multiple organ transplant, kidney graft failure within 3 months post-transplant, or missing data about death censored graft survival. Graft failure was defined as the need for maintenance dialysis post-transplant. The data was divided into training and test dataset with ratio 70:30 in order to train the model and then evaluate its performance on the unseen data. Decision based models for survival analysis were used (decision tree, Random Forest and XGBOOST). Evaluation criteria were Harrell C statistic for discrimination, and Integrated Brier score for calibration. Data collected were transplant, factors donor and recipient demographics, serum creatinine at 3 months post-transplant.
Results: 22,717 patients were included in our study. For the decision tree model, Harrell C-statistics=0.70 (indicating adequate discrimination), Integrated Brier score=0.02 (indicating excellent calibration), AUC for a 10-year post-transplant period was 0.7 (indicating adequate performance). Random Forest and XGBOOST models slightly improved the Harrell C-statistic to 0.72. The key players in making the predictions were serum creatinine at 3 months post-transplant (importance factor=0.67), followed by donor-recipient age difference (importance factor=0.04). Using only pre-transplant factors, our model had a Harrell C-statistic of 0.67 in the training data and 0.635 in the test dataset.
Conclusions: Decision based models can aid in predicting kidney graft survival post-transplant. Our model can make has high discrimination and calibration power. A user-friendly web app can be developed using our model. Key players in prediction were serum creatinine at 3 months post-transplant and donor-recipient age difference. A user-friendly web app can be developed using our model.

BOS7_2 REAL-LIFE IMPLEMENTATION OF A STRATEGY BASED ON CMV-SPECIFIC CELL-MEDIATED IMMUNITY TO GUIDE CMV PREVENTIVE THERAPY IN SOLID ORGAN TRANSPLANTATION

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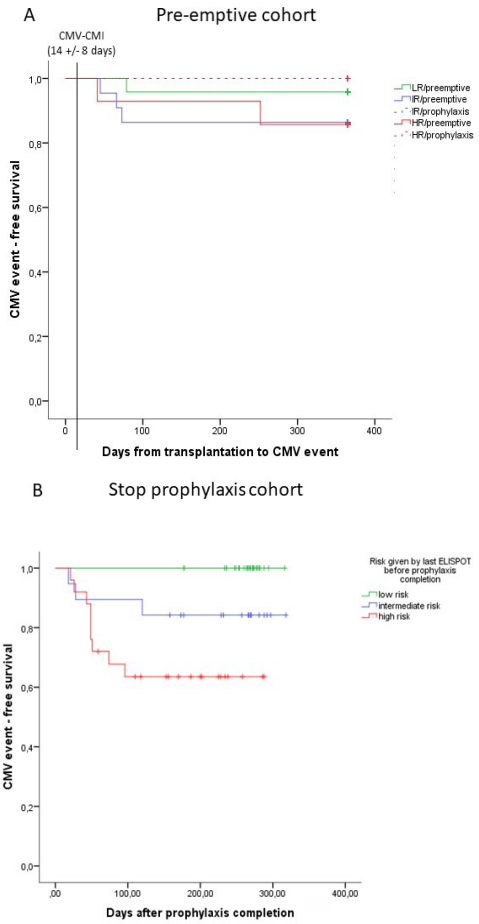
Background: Measuring CMV-specific cell-mediated immunity (CMI) is be a new promising tool to guide CMV preventive therapy after solid organ transplantation (SOT). However, its implementation in clinical practice has not been done yet.
Methods: Between January 2017-December 2019, we evaluated a new strategy for both CMV prevention guided by CMV-specific CMI in a real-life clinical scenario in 147 consecutives SOT recipients. In the preemptive cohort, CMV-CMI was assessed at day 10-15 post-transplantation in 75 CMV R+ SOT not receiving T-cell depletion induction therapy. In the Stop-prophylaxis cohort, CMV-CMI was assessed in 55 CMV R+ and 17 D+/R- kidney transplants (KT) receiving prophylaxis therapy because of use of T-cell depletion. In both groups, decision to continue with either close CMV-PCR assessment or start or extend prophylaxis therapy was at clinician´s discretion according to CMV-CMI results. We assessed CMV-CMI against two major CMV antigens (IE-1/pp65) with the T-SPOT®.CMV assay following IE-1 and pp65 thresholds recently published by our group in a RCT to classify patients into High- (HR), Intermediate- (IR) and Low-risk (LR). Primary outcome was occurrence of High CMV viral load requiring therapy during first year posttransplantation.
Results: The preemptive cohort included 40 (53%) liver, 25 (33%) heart and 10 (13%) KT recipients. Mean time between transplantation and CMI was 14±8 days. No (0/24) LR-CMI patients, 5/27 (19%) of IR-CMI and 10/24 (42%) HR-CMI received prophylaxis. No infections occurred in patients on prophylaxis. Infection occurred in 1/24 (4.1%) LR-, 3/22 (14%) IR- and 2/14 (14%) HR-CMI patients under pre-emptive strategy (figure 1A). In the Stop-prophylaxis cohort, mean time between transplantation and CMV-CMI was 117±43 days. Prophylaxis was withdrawn after first CMI in all LR-CMI patients (28/28), 16/21 (76%) IR- and 16/25 (64%) HR-CMI patients. 12 CMV events occurred, 3 in R+ and 9 in R-. All events occurred after prophylaxis completion, with a last CMV-CMI catagorizing patients as IR (3/12) and HR (9/12) (p<0.01, figure 1B).
Conclusions: CMV-CMI risk stratification in a real-life clinical transplant scenario allowed identification of at-risk patients and proves to be a useful tool to guide type and extension of prophylaxis therapy among D+/R + SOT.



BOS7_3 MACHINE LEARNING MODELS IN RENAL TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS OFPREDICTIVE PERFORMANCE IN GRAFT SURVIVAL

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Background: Kidney transplantation(KT) is currently the renal replacement therapy of choice for most patients with end-stage kidney disease. Despite many advancements, the variations in outcome and frequent occurrence of graft failure continue to pose important clinical and research challenges. The aim of this study was to carry out a systematic review of the current application of Machine Learning(ML) models in KT and perform a meta-analysis of these models in the prediction of graft outcomes.
Methods: This review was registered with the PROSPERO database(CRD42021247469) and all peer-reviewed and preprint original articles that reported the sensitivity and specificity of AI-based models were included in the meta-analysis. The quality of the articles were assessed by the criteria defined by Qiao et al and Risk of Bias assessment was performed using the PROBAST tool. The diagnostic performance of the meta-analysis was assessed by a meta-analysis of the Area under the receiver operating characteristics(AUROC) and a Hierarchial Summary ROC plot.
Results: 25 studies met the inclusion criteria for the review and 22 studies were included in the meta-analysis. More than 15 different ML models were used to predict graft survival in the included studies. Seven studies compared the predictive performance of ML models with traditional regression methods. 6 studies had a high risk of bias and 3 studies had an unclear risk of bias. The area under the HSROC curve was 0.79 and the summary sensitivity and specificity of ML-based models were 0.78(95% CI, 0.69- 0.85) and 0.66(95% CI, 0.6-0.73), respectively.
Conclusions: Our study shows that ML models can accurately predict outcomes following KT by the integration of the vast amounts of non-linear data

BRIEF ORALS

Complications and infections after kidney transplant

BOS7_4 BURDEN OF REFRACTORY/RESISTANT CYTOMEGALOVIRUS OR CYTOMEGALOVIRUS DRUG INTOLERANCE IN SOLID ORGAN TRANSPLANT RECIPIENTS: EUROPEAN SUBGROUP ANALYSIS

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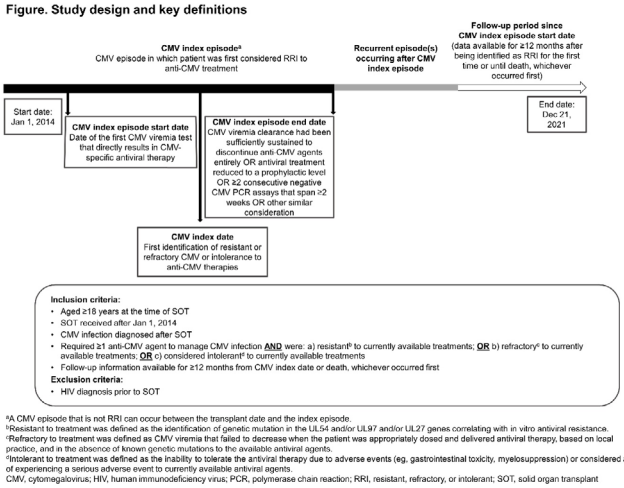
Background: Contemporary real-world data on management and outcomes of cytomegalovirus (CMV) infection post solid organ transplant (SOT) are scarce. Data were collected to describe the burden of resistant/refractory CMV infection or intolerance to conventional anti-CMV therapies (RRI) among SOT recipients enrolled in the Multinational CMV Outcomes, Treatment Patterns and Healthcare Resource Utilization study (OTUS).
Methods: OTUS SOT was a multicenter, retrospective study of adult patients (pts) who had RRI post-SOT. Eligible pts received SOT after Jan 1, 2014 across 13 transplant centers in the US and Europe (Spain, France, Germany, UK). Pts were followed ≥12 months from CMV index date (date of RRI identification) or until death, whichever occurred first (**Figure**). CMV treatment patterns, clinical outcomes, and hospitalizations in pts from the 8 European centers are described.
Results: Overall, 112 pts from Europe with ~3 years (mean) of follow-up post-SOT were analyzed. Median time from transplant to first CMV episode: 94.5 days. 109 (97.3%) pts developed RRI during their first CMV episode. Valganciclovir was used for primary and secondary prophylaxis in all pts for whom prophylaxis was used, and as treatment in 89.3% of pts. In the treatment setting, 16 (14.3%) pts received foscarnet and 58 (53.2%) pts required ≥2 anti-CMV therapies. From first identification of RRI, 23/31 (74.2%) myelosuppression events occurred with valganciclovir use; treatment discontinuations/dose changes occurred in 81/93 (87.1%) pts on valganciclovir and 54/93 (58.1%) pts on ganciclovir. A total of 26 (23.2%) pts failed to achieve viremia clearance during the CMV index episode. CMV recurred in 22 (19.6%) pts. 50 (44.6%) pts had CMV-related hospitalizations with/without emergency department visits. Graft loss was observed in 9 (8.0%) pts (7 pts after RRI identification). All-cause mortality: 22.3%. Mortality 1-year post-RRI identification occurred in 16.1% of pts.
Conclusions: A relevant portion of pts in the European cohort of the OTUS SOT study who had RRI did not achieve CMV clearance during the CMV index episode and had CMV recurrence and/or adverse outcomes. Therapies that achieve and maintain CMV clearance without treatment-limiting toxicities are needed. Funding: Takeda Development Center Americas Inc.

Figure. Study design and key definitions



[a]A CMV episode that is not RRI can occur between the transplant date and the index episode.
[b]Resistant to treatment was defined as the identification of genetic mutation in the UL54 and/or UL97 and/or UL27 genes correlating with in vitro antiviral resistance.
[c]Refractory to treatment was defined as CMV viremia that failed to decrease when the patient was appropriately dosed and delivered antiviral therapy, based on local practice, and in the absence of known genetic mutations to the available antiviral agents.
[d]Intolerant to treatment was defined as the inability to tolerate the antiviral therapy due to adverse events (eg, gastrointestinal toxicity, myelosuppression) or considered at risk of experiencing a serious adverse event to currently available antiviral agents.
CMV, cytomegalovirus; HIV, human immunodeficiency virus; PCR, polymerase chain reaction; RRI, resistant, refractory, or intolerant; SOT, solid organ transplant

BOS7_5 PREVALENCE OF CYTOMEGALOVIRUS ANTIVIRAL DRUG RESISTANCE IN TRANSPLANT RECIPIENTS

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Background: Human cytomegalovirus (CMV) is a significant pathogen after solid organ and allogeneic hematopoietic cell transplantation. Antiviral drug resistance (ADR) to CMV is an important complication for patients on prophylaxis or treatment, and genotypic resistance is well-documented for all current anti-CMV drugs. International guidelines recommend that ADR should be suspected, and genotypic testing performed, with persistent or recurrent CMV DNAemia or disease during prolonged (e.g., ≥6 weeks) antiviral therapy (Transplantation 2018; 102:900).
Methods: A total of 2750 patient samples submitted to Eurofins Viracor's reference laboratory for CMV genotypic resistance testing were de-identified prior to retrospective analysis. Testing was performed for ganciclovir (GCV), cidofovir (CDF), foscarnet (FCN), maribavir (MBV) and/or letermovir (LMV) resistance based on physician orders. Viral UL54, UL56 and/or UL97 genes were amplified by PCR to produce overlapping fragments, which were subjected to consensus (Sanger) sequencing. Resistance conferring mutations were analyzed by viral genes and patient.
Results: Resistance mutations were most common in UL97 with 27.64% and 9.96% of samples positive for GCV and MBV ADRs, respectively. For LMV, ADRs in UL56 were present in 7.17% of samples, and mutations at C325 represented 80.95% of mutations. The five most common mutations for each viral gene are shown in Table 1. Patient samples with ADR to GCV were most common, with 29.38% having mutations (657 in UL97 only, 42 in UL54 only, 95 in both UL97 and UL54). Several ADRs conferring resistance to more than one drug were identified, such as F342Y and C480F in UL97 which confer resistance to both GCV and MBR. Of the 2750 patient samples, 826 (30.03%) had resistance to one or more drug. Resistance to 2 drugs was identified in 216 samples and to 3 or more drugs in 35 samples.
Conclusions: A high prevalence of CMV ADR was identified in patient samples, although this must be taken in the context of physicians submitting samples from patients with suspected resistant CMV strains. For these patients, rapid monitoring for ADR allows physicians to treat based on objective results rather than empiric drug selection, which is particularly relevant given the presence of mutations conferring resistance to more than one drug.

Table 1. Prevalence of the most commonly detected resistance conferring mutations by CMV gene and antiviral drug

UL54 Cidofovir		UL54 Foscarnet		UL54 Ganciclovir		UL97 Ganciclovir		UL97 Maribavir		UL56 Letermovir	
Mut.	% (No.)	Mut.	% (No.)	Mut.	% (No.)	Mut.	% (No.)	Mut.	% (No.)	Mut.	% (No.)
None[1]	94.10% (2202)	None	98.08% (2293)	None	93.85% (2196)	None	72.36% (1723)	None	90.04% (1121)	None	92.83% (1359)
T503I	0.94% (22)	V715M	0.43% (10)	T503I	0.94% (22)	L595S	5.00% (119)	T409M	3.62% (45)	C325Y	2.66% (39)
A987G	0.68% (16)	T700A	0.26% (6)	A987G	0.68% (16)	A594V	4.66 (111)	H411Y	2.17% (27)	C325F	2.25% (33)
P522S	0.64% (15)	Q578H	0.21% (5)	P522S	0.64% (15)	C603W	3.99% (95)	C480F	1.53% (19)	L257F	0.48% (7)
F412L	0.26% (6)	A834P	0.17% (4)	F412L	0.26% (6)	L595F	1.51% (36)	F342Y	0.96% (12)	C325W	0.41% (6)
L545S	0.26% (6)	D515Y	0.17% (4)	L545S	0.26% (6)	H520Q	1.34% (32)	T409M, H411Y	0.64% (8)	C325R	0.20% (3)

[1]No antiviral drug resistance conferring mutations detected for the indicated drug and CMV gene.

BOS7_6 THE RISK OF VENOUS THROMBOEMBOLISM IS ENHANCED AFTER A CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENT

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Background: In immunocompetent patients, past CMV infections have been associated with an increased risk of venous thromboembolism (VTE). In this study, we have investigated in a large prospective cohort of kidney transplanted recipients (KTR) whether the occurrence of a CMV infection which is the most frequent pathogen encountered within the first-year post transplantation could be followed by an increased risk of VTE in addition to the risk of the post-operative period, or repeated hospitalizations.
Methods: We conducted a study on the multicentric DIVAT database which was carried out prospectively and exhaustively on key dates during post-operative follow-up of clinical and biological data for all incident KTR belonging to 8 French transplantation centers (CNIL decision DR-2015-087, N°914184). Multivariable cause-specific time-varying Cox models stratified on centers were used to estimate the relationship between the risk of VTE occurring after well documented first CMV infections (asymptomatic or disease) and which were considered as a time-dependent variable.

Results: 15433 KTR transplanted between 2000 and 2021 were included among whom 1756 presented a CMV infection with a cumulative incidence at 1- and 2 years respectively of 11.6% [95% CI from 11.1% to 12.2%] and 13% [95% CI from 12.4% to 13.5%]). Within the same period of survey VTE occurred in 5.53% (95% CI from 5.17% to 5.92%) and 6.71% (95% CI from 6.31% to 7.14%) at 1- and 2 years respectively. CMV and VTE was observed in 87 KTR. The final multivariable cause-specific time-varying Cox model stratified on centers showed that after a first asymptomatic CMV infection (n=1176) the risk of VTE is 1.61 [95%CI 1.19; 2.17]. The risk enhanced at 2.00 [95%CI 1.32 ; 3.02] after a symptomatic infection (n=574) in comparison to similar patients free of CMV infection and independently of recipient age, past history of TVE and post-transplant surgical complications. Finally, the increased risk of VTE occurrence did not change whatever it was a primo or a reactivation of the CMV
Conclusion: After CMV infections and particularly in case of CMV disease, there is an increased risk of VTE. Since to the high frequency of CMV infection after a kidney transplantation, transplant physicians should be aware of such association for a rapid diagnosis and adapted treatment.

BOS7_7 IMPACT OF PROTON PUMP INHIBITORS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Proton pump inhibitors (PPIs) are frequently used after renal transplantation and often maintained afterward. However, many studies report complications related to the use of PPIs, especially in terms of nephrotoxicity on native kidneys. Nevertheless, data concerning the use of PPIs in renal transplantation remain scare.
Methods: We retrospectively analyzed all kidney transplant recipients at the Nantes University Hospital between 01/01/2000 and 31/12/2020. In order to approach a clinical trial methodology, patients were categorized according to whether or not they were taking PPIs at D15, and then analyzed in Intention to Treat. The primary endpoint was graft survival. Secondary endpoints were biopsy proven rejection, all-cause infections, and digestive bleeding complications. Analyses were performed using a multivariate Cox model.
Results: 2379 patients were included, 1401 in the PPI group and 978 in the non-PPI group. The median follow-up time was 6 years. In multivariate analysis, patients in the PPI group did not have a significant excess risk of graft loss (HR = 0.86; CI95% = 0.69 ;1.06). There was a statistically non-significant trend towards an increase in occurrence of rejection (HR = 1.24; CI95% = 0.95; 1.60) and a higher risk of infectious complications (HR = 1.13; CI95% = 1.01; 1.29) in the PPI group. The occurrence of bleeding complications did not differ between groups (HR = 1.12; CI95% = 0.75; 1.69).
Conclusion: In our cohort analyzed in Intention to Treat, the use of PPIs did not impact graft survival nor the occurrence of bleeding complications but increased the occurrence of infectious complications.

BOS7_8 HYPERCHOLESTEROLEMIA IMPAIRED CAPILLARY VEGF AND NITRIC OXIDE AND, IN TURN, DECREASED MICROVASCULAR DENSITY AND TUBULAR VILLIN IN RENAL ALLOGRAFTS

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Background: The changes during angiogenesis in aging and hypercholesterolemia (HC) are not well defined. Experimental studies showed that aged endothelial cells (ECs) might produce less NO and VEGF, resulting in reduced glomerular capillaries (GCs) and peritubular capillaries (PTCs). Chronic ischemia resulting from reduced GCs and PTCs is considered a significant factor for renal injury. To understand whether the microvascular loss was due to changes in angiogenic factors affected by age and cholesterol, we investigated the impact of age and cholesterol on the density of GCs and PTCs.
Methods: Among 150 patients, 63 (42%) had HC. Biopsies were highlighted with CD31 and HLA-DR to determine the mean number of GCs and PTCs. PCNA, VEGF, and NO expression of GCs and PTCs examined. EC proliferation index (PI) of GCs and PTCs assessed by the number of PCNA-positive cells. Villin expression and PI of tubules were examined to determine the degree of tubular injury.
Results: The mean capillary numbers were 38,4±15,2 and 27,6±14,4 for GCs and PTCs, respectively. VEGF and NO expression of both GCs and PTCs and the PI of all capillaries decreased with increasing donor age and serum cholesterol levels (p<0.001). The PI index of ECs and tubule cells showed a negative correlation with the VEGF and NO expression of both GCs and PTCs (p<0.001). The number of PTCs correlated significantly with PTC inflammation, PTC-VEGF expression, PTC-NO expression, tubular villin, proteinuria, hypertension, IF development, and graft loss (P<0.001 for all). The GC loss was also significantly associated with GC inflammation, GC-VEGF expression, GC-NO expression, tubular villin, proteinuria hypertension, GS development, and graft loss (P<0.001 for all). IF development was found to increase with the decreasing degree of tubular villin and tubular cell PI index.
Conclusions: A marked loss of capillary VEGF & NO expression associated with aging and HC resulted in a significant loss of GCs and PTCs. The loss of PTCs and GCs significantly correlated with the severity of the tubular injury, proteinuria, hypertension, and development of IF and GS. We suggested that donor age and HC influenced graft survival negatively by impairing the microvasculature and tubular integrity in renal allografts.

BOS7_9 ADVERSE OUTCOMES AFTER ALEMTUZUMAB THERAPY FOR KIDNEY TRANSPLANT REJECTION

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Background: Alemtuzumab is used off-label as a lymphocyte-depleting therapy for severe or glucocorticoid-resistant kidney transplant rejection. Despite the efficacy and apparent short-term safety of alemtuzumab, concerns about the long-term adverse effects of lymphocyte depletion remain. To date, the impact of alemtuzumab-therapy on patient survival, infection and malignancy are unclear. In this retrospective study, we report the occurrence of death, infections and malignancy of a large cohort of patients treated with alemtuzumab for kidney transplant rejection.
Methods: We compared clinical data of kidney transplant recipients treated with and without alemtuzumab for rejection between January 1st 2012 and January 1st 2022. Using a multivariable, time-varying Cox proportional hazard model we evaluated the effect of alemtuzumab on the general risk of death and risk of death from infection or malignancy. Additionally, the association between alemtuzumab and malignancy incidence was analyzed with a negative binomial regression model.
Results: During the study period, 213 kidney transplant recipients were treated with alemtuzumab for rejection. 1691 kidney transplant recipients were included who didn't receive alemtuzumab as an anti-rejection treatment. Baseline characteristics were comparable (Table 1). Alemtuzumab-therapy was associated with a higher probability of death (HR 1.63, 95%-CI 1.22 to 2.20) and infection-related death (HR 1.82, 95%-CI 1.08 to 3.05), but not with malignancy-related death. Alemtuzumab-therapy was also not associated with a higher incidence of overall malignancies, solid malignancies, skin malignancies or hematological malignancies.
Conclusions: Treatment with alemtuzumab for kidney transplant rejection is associated with a higher probability of death and infection-related death, but not malignancy-related death or the number of malignancies. These results suggest that infections are the most important long-term complication of alemtuzumab for kidney transplant recipients.

		Patient group		Statistic[1]
		Alemtuzumab (n = 213)	Control (n = 1,691)	P-value
Recipient age at Tx	Median (IQR)	56.00 (39.00, 64.00)	59.00 (49.00, 67.00)	<0.01
Recipient gender	Female/Male (%)	86/127 (40.40%/59.60%)	642/1,049 (38.0%/62.0%)	0.50
Recipient BMI	Median (IQR)	26.91 (23.55, 32.02)	26.35 (23.40, 30.10)	0.04
	Unknown or missing	1 (0.47%)	1 (0.06%)	
Diabetes mellitus at Tx	No/Yes (%)	146/66 (68.90%/31.10%)	1,190/500 (70.40%/29.60%)	0.63
	Unknown or missing (%)	1 (0.47%)	1 (0.06%)	
Cardiac event at Tx	No/Yes (%)	184/29 (86.40%/13.60%)	1,399/289 (82.90%/17.10%)	0.21
	Unknown or missing (%)	0 (0.00%)	3 (0.18%)	
Vascular event at Tx	No/Yes (%)	194/19 (91.10%/8.90%)	1,559/130 (92.30%/7.70%)	0.50
	Unknown or missing	0 (0.00%)	2 (0.12%)	
CVA prior to at Tx	No/Yes (%)	192/21 (90.10%/9.90%)	1,499/190 (88.80%/11.20%)	0.64
	Unknown or missing (%)	0 (0.00%)	2 (0.12%)	
Primary kidney disease	Hypertension (%)	11 (5.20%)	133 (7.90%)	0.21
	Diabetes mellitus (%)	18 (8.50%)	97 (5.70%)	0.13
	Glomerulonephritis (%)	13 (6.10%)	72 (4.30%)	0.22
	PKD (%)	14 (6.60%)	78 (4.60%)	0.23
	Reflux nephropathy (%)	8 (3.80%)	39 (2.30%)	0.24
	Other (%)	139 (65.30%)	1,212 (71.70%)	0.05
	Unknown (%)	10 (4.70%)	60 (3.50%)	0.44

Table 1: Patient baseline characteristics

[1] Kruskal-Wallis (continuous variables) or Fisher's exact (categorical variables) test

BOS7_10 THE OUTCOME PREDICTION VALUE OF PROTEINURIA AND ALBUMINURIA BY DIFFERENT WAYS OF MEASUREMENT IN KIDNEY TRANSPLANTATION

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Background: Increased urinary excretion of protein and albumin are associated with adverse outcomes in kidney transplant recipients. However, the optimal test for proteinuria and albuminuria at one-year posttransplant to identify patients at risk is uncertain.
Methods: We analyzed 1264 adult kidney transplant recipients with stable graft function in this retrospective, observational cohort study. The predictive performance of one-year-posttransplant spot urine protein-creatinine ratio (uPCR), albumin-creatinine ratio (uACR), 24-hour urine protein excretion (24hPE), and 24-hour urine albumin excretion (24hAE) as well as urinary dipstick protein (uDSP) on five-year death-censored graft loss (DCGL) and all-cause mortality were compared.
Results: Patients were followed up for a median of 8.17 (25th-75th percentile, 4.47-11.84) years, during which 58 (4.59%) patients developed graft loss and 88 (6.96%) patients died within five-year posttransplant. The predictive performance of uDSP for DCGL was lower (area under the receiver-operating characteristic curve [AUC] 0.61, *P* = 0.005) than 24hPE, uPCR, 24hAE, and uACR (AUC 0.65, 0.68, 0.72, and 0.74, respectively, all *P* <0.001). Results were similar for the mortality outcome. Elevated uACR was associated with increased DCGL (adjusted hazard ratio [aHR] 7.45, 95% confidence interval [95% CI] 2.05-27.13, *P* = 0.002) as well as cumulative mortality (aHR 2.93, 95% CI 1.23-6.95, *P* = 0.015), whereas, uDSP was not associated with DCGL or cumulative mortality.
Conclusions: In patients with stable graft function, measuring albuminuria and uACR showed the best performance in predicting 5-year outcomes after kidney transplantation. Dipstick proteinuria measurement performed poorly on outcome prediction. Our data suggest that albuminuria measured as spot uACR should be the method of choice for routine care and research, while uDSP test does not reliably predict outcomes.

BOS7_11 TUBULORETICULAR INCLUSIONS: A NEW PROGNOSTIC BIOMARKER IN KIDNEY TRANSPLANTATION

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Background: Tubuloreticular inclusions(TRIs) seen on electron microscopy(EM) are classically associated with lupus nephritis(LN) and systemic viral infections in native biopsies. Traditionally a marker for enhanced type I interferon expression, little is known about their significance post-transplant. We aimed to look at a large cohort of transplant biopsies showing TRIs to investigate associations and outcomes.
Methods: A retrospective analysis was performed on two prospective databases; an in-centre transplant registry and a histopathology database holding data on all kidney biopsies performed at our centre. All patients biopsied since 2015, who had EM examination were included. Where patients had more than one biopsy showing a TRI the earliest one was included. Demographic, clinical and transplant data was collected from the laboratory records. ABO incompatible transplants were excluded.
Results: 998 kidney transplant biopsies were performed between December 2005 and December 2022; 1740 (21.7%) had EM performed. Of 1740 with EM, 256 (14.7%) had evidence of TRIs on at least one biopsy. Of 256 patients, 34% were female, the median age was 52.3 years (38.9-59.4), 28% had underlying glomerulonephritis as their cause of ESKD, 61% were deceased donors and 68% were of non-white ethnicity. TRIs were associated with serological evidence of autoimmunity (17%), viral infections (28%) and donor specific antibodies (35 %), with no association found in 34%. Rejection occurred in 127 (50%), including 38(44%) of patients with no recognised association with TRIs. Allograft outcomes were poor, with all-cause allograft survival and death-censored allograft survival of 54% and 70% after a follow up of 5.7 +/- 3.8 years post index biopsy. A comparison with a matched control group is underway.
Conclusions: In extension to previous work, we show that TRIs appear to be associated with alloimmunity. In this regard they may be a useful biomarker especially in cases where the diagnosis is unclear or biopsy findings are 'subthreshold'. Irrespective of aetiology, TRIs are associated with poor outcomes and warrant further consideration.

BOS7_13 RISK OF BLEEDING AFTER PERCUTANEOUS GRAFT KIDNEY BIOPSY IN PATIENTS RECEIVING LOW DOSE ASPIRIN A SINGLE CENTER RETROSPECTIVE STUDY

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Background: Although discontinuation of low-dose aspirin (ASA) at least 5 days before kidney biopsy is recommended by most guidelines and commonly advised by nephrologists, the evidence behind this practice is very low. Indeed, few non-randomized studies previously showed a similar rate of bleeding after native kidney biopsy in patients who received ASA and those who did not; data on kidney transplant biopsy are scant. Withdrawal of antiplatelet agents has been associated with an increase in cardiovascular events.
Methods: We conducted a single center cross-sectional study comparing the risk of complications after percutaneous ultrasound-assisted graft kidney biopsy in patients who received ASA within 5 days from biopsy and those who did not. The main outcome was the difference in the proportion of major complications (red blood cells transfusion, need for selective arterial embolization, surgical revision, nephrectomy).
Results: We analyzed 272 biopsies; 160 (58,82%) were conducted in patients receiving ASA (within 5 days from biopsy). Characteristics of our cohort are reported in table 1. A single (or a combination of) major complication occurred in 0/112 of patients without and in 1/160 (bleeding requiring endovascular embolization) patients with ASA, with non-significant difference (percentage point difference 1%, 95% CI -1% to 2%, p=0,4). There were 14/112 (12,5%) minor complications in patients without and 13/160 (8,13%) in patients with ASA, with non-significant difference (percentage point difference 4%, 95% CI -12% to 3%, p=0,23). All events occurred within 24h from biopsy. There was no difference in the proportion of complications in patients who received ASA in the last 48 hours or 3-5 days before the procedure. At the univariate logistic regression, no clinical or laboratory parameter were significantly associated with the occurrence of complications. There were also no differences comparing biopsies according to needle size (16 or 18 gauge); nevertheless, procedures with 18 gauge needle resulted in a significantly lower number of glomeruli in sample.
Conclusions: Receiving low-dose ASA within 5 days from percutaneous graft kidney biopsy did not increase the risk of major or minor complications in our cohort.

Table 1. Clinical, demographic and laboratory characteristics.

Variable	All patients	No antiplatelet	Antiplatelet	p
n. of biopsies	272	112	160	
age, yr	52,85 (12,84)	51,65 (13,33)	53,69 (12,46)	0,197
male, nr (%)	177 (65,07)	69 (61,61)	108 (67,5)	0,366
body weight, kg	72,5 (15,8)	72,46 (16,02)	71,79 (16,04)	0,825
body mass index	24,69 (22,49-27,43)	24,49 (22,41-28,27)	25,18 (22,46-27,26)	0,534
Systolic blood pressure, mmHg	139,7 (18,69)	140,5 (17,61)	139,2 (19,44)	0,358
Diastolic blood pressure, mmHg	81,27 (11,1)	83,08 (11,18)	80,04 (10,91)	0,028
Platelet count, n*10^3/ul	190 (146,25-251,75)	184,5 (130,25-252,75)	198,5 (159,25-249,75)	0,203
I.N.R.	1,06 (0,99-1,13)	1,08 (0,99-1,15)	1,06 (0,99-1,12)	0,214
aPTT ratio	0,97 (0-9-1,05)	0,98 (0,9-1,08)	0,96 (0,89-1,04)	0,102
Hemoglobin pre-biopsy, g/dl	10,6 (9,6-11,5)	10,5 (9,5-11,5)	10,6 (9,7-11,48)	0,786
Hemoglobin 24h post-biopsy, g/dl	10,6 (9,7-11,63)	10,5 (9,55-11,95)	10,7 (9,8-11,4)	0,646
serum creatinine, mg/dl	2,5 (1,83-3,41)	2,75 (1,85-3,81)	2,35 (1,81-3,34)	0,144
estimated GFR, ml/min per 1.73 m2	25,65 (17,23-38)	25 (14,25-36,53)	27,35 (19-39,75)	0,102
eGFR < 30 ml/min, nr (%)	158 (58,1)	71 (63,39)	88 (55)	0,172
eGFR < 15 ml/min, nr (%)	56 (20,6)	28 (25)	28 (17,5)	0,170
serum urea, mg/dl	88 (64,25-133,8)	90 (64,25-149,8)	86 (64,5-128)	0,391
proteinuria / creatininuria	0,9 (0,3-2,78)	1,33 (0,4-4)	0,76 (0,3-2,4)	0,068
serum albumin, g/dl	3,6 (3,2-3,9)	3,5 (3,1-3,9)	3,6 (3,26-4)	0,054
urgent biopsy, nr (%)	127 (46,69)	53 (47,32)	74 (46,25)	0,902
Acute kidney injury, nr (%)	55 (20,22)	30 (26,79)	25 (15,63)	0,031
Nephrotic syndrome, nr (%)	18 (6,62)	6 (5,36)	12 (7,5)	0,622
hypertesion,nr (%)	225 (82,72)	92 (82,14)	133 (83,13)	0,871
chronic viral infection, nr (%)	55 (20,22)	25 (22,32)	30 (18,75)	0,540
diabetes mellitus, nr (%)	42 (15,44)	14 (12,5)	28 (17,5)	0,308
use of anticoagulants within 5 days, nr (%)	14 (5,15)	11 (9,82)	3 (1,88)	0,005

BRIEF ORALS

Complications and infections after kidney transplant

BOS7_14 IMPACT OF ALLOGRAFT CELLULAR INFLAMMATION ON THE IGA NEPHROPATHY RECURRENCE AFTER KIDNEY TRANSPLANTATION

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Background: The recurrence of IgA nephropathy (rIgAN) after kidney transplantation (KT) is relative frequency and impairs KT outcomes, representing the third cause of loss in KT recipients. Several variables at the time of recurrence, (e.g. impaired allograft function, heavy proteinuria, steroid withdrawal, and MEST-C histological findings have been associated with a higher risk of graft loss after rIgAN. The presence of allograft clinical or subclinical inflammation has been associated with a higher risk of graft loss, but it is not precisely known how it influences the outcome of patients with rIgAN.
Methods: A multicenter retrospective study was carried out including KT recipients with biopsy-proven IgA nephropathy as the underlying disease in which the recurrence of the primary disease had been proven by means of graft biopsy and in which the Banff criteria were available or could be reviewed. Allograft cellular inflammation was defined according to Banff scores as “t” or “i” ≥2. The main endpoint was progression to CKD stage 5 or death censored-graft loss (DCGL).
Results: 118 KT recipients were included (47±14 ys. at recurrence), 80% male, with a mean time to biopsy of 65±69 mo. and a post-transplant follow-up of 118 ± 70 months. After recurrence, 34 (28.8%) allografts were lost after 35±28 mo., excluding death. By univariate Cox regression, the factors related to CKD stage 5 or graft loss were systolic blood pressure (HR 1.039, 95%CI 1.016-1.064, p = 0.001), glomerular filtration rate (HR 0.948, 95%CI 0.922-0.974, p <0.001), the logarithm of proteinuria (HR 15.836, 95% CI 5.504-45.565, p < 0.001), Oxford-C score (HR 3.490, 95% CI 2.137-5.699, p <0.001), interstitial fibrosis (HR 2.173, 95% CI 1.362-3.468, p = 0.001) and cellular inflammation (HR 2.458, 95% CI 1.237-4.884, p = 0.010). By multivariate analysis, allograft inflammation remained significantly related to CKD stage 5 or DCGL (HR 2.338, 95% CI 1.077-5.075, p = 0.032), independently of systolic blood pressure, glomerular filtration rate, proteinuria and Oxford-C score.
Conclusions: Allograft cellular inflammation influences worsens KT outcomes after rIgAN. We suggest to considering the Banff criteria for acute cellular inflammation to better understand the subsequent evolution of patients with rIgAN.

Kidney allograft immunopathology

BOS8_1 HUMAN LEUKOCYTE ANTIGEN MISMATCHES AND GRAFT OUTCOMES IN THE CONTEMPORARY ERA OF IMMUNOSUPPRESSION: A UK REGISTRY ANALYSIS

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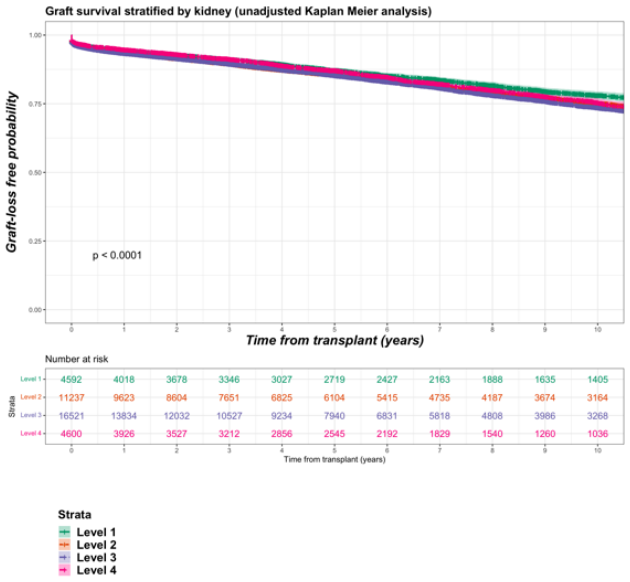
Background: The impact of human leukocyte antigen (HLA) mismatching on kidney transplant outcomes is unclear. A recent meta-analysis of 23 cohort studies concluded HLA mismatching was a critical prognostic factor for graft loss, especially HLA-DR, but the majority of included studies did not reflect contemporary use of immunosuppression. The aim of this study was to investigate this using contemporary UK transplant registry data.
Methods: A retrospective cohort study was undertaken of prospectively collected registry data of all kidney transplant recipients in the United Kingdom from January 1, 2000 until September 30, 2019 inclusive. HLA mismatch levels were defined by national criteria; level 1 (HLA mismatch 0), level 2 (HLA mismatch 0 DR and 0/1 B), level 3 (HLA mismatch 0 DR and 2B, or 1 DR and 0/1 B), and level 4 (1 DR and 2B, or 2 DR). The primary outcome was death-censored graft loss. Time-to-graft loss was modelled using weighted estimation of Cox regression to account for non-proportional hazards, with covariate adjustment. All analyses were done using R statistical software (version 4.2.2).
Results: A total of 37,251 kidney transplant recipients formed the study cohort. HLA mismatches were as follows; level 1 (12.4%, n=4,592), level 2 (30.4%, n=11,237), level 3 (44.7%, n=16,521), level 4 (12.4%, n=4,600). Increasing level of HLA mismatches were associated with risk for 3-month rejection; level 1 (11.0%), level 2 (13.4%), level 3 (14.4%) and level 4 (18.1%) (p<0.001). In an adjusted weighted Cox regression model with level 1 the reference, there was no increased risk for death-censored graft loss with level 2 (HR 1.18, 95% CI 0.77-1.82), level 3 (HR 1.11, 95% CI 0.76-1.62) and level 4 (HR 1.31, 95% CI 0.88-1.97). Exploring HLA mismatches in isolation, no significant difference was observed with either 1 or 2 HLA A or B mismatches. Just exploring HLA DR mismatches, no significant difference was observed with 1 (HR 1.01, 95% CI 0.85-1.19) but borderline association with observed with 2 (HR 1.30, 95% CI 0.99-1.71) HLA DR mismatches.
Conclusions: In the current era of immunosuppression, level of HLA mismatches does not contribute to long-term death-censored graft survival. Unless clinically indicated (e.g., younger kidney transplant candidates), HLA mismatching should not influence choice of allograft.



BOS8_2 PATTERNS OF MAJOR-HISTOCOMPATIBILITY-COMPLEX (MHC) CLASS I–RELATED CHAIN A (MICA) ALLOIMMUNE RESPONSES REVEALED BY MACHINE LEARNING ALGORITHMS

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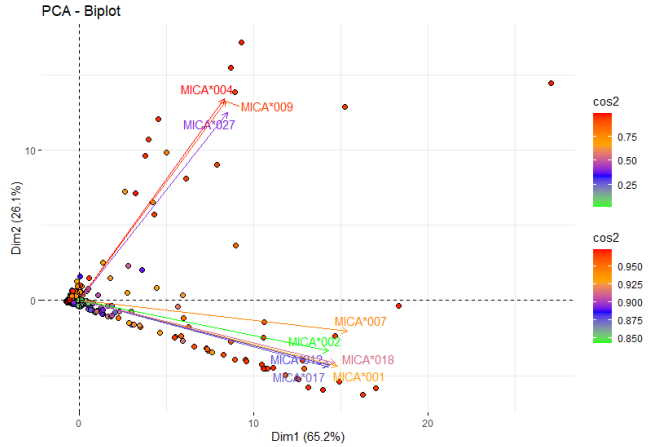
Background: Antibodies against Major histocompatibility complex class I–related chain A antigens (anti-MICA) in kidney transplantation (KTx) have been associated with rejection episodes and reduced graft survival. MICA cross-reactive epitope groups (CREGs) are not full described. This study aimed to the unsupervised identification of MICA CREGs in KTx patients, thus providing more information regarding their role in immune responses.
Methods: A cohort of 1208 KTx patients were enrolled from 2006-2022 and tested by single antigen bead assay (One Lambda). Initially, the antibody responses to 9 common MICA between different lots, were analyzed in all patients. In 336 patients, the analysis was repeated adding 6 additional MICA alleles to the antibody response control, studying a total of 15 MICA. Knowing that the immune system usually responds to "shared" immunogenic targets, the clustering patterns of anti-MICA responses without any a priori hypothesis using Principal Component Analysis (PCA), was studied. MICA protein sequence alignment was performed utilizing the IMGT/HLA alignment tool. The response clusters polymorphisms were determined with the 57 verified MICA epitopes in the Registry of HLA Epitopes.
Results: PCA projection, revealed that anti-MICA responses can be explained by two major distantly related CREGs filling the upper and lower quadrant of the PCA biplot respectively (figure 1). Protein sequencing alignment of the two groups, showed that they express dimorphism at positions 36Y/C, 129V/M and 173 E/K corresponding to 6 confirmed functional MICA antigenic epitopes. Three additional nonlinear epitopes were identified in the upper (206S) and lower (206GWS and 215S) quartile group respectively. Responses to 6 additional alleles (MICA*005,*006,*015,*019,*028, *046) did not affect the clustering of previous responses confirming the antigenicity of the above epitopes.
Conclusions: Machine learning approaches can be considered for objective clustering and measuring of antigenic distances of anti-MICA responses. Two major bead-array defined CREGs were clearly identified and were explained by specific amino acid differences. Knowledge of MICA associations may guide allograft and immunosuppression strategy selection, thus improving long graft survival and KTx success.

Figure 1.



BOS8_3 EARLY SYSTEMIC VASCULAR INFLAMMATION SCORE IS ASSOCIATED WITH I-IFTA IN BIOPSIES 6-WEEKS AND 1-YEAR AFTER KIDNEY TRANSPLANTATION

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Background: Inflammation in areas with interstitial fibrosis and tubular atrophy (i-IFTA) is associated with progression of interstitial fibrosis and reduced kidney graft survival. The presence of i-IFTA in early surveillance biopsies is also associated with the development of de novo donor-specific HLA-antibodies one year after kidney transplantation (KT). We have previously shown associations between systemic inflammation scores, based on combinations of 21 plasma biomarkers to cover relevant pathways, and patient survival. In this study, we have investigated the association between these scores six weeks after transplantation and i-IFTA in biopsies after six weeks and one year after KT.
Methods: Between 2009-2012, early surveillance biopsies were performed in 695 patients, and biopsies at one year were performed in 574 patients. The lesions were graded according to the Banff criteria, and they were classified into four groups: 1) normal histology, 2) inflammation, 3) IFTA, and 4) i-IFTA. Logistical regression analyses were performed to study predictors, including pathway-specific inflammation scores, of the different histological groups.
Results: The histological diagnosis at 6 weeks was: normal (n=265), inflammation (n=40), IFTA (n=285), and i-IFTA (n=105), and at 1 year after transplantation: normal (n=237), inflammation (n=30), IFTA (n=228), and i-IFTA (n=79). In the multivariable logistic regression model with i-IFTA at 6 weeks as outcome variable (table 1), multiple transplantations, number of HLA-DR mismatches and vascular inflammation score (both as continuous and categorical variable) showed significant associations. In the model regarding i-IFTA at one year, HLA-DR mismatches, usage of cyclosporine, and vascular inflammation score were statistically significant. Inflammation scores representing other pathways did not come out statistically significant regarding i-IFTA. When the individual systemic biomarkers were included in the logistic regression model, CXCL16, sTNFR1, PTX3, syndecan1, and osteopontin were significantly associated with i-IFTA at six weeks. Only sTNFR1 was associated with i-IFTA at one year.
Conclusions: Subclinical systemic vascular inflammation early after KT is associated with i-IFTA in biopsies both six weeks and one year after transplantation.

Table 1: Multivariable logistic regression model showing associations between predictors and i-IFTA in biopsies six weeks and one year after kidney transplantation.

	Six weeks after transplantation			One year after transplantation		
	OR	95% CI	P-value	OR	95% CI	P-value
Age (years)	0.98	0.96-1.00	0.096	0.99	0.97-1.01	0.377
Donor age (years)	1.01	0.99-1.03	0.155	1.00	0.99-1.03	0.403
Ischemic time (hours)	0.99	0.96-1.03	0.994	1.68	0.97-2.90	0.064
HLA DR mismatches (n)	2.26	1.37-3.74	0.001	2.32	1.31-4.11	0.004
PRA (> 20%)	1.66	0.60-4.62	0.331	2.18	0.70-6.82	0.180
Cyclosporine (yes)	1.63	0.98-2.70	0.331	1.83	1.03-3.26	0.039
Delayed graft function (yes)	1.12	0.54-2.34	0.761	1.09	0.44-2.67	0.854
dnDSA at time of biopsy	0.68	0.19-2.47	0.553	1.33	0.51-3.46	0.563
Vascular inflammation score (continuous)	1.06	1.022-1.098	0.002	1.05	1.01-1.10	0.016
Vascular inflammation score (categorical – 4th quartile)	2.87	1.50-5.50	0..001	2.88	1.36-6.10	0.006

BOS8_4 EARLY SYSTEMIC SUBCLINICAL INFLAMMATION SCORES ARE ASSOCIATED WITH SIGNIFICANT RISK FOR LONG-TERM KIDNEY GRAFT FAILURE

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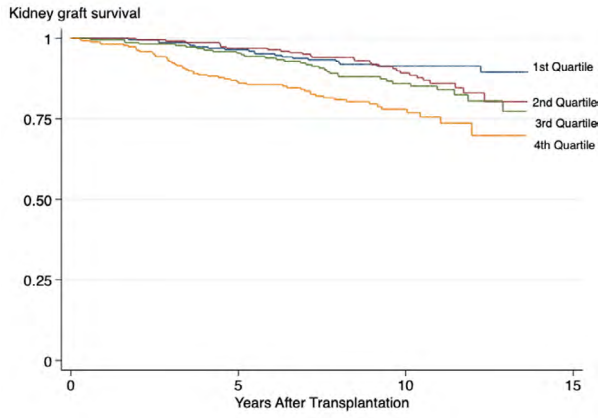
Background: Early graft failure after kidney transplantation (KT) is mainly a result of acute rejection or surgical complications, while long-term graft failure is due to multifactorial conditions. An inflammatory profile in kidney transplant recipients is associated with increased long-term mortality, and specific inflammatory biomarkers have shown association with long-term graft failure. In this study we have examined the association between early subclinical systemic inflammation scores following kidney transplantation and long-term kidney graft failure.
Methods: We measured 21 inflammatory biomarkers 10 weeks after KT in 1044 patients. Low-grade inflammation was assessed with predefined inflammation scores based on specific biomarkers: one overall inflammation score and five pathway-specific scores representing fibrogenesis, vascular inflammation, metabolic inflammation, angiogenesis, and leukocyte activation. The scores were tested in Cox regression models adjusted for established risk factors. Death-censored kidney graft failure was the primary outcome variable.
Results: Median follow-up time was 9.8 years (interquartile range 7.6-11.4 years). When tested as a continuous variable, the overall inflammation score was associated with long-term kidney graft failure (HR 1.03, 95% CI: 1.02-1.05, p-value <0.001). When the score was assessed as a categorical variable with the 1st quartile as reference, the 4th quartile was also associated with long-term death-censored kidney graft failure (HR 3.12, 95% CI: 1.71-5.69, p-value <0.001, table 1, figure 1). In the pathway-specific analyses, fibrogenesis activity and vascular inflammation stood out (table 1).
Conclusions: In conclusion, based on total inflammatory- and pathway-specific scores, we have described a significant association between an inflammatory environment early after kidney transplantation and long-term kidney graft failure. Vascular inflammation and increased fibrogenesis activity stood out among the tested pathways and could be potential targets in future intervention studies.

Table 1: Adjusted Cox regression analyses of inflammation scores and death-censored kidney graft failure

Pathway-specific inflammation score	Score as continuous variable (HR, 95% CI, p-value)	2nd Quartile (HR, 95% CI, p-value)	3rd Quartile (HR, 95% CI, p-value)	4th Quartile (HR, 95% CI, p-value)
Overall inflammation score	1.03 (1.02-1.05, p<0.001)	1.21 (0.68-2.16, p=0.524)	1.69 (0.95-3.00, p=0.074)	3.12 (1.71-5.69, p<0.001)
Fibrogenesis	1.05 (1.02-1.08, p=0.004)	1.34 (0.78-2.32, p=0.292)	1.50 (0.85-2.63, p=0.163)	2.05 (1.22-3.73, p=0.020)
Vascular/general inflammation	1.07 (1.03-1.10, p<0.001)	1.58 (0.89-2.80, p=0.115)	2.38 (1.37-4.15, p=0.002)	2.83 (1.60-5.02, p<0.001)
Metabolic inflammation	1.03 (0.99-1.07, p=0.109)	1.40 (0.80-2.44, p=0.240)	0.93 (0.52-1.64, p=0.792)	1.65 (0.93-2.92, p=0.087)
Growth-/angiogenesis	1.02 (0.98-1.06, p=0.373)	1.01 (0.61-1.65, p=0.982)	1.03 (0.60-1.18, p=0.926)	1.21 (0.73-2.00, p=0.470)
Leukocyte activation	1.03 (1.00-1.07, p=0.097)	1.10 (0.65-1.88, p=0.724)	1.47 (0.88-2.48, p=0.144)	1.43 (0.81-2.53, p=0.212)

Figure 1: Kaplan-Meier plot: association between the overall inflammation score and kidney graft survival.



BOS8_6 PRECISE COMPOSITION AND LOCALIZATION OF THE INFLAMMATORY BURDEN OF 125 KIDNEY TRANSPLANT REJECTIONS: DETERMINANTS AND PROGNOSIS IMPACT

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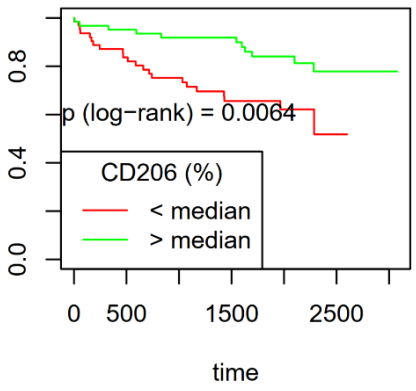
Background: The exact composition of the inflammatory burden during kidney transplant rejection has not been studied on large cohorts. We have recently shown an important heterogeneity in the cellular composition from one patient to another for the same type of rejection. We aim to study the determinants and impact of the cellular composition of infiltrates in a large cohort of 125 first episode rejection biopsies.
Methods: We used multiplex immunofluorescence on a cohort of 125 rejections (ABMR n=69; TCMR n=18; Borderline n=23; mixed n=15) to phenotype T and B lymphocytes, M1 (CD68+CD206-) and M2 (CD68+CD206+) macrophages and NK cells on the same biopsy slide with automated localization (intra- or extravascular) and quantification.
Results: The total cellular density was maximal during mixed rejection (1242/mm2), significatively superior to ABMR (604/mm2) or BL (564/mm2). During TCMR, the mean cellular density was 892/mm2. In all rejection types, most cells were located within the interstitium but there were more cells in the microcirculation during ABMR. In all types of rejection, the 2 main cell types were macrophages (59.2%), mostly M2, and T lymphocytes (33.2%), with few NK cells and B lymphocytes. However, ABMR was significantly enriched in macrophages, mainly M2, compared to TCMR (64.2% vs 50.8%; p=0.03). In the microcirculation, T lymphocytes were the main population in all types of rejections (55.2%). We confirmed the vast heterogeneity of the cellular composition within the same type of rejection. We found a global decrease in macrophage density and increase in T lymphocytes density with time post transplantation. Using a Cox model, we found that the most impactful population was macrophages. The intravascular density of M2 macrophages was associated with a better graft survival.
Conclusions: Multiplex IF applied on a large cohort of 125 rejection confirmed the predominance of macrophages, mainly M2, and T lymphocytes during all types of rejection, with a majority of cells located within the interstitium, and a large heterogeneity from one patient to another. Macrophages density is associated with prognosis with a positive correlation between M2 macrophages and graft survival.



BOS8_7 HIGH REJECTION RATES WITH NO INDUCTION+RAPID STEROID WITHDRAWAL IN WELL MATCHED LIVING DONOR KIDNEY TRANSPLANTS WITH PREFORMED TCELL ALLOREACTIVITY

Maria Meneghini*[1], Eduard Palou[2], Francesc Moreso[1], Edoardo Melilli[3], Marta Crespo[4], Laura Cañas[5], Carme Facundo[6], Ignacio Revuelta[7], Alba Torija[8], Elena Crespo[8], Oriol Bestard[1]

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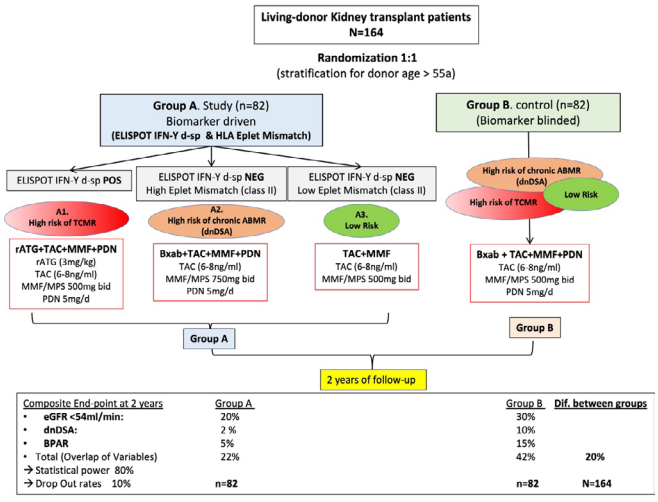
Background: Both *de novo* and preformed alloimmunity drive posttransplant immune-mediated events, that may be predicted by the assessment of donor/recipient HLA molecular mismatch and pretransplant circulating donor-reactive memory T cells (dR_mTc). To investigate the value of these biomarkers to allow safe immunosuppression (IS) individualization, we conducted a prospective, multicentre clinical trial in which first, living-donor kidney transplants (LDKT) were randomized to biomarker-guided IS regimens or to standard-of-care (SoC) therapy.

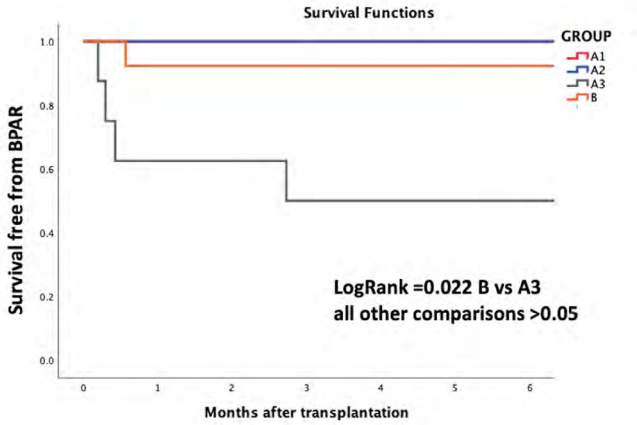
Methods: In this 2-year follow-up trial, run in 6 adult KT centres, IS individualization based on preformed dR_mTc (IFNg ELISPOT) and HLA-DR/DQ Eplet Mismatch (HLAMatchmaker) (group A) was compared to SoC IS (TAC/MMF/PDN; group B) on a composite endpoint made of loss of renal function, incidence of biopsy-proven acute rejection (BPAR) and *de novo* DSA. Patients with high dR_mTc frequencies (>25 IFNg spots/3x10^{5}PBMC) received Thymoglubulin induction (A1), patients with high DR/DQ Eplet MM received basiliximab and TAC-based triple therapy with higher MMF exposure (A2), and KT with both low DR/DQ Eplet MM and low dR_mTc received TAC/MMF with no induction and rapid (7-day) steroid withdrawal (A3).

Results: The study was prematurely halted when 39 LDKT were recruited due to exceeded BPAR rates in the A3 group (4/8; 50%), whereas none occurred in the other 2 biomarker-guided groups (A1, A2) and only 1/13 (8%) in SoC (group B). All rejections were T-cell mediated (3 Banff IA, 2 IIA) and occurred within the first weeks after transplant (25±32days) (figure). Assessment of baseline biomarkers revealed that LDKT developing BPAR within group A3, albeit lower than 25, these patients displayed detectable and significantly higher IFNg-producing mTc than those that did not reject (10.8±2.3 vs 2.3±4.0, p=0.05). Conversely, no differences on distinct donor/recipient HLA MM algorithms were observed. Notably, the patient in group B developing TCMR showed high frequencies of dR_mTc (>25 IFNg spots).

Conclusions: Rapid steroid withdrawal in absence of induction therapy in a TAC/MMF-based IS regimen should be highly discouraged in presence of low but detectable preformed donor-reactive mTC, despite good donor/recipient HLA molecular matching.



Composite End-point at 2 years	Group A	Group B	Dif. between groups
• eGFR <54ml/min:	20%	30%	
• dnDSA:	2 %	10%	
• BPAR	5%	15%	
• Total (Overlap of Variables)	22%	42%	20%
→ Statistical power 80%			
→ Drop Out rates 10%	n=82	n=82	N=164



BOS8_8 EUROPEAN SURVEY ON CLINICAL PRACTICE OF DETECTING AND TREATING T-CELL MEDIATED KIDNEY TRANSPLANT REJECTION

Priyanka Koshy*[1], Lucrezia Furian[2], Peter Nickerson[3], Gianluigi Zaza[4], Maria Haller[5], Aiko De Vries[6], Maarten Naesens[7]

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Background: The 2009 KDIGO guideline for treatment of acute rejection recommends the use of corticosteroids as the initial treatment and suggests using lymphocyte-depleting antibodies or OKT3 if the patient is nonresponsive to corticosteroids or if there is recurrence of acute cellular rejection. OKT3 is unavailable and it is unclear what is the current clinical standard of care in acute T-cell mediated rejection (TCMR) in EU. Adapting treatment guidelines to the current EU reality is necessary, also for novel clinical trial design.

Methods: An invitation was sent through ESOT/EKITA newsletters and through a social media campaign to transplant professionals in Europe for taking part in the survey. The survey was web-based through SurveyMonkey and was conducted in 2022.

Results: A total of 129 European transplant professionals responded to the survey, most were transplant nephrologists (78.1%). 92 major university hospitals across Europe were represented. There was equal representation of small sized and large sized transplant centres. There was heterogeneity between centres in the performance of protocol biopsies (always-36.2%; in specific groups-21.3%; never-42.5%). The kidney biopsies performed for the diagnosis of TCMR were evaluated by renal pathologists (91.7%). The common practices observed were that majority of the centres treat borderline changes (BL) and TCMR (Grade IA-B, IIA-B), in indication biopsies (99% for BL; 100% for TCMR) and in protocol biopsies (69.9% for BL; 100% for TCMR), with primarily steroids as the first line treatment. Thymoglobulin is used as second line treatment for TCMR Grade IA-B(72.1%) & TCMR IIA-B(74.8%). Alemtuzumab is not routinely administered since many centres in EU have not approved the drug for clinical use and it is not reimbursed. There were no differences observed between the large and small centres for the management of TCMR. No consensus was observed in the dosages of steroid therapy for the treatment of borderline changes and TCMR.

Conclusions: This survey highlights the common practices and diversity in clinics for management of TCMR in Europe. It also highlights the differences in clinical practices in EU from US and Canada.

BOS8_9 PROFILING THE IMMUNE CELL INFILTRATE OF KIDNEY ALLOGRAFTS IN RELATION TO THE EXISTING BANFF HISTOLOGY

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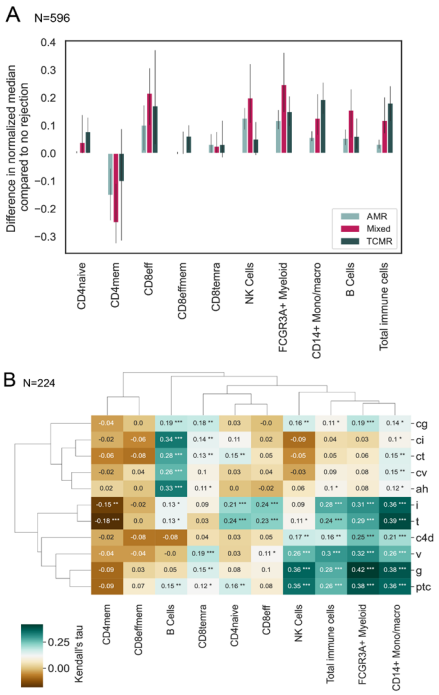
Background: The histological Banff classification for kidney transplant rejection currently includes limited information on the cell type composition of the immune infiltrate. Improved understanding of rejection's immune cell composition could help in developing targeted therapies. This study aims to explore the association of intragraft immune cell populations and Banff histology.
Methods: The proportions of nine infiltrating immune cell types were estimated via the deconvolution of two transcriptomic datasets (N_{total}=596) of kidney transplant biopsies using a novel signature matrix derived from single cell transcriptomics. Differences in cells proportion between No rejection and AMR, TCMR or Mixed rejection were assessed with Student t-tests. The association between cellular proportions and the ordinal Banff scores (t i v g ptc c4d [acute lesions] and cg ct ci cv and ah [chronic lesions]) was assessed with Kendall's tau on the first dataset (N=224).
Results: CD4 memory (CD4mem) cells were the only cells whose fractions were significantly higher in No rejection (on average +3.1% p<0.001) compared to Rejection. All other immune cells were significantly higher in Rejection. Mixed rejection was marked by the largest difference with No rejection in NK cells (+1.7% p<0.001), FCGR3A+ myeloid cells (+2.6% p<0.001), B cells (+2.2% p<0.001), and CD4mem (-5.1% p<0.001), although there were large overlaps in the cell composition between the rejection subtypes (Fig. 1A). TCMR demonstrated the highest degree of general inflammation (total immune cells, T_{ic}) (+16.5% p<0.001) and the largest increase in CD4 naïve (+1.8% p<0.001) and CD14+ monocytes (+5.9% p<0.001) compared to No rejection. Monocytes, NK cells and T_{ic} were positively associated with acute lesion scores (Fig. 1B). CD4 naïve and CD8 effector were positively associated with lesions *t* and *i*, whereas CD4mem was negatively associated. Overall, the immune cell types were poorly associated with the chronic lesions, except for B cells which positively associated with all chronic lesions (Fig. 1B).
Conclusions: Profiling kidney graft infiltrating immune cells showed an important involvement of monocytes and NK cells in acute rejection phenotypes. We are currently investigating how the complex immune cell composition of rejection relates to transplant outcomes.



BOS8_10 OUTCOMES OF STANDARD VERSUS DELAYED INITIATION OF TACROLIMUS IN RECIPIENTS OF DONATION AFTER CARDIOCIRCULATORY DEATH KIDNEY

Lan Zhu*[1], Zhangfei Shou[2], Jinliang Xie[3], Jianghua Chen[4], Changxi Wang[5], Wenli Song[6], Min Gu[7], Xiaofeng Zhou[8], Jing Wu[9], Martin Blogg[10], Mohamed Soliman[11], Ruijin He[9], Wujun Xue[12], Zhishui Chen[1]

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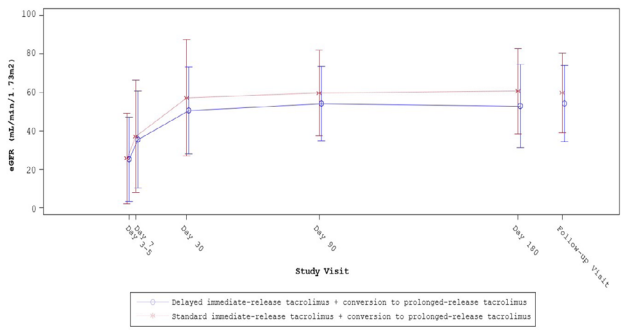
Background: The impact of tacrolimus initiation timing on graft function after receiving a donation after cardiocirculatory death (DCD) kidney transplant is not known. Therefore, this prospective phase IV open-label study explored clinical outcomes, including delayed graft function (DGF), in patients at 15 Chinese centers from 22 October 2018 to 15 July 2022.
Methods: Adults aged ≥18 years with end-stage kidney disease suitable for primary DCD kidney transplantation were randomized 1:1 to Group A (induction therapy + standard immediate-release tacrolimus initiated ≤24 h post-transplant) or Group B (induction therapy + delayed immediate-release tacrolimus initiated 48–120 h post-transplant). All patients were converted to maintenance immunosuppression with prolonged-release tacrolimus at 1-month post-transplant + conventional mycophenolic acid + corticosteroids. The primary endpoint was the incidence of DGF, defined as requirement for dialysis, within 7 days post-transplant. An upper limit of <15% for the 95% confidence interval (CI) of the relative difference in DGF incidence between the two groups was considered to show non-inferiority of delayed initiation of tacrolimus. Secondary endpoints included renal function (estimated glomerular filtration rate, eGFR) at 1 and 6 months and incidence of treatment-emergent adverse events (TEAEs).
Results: 278 recipients of DCD kidney transplants were randomized; 141 to Group A and 137 to B. The groups were similar in terms of baseline age, body mass index, sex, ABO blood groups and human leukocyte antigen mismatch. Incidence of DGF within 7 days post-transplant was non-inferior with delayed tacrolimus initiation (20.0%) versus standard tacrolimus initiation (23.9%; difference: −3.9% [95% CI −13.6 to 5.8]). eGFR remained stable over the 6-month study period and was consistent between both groups (Figure). Incidence of drug-related TEAEs was similar between groups (35.5% in Group A and 35.8% in Group B), and 19.8% of patients had drug-related serious TEAEs.
Conclusions: Delayed initiation of immediate-release tacrolimus was non-inferior to standard initiation for DGF within 7 days of DCD kidney transplantation. For both groups, post-transplant renal function remained stable over the 6-month study period and incidence of TEAEs was similar.

Figure. Renal function (eGFR) over time after cardiocirculatory death kidney transplant



Data show mean with error bars depicting ± standard deviation.
eGFR, estimated glomerular filtration rate.

BOS8_11 REAL-LIFE ASSESSMENT OF NON-INVASIVE MOLECULAR BIOMARKERS FOR PREDICTING CLINICAL AND SUBCLINICAL HISTOLOGICAL LESIONS IN KIDNEY TRANSPLANT RECIPIENTS

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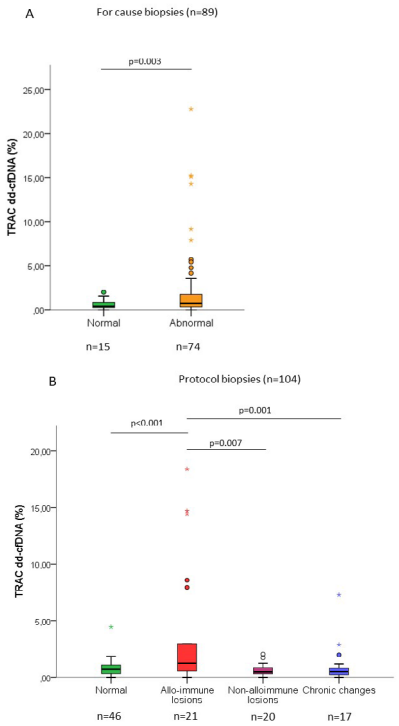
Background: Non-invasive biomarkers are intended to rule out alloimmune-mediated graft damage in kidney transplant patients. While TruGraf®, a gene set signature has been shown to accurately exclude the presence of subclinical rejection, especially TCMR as well as borderline lesions, elevated dd-cfDNA levels accurately capture clinical and subclinical ABMR. This study evaluated the ability of TruGraf® and dd-cfDNA (Viracor TRAC®) to diagnose rejection when assessed at the time of for-cause or surveillance biopsies.
Methods: We performed a multicenter, observational study with 310 unselected, consecutives kidney transplant recipients undergoing either for-cause or protocol biopsies (Banff 2019 classification) with paired blood samples, from Dec. 2021 to Oct. 2022. TruGraf® and Viracor TRAC® were run blinded by a central lab. Of 310 patients, 230 had paired core biopsies.
Results: In the for-cause biopsy group (n=89), mean dd-cfDNA values were different between patients with normal and abnormal biopsies (0.596±0.579% vs 2.106±4.030% (p=0.003) (Figure 1A) and was significantly higher in allo-immune mediated lesions (rejection, BL, MVI) than other findings (IFTA, recurrent GN, ATN) (3.116±5.244 vs 1.107±2.153 p=0.042). Viracor TRAC® discriminated any rejection from non-rejection (AUC=0.714) as compared to serum creatinine (AUC=0.584). In protocol biopsies (n=104), mean dd-cfDNA values were significantly different between patients with normal vs abnormal features (0.812±0.747 vs 1.935±3.743 (p=0.029), although with a low AUC of 0.514. These differences were significantly stronger when discriminating allo-immune-mediated lesions (ABMR, TCMR, BL) from any other feature such as recurrent GN, IFTA and pristine biopsies (3.905±5.536% vs 0.633±0.552 vs 1.032±1.781%, 0.812±0.747%, p=0.007, p=0.001 and p<0.001, respectively) (Figure 1B). Viracor TRAC® discriminated between rejection and non-rejection and between ABMR and no ABMR with AUC of 0.758 and 0.861 respectively. In this study, TruGraf® did not discriminate rejection and other diagnosis neither in for cause nor protocol biopsies.
Conclusions: Viracor TRAC® showed good performance to capture subclinical rejection, especially ABMR, and to discriminate normal vs abnormal histology in patients with graft dysfunction.



BOS8_12 INHIBITION OF MTOR PATHWAY PREVENTS MISSING SELF-INDUCED NK CELLS-MEDIATED REJECTION

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Background: Our team recently reported that the inability of graft endothelial cells to deliver HLA-I-dependent inhibitory signals to circulating recipient NK cells (missing self, MS) was the cause of DSA-independent microvascular inflammation (MVI) leading to chronic vascular rejection. The purpose of this translational study was to identify the signalling pathways involved in NK cells activation and to evaluate the therapeutic potential of their pharmacological blockade.
Methods: The coculture of human purified NK cells with allogeneic microvascular endothelial cells recapitulated MS-induced NK cell rejection *in vitro*.
In vivo validation was made in an adapted mouse heterotopic heart transplantation model, in which donor animals were from the same genetic background as recipients [C57B6 ($H2^b$)] but KO for MHC-I. This trick allowed stimulating recipient's NK cells by missing self in the absence of any other allogeneic stimulation. Finally, a monocentric pilot clinical study was conducted in 46 renal transplant patients with MS-induced NK rejection.
Results: The coculture model revealed the crucial role of the mTOR pathway for MS-induced activation of NK cells. The addition of an mTOR inhibitor to the cocultures blocked NK cells activation and prevented the destruction of endothelial cells. These results were confirmed in the mouse heart transplantation model, in which the MVI lesions observed in the grafts of untreated controls were completely abrogated in recipients treated with mTOR inhibitor.
Finally, the replacement of MMF by an mTORinh in 16 kidney recipients diagnosed with MS-induced NK rejection resulted in the reduction of graft MVI lesions in control biopsy and an improved graft survival as compared with historical controls (n=30) left on the same immunosuppression (MMF+CNI).
Conclusions: The introduction of an mTOR inhibitor in patients diagnosed with MS-induced NK rejection could reduce rejection lesions and improve graft survival.

BOS8_13 THE INFLUENCE OF MYCOPHENOLATE MOFETIL ON TOP OF TACROLIMUS ON BLOOD PRESSURE IN A RANDOMIZED COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: Animal experimental data suggest a blood pressure lowering effect of mycophenolate mofetil(MMF). However, data from a randomized controlled trial in humans are lacking.
Methods: A randomized controlled weaning trial was performed in low immunologically risk kidney transplant recipients (EudraCT nr.: 2014-001372-66). Recipients were randomized to standard tacrolimus (TAC)/MMF or to TAC monotherapy (TACmono), from 9 months onwards after transplantation, without steroids. Outpatient clinic blood pressure measurements were performed at month 6 (baseline), 9 and 12 after transplantation. At each timepoint, blood pressure was measured 7 times with 5-minute intervals by a research nurse after 30-minutes rest. The WHO developed Daily defined dose (DDD) was used to compare the number and type of antihypertensive drugs. At each timepoint 24-hour urinary sodium, potassium and protein excretion was also assessed.
Results: Between 2015 and 2018, 79 recipients were randomized, of whom 73 completed 12 months follow-up in the blood pressure study (39 TAC/MMF and 34 TACmono). At baseline six months after transplantation, patients were 62 (56-69) years of age with an eGFR of 55(±16) ml/min and proteinuria of 14.0 (10.0-23.0) mg/mmol, TAC trough levels of 7.4 (2.5) µg/L in both groups and MMF dose of 1000 mg daily (1000-1500) in TAC/MMF. Systolic blood pressure at baseline, was comparable in TAC/MMF compared to TACmono (134.3(±15.2) mmHg vs 133.2 (±10.4), p = 0.63) and did not change significantly from month 6 to 12 after transplantation between TAC/MMF and TACmono, p = 0.75. DDD of TAC/MMF and TACmono was comparable at baseline. From month 6 to 12 the DDD changed from 1.5 (0.7-2.7) to 1.1 (0.7-2.3) in the TAC/MMF group, compared to an increase from 2.0 (1.0-4.0) to 2.3 (1.1-3.8) in TACmono (p=0.02). Urinary sodium, potassium and protein excretion were comparable between both groups. Sodium excretion increased from 146 (106-180) at month 6 to 173 (123-231) mmol/day at month 12 after kidney transplantation (p<0.001).
Conclusions: Discontinuation of MMF after kidney transplantation in a tacrolimus/MMF immune suppressive regimen increased the use of antihypertensive drugs significantly. These data support the concept of a blood pressure lowering effect of MMF.

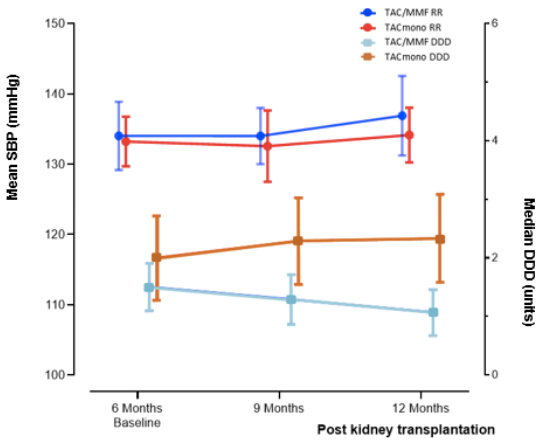
Table 1. Baseline characteristics of kidney transplant recipients randomized to either tacrolimus monotherapy or tacrolimus with mycophenolate mofetil

	TAC-mono (n =34)	TAC/MMF (n = 39)	*p-value*
Age, median (range in years)*	63 (38-71)	61 (30-80)	0.77
Sex, n male (%)*	25 (74)	28 (72)	0.87
BMI, mean (SE)#	28 (0.6)	27 (0.7)	0.13
Transplant type, n living donor transplant (%)*	23 (68)	21 (54)	0.23
Proteinuria protein/creatinine ratio, median (range in mg/mmol)*	12.1 (0-34.5)	12.0 (6.8-46.6)	0.86
CKD-EPI eGFR, mean (SE)#	59 (3.2)	51 (2.1)	0.05^
TAC trough level, median in ug/l (IQR)*	7.4 (2.9)	7.0 (2.9)	0.41
MMF trough level, median in mg/l (IQR)*	2.2 (1.5)	2.0 (1.4)	0.99
Daily dose TAC, median in mg (IQR)*	6.0 (5.0)	5.0 (4.0)	0.44
Daily dose MMF, median in g (IQR)*	1.0 (1.0)	1.0 (0.5)	0.74

#:normally distributed *:not normally distributed ^: 0.046 TAC-mono: tacrolimus monotherapy n: number BMI: body mass index eGFR: estimated glomerular filtration rate TAC: Tacrolimus MMF: Mycophenolate mofetil SE: standard error IQR: Interquartile range

Figure 1. Systolic blood pressure and use of antihypertensive drugs in kidney transplant recipients treated with tacrolimus monotherapy versus tacrolimus and mycophenolate mofetil.

Antihypertensive drug use was defined in WHO daily defined dose units (DDD). In the intervention arm six months after transplantation, MMF was halved and at month 9 discontinued.



TACmono: tacrolimus monotherapy TAC/MMF: tacrolimus and mycophenolate mofetil
SBP: systolic blood pressure DDD: daily defined dose

BOS8_14 A COMPREHENSIVE MONITORING OF MEDICATION ADHERENCE OVER THE FIRST TWO YEARS AFTER RENAL TRANSPLANTATION - A PROSPECTIVE, NON-INTERVENTIONAL STUDY

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Background: Optimal adherence to immunosuppressive regimens is key for prolonged allograft survival. However, granular data on adherence after kidney transplantation is still expandable, while the implementation of assessments in routine care remained limited. Therefore we designed the prospective ADTORQUE trial including a multi-component monitoring over first two years after renal transplantation.
Methods: A total of 226 adult kidney graft recipients consecutively transplanted at the Medical University of Vienna from January 2018 to December 2019 were prospectively monitored for up to 24 month with six study visits (V1-V6). The study visits were scheduled in three month intervals within the first year and at 24 months post-transplant. The adherence monitoring based on multicomponent assessment, complemented by concurrent immune monitoring by the quantification of the Torque Teno virus level in peripheral blood. Medication adherence was assessed by self-reports, electronic drug monitoring, pharmacy refill records, tacrolimus trough level and individual evaluation by a transplant psychologist. Herein we present preliminary analysis of the data on the self-reported adherence using the BAASIS© questionnaire.
Results: Non-adherence was detected in 55% of recipients across all timepoints: 58 (26%) of the transplant recipients reported non-adherence at least once within the first year post transplantation, while 67 recipients (30%) revealed non-adherence at multiple times. The proportion of non-adherence increased within the first three month post transplantation, from 11% at V1 to 31% at V2. At following visits, and remained at 27%, 27%, 32% and 32% over subsequent visits. Deviations from dose-timings were indicated in 44% of all recipients and constitutes for the most frequent cause for non-adherent ratings. Patient revealed non-adherence once had a significantly higher rate of biopsy proven rejections than adherent patients (21% vs. 7%, *p*=0.006).
Conclusions: Inappropriate adherence was substantially reported already in early phases post-transplantation, whereby taking doses on time was the main barrier. The analysis of the whole adherence monitoring might provide granular data to define an optimal diagnostic setting for clinical meaningful non-adherence.

BRIEF ORALS

Management and selection of kidney transplant candidates

BOS9_1 REPEAT HLA CLASS 2 MISMATCHES REMAIN ASSOCIATED WITH GRAFT LOSS OF THE SECOND KIDNEY TRANSPLANT : A COLLABORATIVE TRANSPLANT STUDY REGISTRY ANALYSIS

Lissa Pipeleers*[1], Christian Unterrainer[2], Marie-Paule Emonds[3;4], Karl Martin Wissing[5], Thuong Hien Tran[2]

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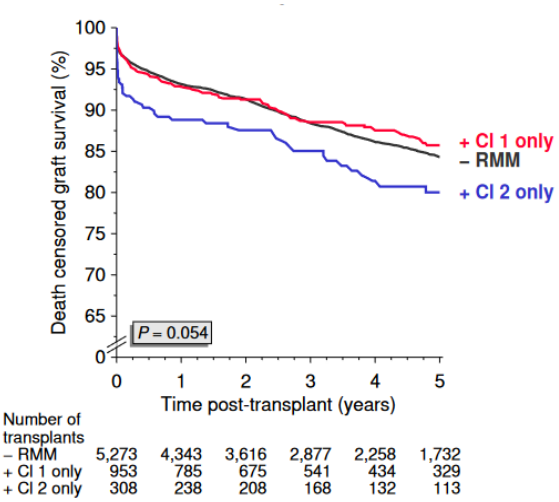
Background: For a second kidney transplantation (2nd KT), many transplant centers systematically avoid repeat HLA antigen mismatches (RMM) with the previous donor. This precaution comes at the price of a potential increase in waiting time. We hypothesized that, since highly sensitive anti-HLA antibody assays have become standard of care, 2nd KT with 1 or more RMM have no inferior graft survival compared to 2nd KT with no RMM because harmful RMM could now be accurately identified and selectively avoided.
Methods: We performed an analysis of the Collaborative Transplant Study (CTS) registry including data of 6711 patients who had received a 2nd KT between 2010 and 2021, with at least one HLA-A, -B or -DR mismatch.
Results: No significant difference in death-censored graft loss (DCGL) was observed between 2nd KT with no RMM compared to 2nd KT with ≥1 RMM (HLA Class 1 or Class 2) in univariate and multivariate analysis. However, a higher DCGL was observed for recipients with ≥ 1 Class 2 only RMM compared to ≥ 1 Class 1 only RMM and no RMM with significance at 1 year in univariate analysis (P=0.011) (Figure). Multivariate analysis showed a doubling of the risk of 1-year DCGL (HR 2.02; 95% CI 1.40 to 2.91; P<0.001) and a 56% increase of the risk of 5-year DCGL (HR 1.56; 95% CI 1.16 to 2.11; P=0.003) for 1 Class 2 only RMM compared to no RMM. For recipients with a Class 1 RMM only, no significantly increased risk was observed in 1-year DCGL (HR 1.07; 95% CI 0.81 to 1.40; P=0.64) and 5-year DCGL (HR 0.98; 95% CI 0.79 – 1.21; P=0.82) compared to no RMM.
Conclusions: Our observations suggest that HLA Class 1 RMM with the first donor do not need to be systematically avoided. On the other hand, HLA Class 2 RMM have a detrimental impact on early and late graft survival in patients who receive a 2nd KT at present times, suggesting modern anti-HLA antibody assays lack accuracy to identify harmful Class 2 RMM. Based on our observations, caution remains warranted for the acceptance of HLA Class 2 RMM.

Figure: Kaplan Meier analysis of 5-year death-censored graft survival after a second kidney-only transplant without a repeat mismatch (-RMM) or with a RMM stratified by repeatedly mismatched HLA class 1 or 2 (CI 1 = HLA class 1 RMM; CI 2 = HLA class 2 RMM). Log rank test after 5 years: P = 0.054. Log rank after 1 year: P = 0.011. Subjects with both class 1 and class 2 RMM were not included (N= 177).



BOS9_2 SENSITIVE HLA ANTIBODY DETECTION AND THE RISK OF ANTIBODY-MEDIATED REJECTION AND GRAFT FAILURE

Tim Debyser[1], Karolien Wellekens[2], Aleksandar Senev[1], Maarten Coemans[2], Priyanka Koshy[1], Elisabet Van Loon[2], Jasper Callemeyn*[2], Dirk Kuypers[2], Marie-Paule Emonds[1], Maarten Naesens[2]

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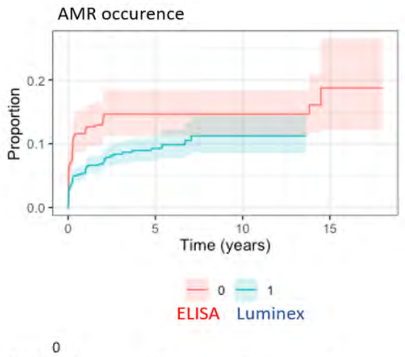
Background: Detection of HLA antibodies relies on single-based antigen bead (SAB) technology (Luminex), which has been shown to be a more sensitive and specific method compared to enzyme-linked immunosorbent assays (ELISA). We aim to elucidate the impact of more sensitive HLA testing on antibody-mediated rejection (AMR) occurrence and long-term allograft survival.
Methods: In this single-center observational study, we made use of a retrospective cohort consisting of all adult patients (n=1818) who received a kidney transplant between March 2004 and May 2021. In April 2008, our transplant center switched from ELISA to SAB HLA testing. We included 393 (21.6%) patients before and 1425 (78.4%) patients after the transition from ELISA- to Luminex-based testing. Bio-banked sera of both groups were retested with the Luminex screening and identification method.
Results: In 90 of 393 patients (23%) of the ELISA-only and 387 of 1425 patients (27%) of the Luminex-only period, circulating HLA antibodies were detected prior to transplantation. HLA-DSA were observed in 11 and 7.6% of patients of the ELISA-only and Luminex-only cohort respectively. Consequently, the preDSA-to-preHLA ratio significantly decreased in the Luminex-only period (43/90), compared to the ELISA-only period (109/387) (48% vs. 28%, P <0.01). Throughout 61 months of follow-up post-transplantation, 166 of 1818 (9.1%) patients developed AMR. After implementing Luminex-based testing, the risk of AMR was significantly decreased with correction for competing risk (Figure 1). However, death-censored graft survival did not significantly differ between both testing methods.
Conclusions: Transition from ELISA- to Luminex-based testing resulted in a significantly decreased preDSA-to-preHLA ratio, indicating that less preformed DSA positive patients are transplanted since the implementation of SAB HLA testing. Consequently, Luminex-based testing led to a significant decrease in AMR occurrence post-transplantation. Since the decline of AMR did not translate into improved graft survival, Luminex-based testing has the added-value of preventing low-risk AMR cases. Therefore, Luminex' high sensitivity must be balanced against the waiting time for a suitable organ.

Figure 1: Competing risk analysis: ELISA- versus Luminex-based HLA testing.



Characteristic	N Event	N	Year 5	Year 10	p-value[†]
1 **Graft failure without AMR**					
txdate	195	1,817			0.093
0 ELISA	61	393	9.5% (6.7%, 13%)	22% (17%, 28%)	
1 Luminex	134	1,424	14% (11%, 17%)	29% (23%, 36%)	
2 **Recipient death without AMR**					
txdate	401	1,817			0.2
0 ELISA	132	393	24% (19%, 28%)	44% (37%, 50%)	
1 Luminex	269	1,424	30% (27%, 34%)	46% (40%, 52%)	
3 **AMR occurence**					
txdate	166	1,817			0.001
0 ELISA	58	393	15% (11%, 18%)	15% (11%, 18%)	
1 Luminex	108	1,424	9.3% (7.4%, 11%)	11% (8.5%, 14%)	

[†] Gray's Test

BRIEF ORALS

Management and selection of kidney transplant candidates

BOS9_3 DEVELOPMENT AND VALIDATION OF A MULTIDIMENSIONAL PROGNOSTICATION SYSTEM FOR KIDNEY TRANSPLANT PATIENT SURVIVAL: THE MORTALITY MBOX

Charlotte Debiais-Deschamps[*1], **Olivier Aubert**[1], **Gillian Divard**[1], **Juliette Gueguen**[1], **Christophe Legendre**[1], **Dany Anglicheau**[1], **Carmen Lefaucheur**[1], **Alexandre Loupy**[1]

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Background: Predicting kidney transplant patient mortality has been hampered by registry-based studies and low level phenotyped cohorts without specific design towards mortality prediction. This represents a limitation for decision making and patient care. We aimed to build and validate a robust patient mortality prognostication system.
Methods: We enrolled 1,446 patients transplanted in France between 2004 and 2014 in whom a protocol-based collection including more than 160 parameters from the recipient, donor and graft, biological and imaging data, was performed on the day of transplantation (TX) and during the first year of TX. Multivariable Cox model was used to develop an individual predictive score of mortality using the strongest predictors of mortality. We externally validated the score in a multicentric French cohort gathering 1198 transplanted kidney recipients.
Results: Among the 1,446 kidney transplant recipients included, 364 patients died after a median post-TX follow-up time of 9.6 years (IQR 6.93-12.71). Among the 160 parameters 16 predictors were selected using multivariable Cox regression. The strongest predictors of patient survival were 1) Baseline recipient factors (age, presence of Donor Specific Antibodies at the time of TX, cardiovascular events, psychiatric history, VHC status and Left Ventricular Mass) 2) Post-TX parameters (complications in the first year of TX) and 3) 6 biological variables measured at one year post-TX (HbA1c, Leucocyte counts, Gamma-Glutamyl Transferase, Uric acid, and Urinary protein). The score showed accurate calibration and discrimination for predicting patient mortality up to 10 years (C-statistic = 0.81, CI: 0.79-0.83). Performances of the score in the validation cohort showed accurate calibration and a C-statistic reaching 0.77 for a prediction at 5 and 10 years.
Conclusions: We generate and validate the first integrative patient survival score that shows a superior prediction performance when compared to previous prognostic systems, reaching 81% prediction accuracy at 10 years. This tool will enable improved patient monitoring and therapeutic decision making to alter the course of an unfavorable patient survival outcome and may provide a surrogate endpoint in clinical trials. Additional external validation (Europe and US) are in progress.

BOS9_4 OUTCOMES OF RENAL TRANSPLANTATION USING DONOR AFTER CARDIOCIRCULATORY DEATH FOR HIGHLY SENSITIZED PATIENTS IN SPANISH AND CATALAN PROGRAMS

Edoardo Melilli[*1], **Jordi Comas**[2], **Francesc Moreso**[3], **María José Pérez-Saez**[4], **Anna Vila-Santandreu**[5], **Fritz Diekmann**[6], **Lluis Guirado**[7], **Nuria Montero**[1], **Jaume Tort**[2], **Josep Maria Cruzado**[1]

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Background: In Spain and autonomous communities, special programs for highly sensitized patients on the waiting list allows for using aging donors and/or donors after cardiocirculatory death (controlled, cDCD). Nonetheless, such donors conferred a high risk of delayed graft function that could affect renal and patient outcomes. Our scope was to evaluate how cDCD donors perform in this clinical scenario compared to DBD donors.
Methods: Data from the Registry of Renal Patients of Catalonia were extracted. Inclusion criteria were: cPRA > 90 %, renal transplantation period from 2012 to 2020. A search for pairs of cases (Transplants with cDCD) with a control (Transplants with DBD) was realized by propensity score matching methodology without replacement. Pairs were matched by the age of the donor/ recipient, sex, presence of DSA at the time of transplantation, and by year of the transplant. We analyzed the impact of donor type on DGF, bPAR, renal, and patients' survival up to 36 months after transplantation. We compared survival curves (Kaplan-Meyer) with the long-rank test and performed survival models with multivariant regression cox analysis.
Results: In the period analyzed, 409 hypersensitized patients were transplanted. After match pairs, 278 patients were included (139 DBD vs 139 cDCD). No statistical differences in basal characteristics were observed. Incidence of DGF was higher in patients from a cDCD donor (40 % vs 28 % p. 0.04) and worse renal function at 12 and 24 months (eGFR-CKD-epi 40±22 and 43±19ml/min for DCD-MAIII and eGFR-CKD-epi 46 ± 20ml/min and 50±20 for DBD vs; p=0.022 and 0.021, respectively) but not at 36 months (44±16 vs 45±19; p=0.3). Acute rejection incidence was similar (24 vs 25 % for cDCD vs DBD, p.0.8). At 36 months, death-censored graft survival and patients' survival, were not different according to donor type (83 % vs 84 % and 83% vs 85 % for DBD and cDCD respectively. NS)
Conclusions: cDCD donors lead to similar outcomes compared to DBD in highly sensitized recipients.

BRIEF ORALS

Management and selection of kidney transplant candidates

BOS9_5 DIETARY OXALIC ACID INTAKE AND PLASMA OXALIC ACID CONCENTRATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Gideon Post Hospers*[2], Wesley Visser[1], Anneke van Egmond[1], Mirjam Laging[2], Jeroen Verhoeven[2], Sara Baart[3], Chris Ramakers[4], Dennis Hesselink[2], Jacqueline van de Wetering[2], Marlies Reinders[2], Ewout Hoorn[2], David Severs[2], Joke Roodnat[2]

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Background: High oxalic acid concentration may be caused by genetic disorders, enteric diseases, but also by kidney insufficiency per se. It may result in kidney oxalic acid stones, kidney function decline, and failure. This study aimed to investigate whether dietary oxalic acid intake influences plasma oxalic acid concentration in a population undergoing kidney transplantation.
Methods: Dietary oxalic acid intake was assessed using a Food Frequency Questionnaire. Based on frequency and portion size, average daily oxalic acid intake in the past year and in the last 24 hours was calculated. A blood sample for determination of plasma oxalic acid concentration was drawn on the operation ward before transplantation. For multivariable analysis seventeen recipient related variables were gathered.
Results: 418 patients were included. The median age of the participants was 62 year, 60% were male, all had an eGFR <20 ml/min/1.73 m^2, and 66% were on dialysis with a median dialysis vintage of 13 months. The median plasma oxalic acid concentration was 32.2 µmol/L (range 4.6-243.2). In 98.3% of patients oxalic acid concentration was above the upper limit of normal. The average oxalic acid intake was 199 mg/day (range 4-1599), while it was 138 mg/day in the last 24 hours before transplantation (range 0-3906). Multivariable linear regression analysis showed that plasma oxalic acid concentrations were significantly higher in recipients with higher average (p<0.001) and last 24 hours oxalic acid intake (p=0.002), lower age (p<0.001), lower residual diuresis (p<0.001), higher body mass index (p<0.001), longer dialysis vintage (p=0.032), hemodialysis (p<0.001), and peritoneal dialysis (p<0.001) versus preemptive status.
Conclusions: In pre-kidney transplant patients, plasma oxalic acid concentration is above upper normal limit in 98.3% of patients and is multifactorially determined. As all other factors are not modifiable, the only way to decrease plasma oxalic acid concentration is dietary restriction.

BOS9_6 CIRCULATING TNF-A LEVELS IN DECEASED DONORS ASSOCIATE WITH POSTTRANSPLANT FUNCTION IN KIDNEY TRANSPLANTATION

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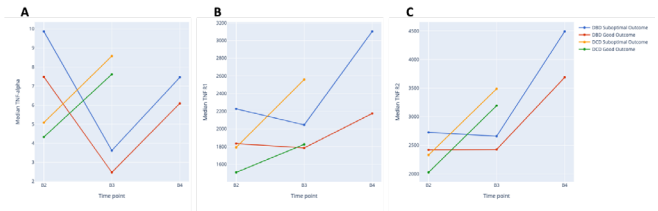
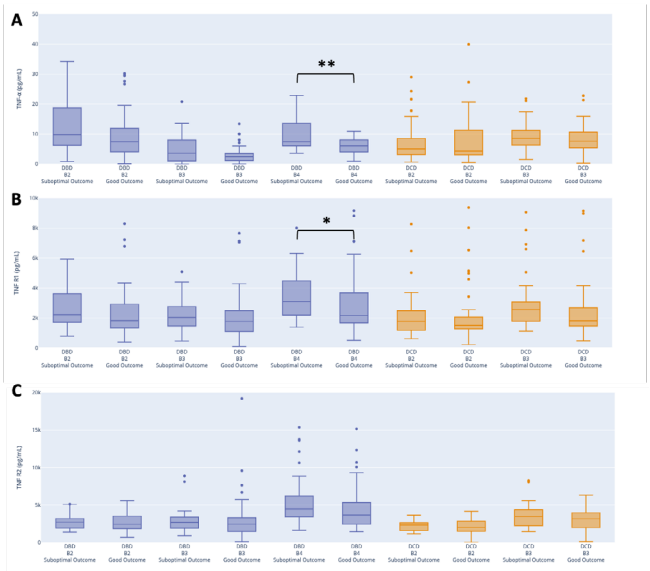
Background: Organ transplantation is a life-saving treatment of end-stage diseases. Yet, shortage of donors and uncertainty for the quality of donor organs limits the full benefit of organ transplantation. Recent research suggests that biomarkers of the TNFα pathway are associated with kidney function decline. Soluble TNFα, TNFR1 and TNFR2 receptors are inflammatory markers with strong prognostic value of progression from acute injury to chronic kidney dysfunction. In this study, we evaluated donor longitudinal circulating levels of TNF-α, TNFR1 and TNFR2 during donor management and compute relevant associations with 12-month posttransplant function
Methods: A cohort of 475 plasma samples were obtained from 189 deceased donors (DBD=95, DCD=94). Samples were provided by the Quality in Organ Donor (QUOD) biobank. Plasma samples from living donors (n=20) obtained from the Oxford Transplant Biobank, provided a baseline reading for these analytes. Using Luminex assay, we quantified the circulating levels of TNF-α and receptors in serial donor plasma collected longitudinally during donor management at three time points (time of brain stem death test; B2, start of retrieval; B3, prior to cross clamp; B4) in DBD and two corresponding time points in DCD (prior to withdrawal of life support; B2, start of retrieval; B3).
Results: Circulating levels of TNF-α and receptors differ among donor types. In DBDs, initial high levels of TNF-α and TNFR2 following brain death reduced during donor management before reaching their highest level prior to kidney retrieval (time point B4). TNFR2 levels remained roughly constant at all time points (Fig 1). In contrast, in DCDs the levels of circulating analytes show a steady increase that peaked just before withdrawal of life support. Notably, only in DBDs plasma levels of TNF-α (p=0.002) and TNFR1 (p=0.018) strongly associated to 12-month suboptimal function (eGFR<=30ml/min) posttransplant (Mann-Whitney U test) (Fig 2). All analytes had baseline levels in living donor plasma prior to kidney procurement.
Conclusion: Our study demonstrates that circulating inflammatory levels differ in DBDs when compared to DCDs. Increased levels of TNF-α mediators in deceased donor may deem donor organs susceptible to posttransplant injury and suboptimal function at 12-m post-transplant function.





BOS9_8 ASSOCIATION BETWEEN ABDOMINAL CT MEASUREMENTS OF BODY COMPOSITION AND WAITLIST MORTALITY IN KIDNEY TRANSPLANT CANDIDATES

Evelien Quint*[1], Yi Liu[2], Omid Shafaat[3], Robert Pol[1], Dorry Segev[2], Clifford Weiss[3], Mara Mcadams-Demarco[2]

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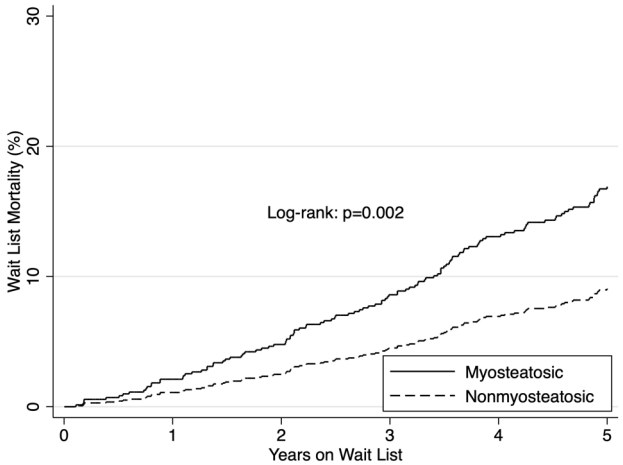
Background: Obesity is considered a risk factor for developing adverse outcomes in the kidney transplant (KT) population, however, there are inherent limitations of BMI measurements. Objective measures of body composition, measured using abdominal CT scans, may improve pre-transplant risk stratification. The goal of this study was to determine the association between various CT-based body composition measurements and waitlist mortality in KT candidates.
Methods: We leveraged a perspective cohort of adult first-time KT candidates (n=836) from 2010 to 2022 who underwent abdominal CT scans during KT evaluation, including L3 vertebral level, at Johns Hopkins Hospital. Body composition measurements were obtained, including skeletal muscle index (SMI) and skeletal muscle radiation attenuation (SM-RA). Sarcopenia was defined as an SMI< 50 cm2 /m2 for males and an SMI<39 cm2 /m2 for females. Myosteatosis was defined as an SM-RA<41 mean HU for recipient with a BMI< 25 kg/m2 and an SM-RA<33 mean HU for recipient with a BMI≥ 25 kg/m2. Sarcopenic obesity was defined as a BMI≥ 30 kg/m2 for sarcopenic recipients. Fine and Gray proportional subhazard models were used to quantify the associations of each measurement with waitlist mortality. P values <.05 were considered significant.
Results: Among 836 KT candidates, the mean age was 55.3 years (SD, 12.8 years) and 38.8% were women. The 1- and 5-year cumulative incidence of mortality were 1.8% and 14.5% respectively. For myosteatosis, cumulative incidence of waitlist mortality was higher among those with myosteatosis (cSHR=1.95, 95%CI: 1.29-2.94, p=0.002). Regarding patients with sarcopenic obesity, cumulative incidence of waitlist mortality was higher when compared to their non-sarcopenic obese counterparts (cSHR=1.55, 95%CI: 1.01-2.39, p=0.047). None of the body composition profiles carried a higher risk of waitlist mortality after adjusting for potential confounders.
Conclusions: Cumulative incidence of waitlist mortality is higher among kidney transplant candidates with myosteatosis and those with sarcopenic obesity. Transplant centers should consider using body composition metrics, when a CT scan is available, to improve risk stratification at KT evaluation.

Figure 1: Cumulative Incidence of Waitlist Mortality by Myosteatosis Status



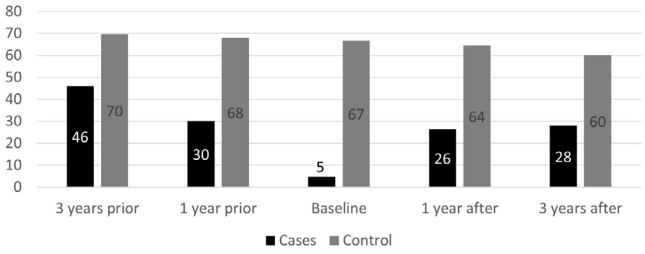
BOS9_9 EMPLOYMENT BEFORE, AT OR AFTER KIDNEY TRANSPLANTATION IN DENMARK – A NATIONAL CASE-CONTROL STUDY

Rasmus Carlsen*[1;2;3], Lilli Kirkeskov[4], Margit Riis[5], Rikke Jacobsen[5], Frederikke Gronemann[5], Merete Osler[5], Janne Petersen[5], Niels Henrik Buus[1]

[1]Aarhus University Hospital, Department of Renal Medicine, Aarhus, Denmark, [2]Oslo University Hospital and Oslo University, Department of transplantation medicine, Oslo, Norway, [3]Regional Hospital of Viborg, Department of Internal Medicine, Vlborg, Denmark, [4]Centre of Social Medicine, University Hospital Bispebjerg-Frederiksberg, Copenhagen, Denmark, [5]University Hospital Bispebjerg-Frederiksberg, Centre for Clinical Research and Prevention, Copenhagen, Denmark

Background: Kidney transplant patients have difficulties at maintaining their employment with an estimated proportion of 38% patients in work after transplantation. Prior studies on employment have previously used self-reported employment as main endpoint, with no control group and only sparse information on employment prior to transplantation. This study aimed to establish the rate of employment in kidney transplant patients from 3 years before to 3 years after kidney transplantation and associated predictors for employment after transplantation.
Methods: All kidney transplantation patients from 2005-2019 were identified using The Danish Nephrological Register linked with DREAM database for information of government benefits, Statistics Denmark for socioeconomic information and The Danish Health Data Authority National Patient Register for comorbidities. Inclusion criteria were kidney transplantation, age 18-65 years. Exclusion criteria were emigration during period of interest. Each transplant patient was matched with 1-3 controls on age, gender and municipality.
Results: In total 2294 kidney transplant patients (median age 49 years, 64 % males) were included with 6790 controls. Employment rate for kidney transplant patients and controls 3 years prior, 1 year prior, at transplantation, 1 year after and 3 years after are shown in Figure 1. At all timepoints kidney transplant patients had a lower employment rate (P<0.001). Associated cause specific hazards of employment after transplantation were male, HR 1.5 (1.3-1.8), non-Danish ethnicity, HR 0.6 (0.5-0.8), education with university degree or higher compared to basic schooling, HR 2.2 (1.6-2.9). Other predictors of employment were hemodialysis compared to preemptive transplantation, HR 0.7 (0.6-0.9), peritoneal dialysis compared to preemptive transplantation, HR 0.8 (0.7-0.97) and diabetes, HR 0.7 (0.5-0.8).
Conclusions: Kidney transplant patients have a low employment rate in Denmark with male gender, Danish ethnicity, preemptive transplantation and education associated with improving the hazard of employment and dialysis and diabetes decreasing the hazard of employment.

Figure 1. Employment rates of kidney transplant patients (cases) and controls according to time of transplantation (baseline).



BOS9_10 DOES TYPE OF DIALYSIS MODALITY INFLUENCE POST-TRANSPLANTATION OUTCOMES? A POPULATION-COHORT ANALYSIS USING REGISTRY DATA

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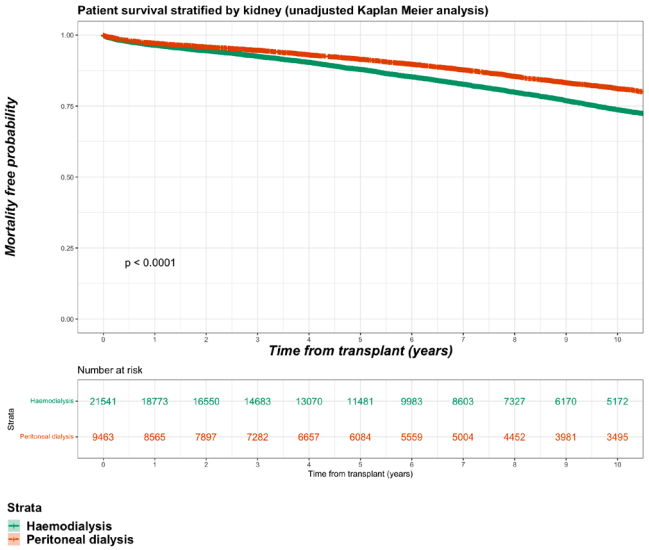
Background: There is conflicting data with regards to whether kidney transplant candidates using peritoneal dialysis (PD) versus haemodialysis (HD) at the time of kidney transplant surgery have better short- and long-term post-transplant outcomes.
Methods: A retrospective cohort study was undertaken of prospectively collected registry data of all kidney transplant recipients in the United Kingdom from January 1, 2000 until September 30, 2019 inclusive. Outcomes studied included short-term and long-term graft outcomes. Time-to-event analyses were performed using weighted estimation of Cox regression models to account for non-proportional hazards, with covariate adjustment as indicated. All analyses were done using RStudio (version 2022.07.2), with survival analyses performed using the *coxphw* package.
Results: A total of 37,194 kidney transplant recipients formed the study cohort, of whom 71.6% (n=26,639) were receiving HD and 28.4% (n=10,555) were receiving PD. Rates of living and donation after brain or circulatory death were similar among patients. PD was more common in the following kidney transplant candidates; younger, females, White ethnicity, non-diabetics and first transplant recipients. Kidney transplant candidates on PD versus HD had lower risk for delayed graft function (13.5% versus 24.4% respectively, p<0.001), but a slightly higher risk for 3-month rejection (15.0% versus 13.8% respectively, p=0.004). Creatinine at 1-year (in umol/L) was slightly better in PD versus HD patients (128 versus 130 respectively, p<0.001). In adjusted survival models, PD versus HD had a significant association with patient mortality (Hazard Ratio 0.71, 95% CI 0.59-0.84, p<0.001) and overall graft loss (Hazard Ratio 0.75, 95% CI 0.68-0.83, p<0.001) but not death-censored graft loss (Hazard Ratio 0.88, 95% CI 0.71-1.10, p=0.251).
Conclusions: Kidney transplant recipients on PD at the time of transplant surgery have a reduced risk for post-transplant mortality compared to the those on HD. While confounding by residual selection bias cannot be ruled out, our data supports encouragement of PD as a bridge to kidney transplantation for eligible kidney transplant candidates.

Figure. Unadjusted Kaplan Meir plot of post-transplant mortality by pre-transplant dialysis modality



BOS9_11 CHARACTERISTICS OF PRE-TRANSPLANT HOSPITALIZATIONS ARE ASSOCIATED WITH ELDERLY PATIENT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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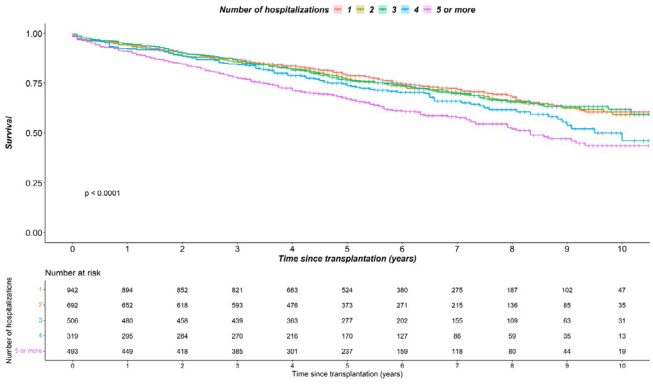
Background: In elderly patients, kidney transplantation is not systematically associated with a benefit in terms of survival, compared to dialysis. Screening of comorbidities is not sufficient to identify those at high risk of mortality, possibly due to unmeasured frailty in some patients. The profile of hospitalizations may be a good proxy of this frailty. Thus, our aim was to study if the number and length of hospitalizations during the three years preceding kidney transplantation were associated with post-transplant mortality.
Methods: We included all patients older than 65 years the day of transplantation who received a kidney transplant between 2006 and 2016. Recipient and donor characteristics were retrieved from French national registries (Renal Epidemiology and Information Network (REIN) and CRISTAL). Data on hospitalizations were obtained by indirect matching with the National Health Data System. Patients with pre-emptive kidney transplantation were excluded. Cox models were used to identify factors associated with mortality.
Results: We included 3882 patients, 930 (24.0%) without pre-transplant hospitalization, and 2952 (76.0%) cumulating a total of 9373 hospitalizations. 67% of patients were male and 14% were older than 75 years. In univariate analysis, patients with history of pre-transplant hospitalization had a lower probability of survival (p<0.001). In hospitalized patients, we observed a dose-response relationship between the number of hospitalizations and survival (Figure). History of hospitalization was associated with a higher mortality (HR 1.26 [1.08:1.48]) after adjustment for recipient comorbidities, duration of dialysis, ECD donors, and cold-ischemia time. For patients with a history of hospitalization, the number of pre-transplant hospitalizations, rather than their cumulative length, was associated with a higher mortality (adjusted HR 1.07 [1.04:1.10] per one hospitalization increase). Being hospitalized at least once for a cardiac or a respiratory condition was independently associated with a higher risk of mortality.
Conclusions: Taking into account the characteristics of pre-transplant hospitalizations during evaluation of elderly candidates to transplantation may help to identify patients with a higher risk of post-transplant mortality.



BRIEF ORALS

Management and selection of kidney transplant candidates

BOS9_12 SARCOPENIA OF KIDNEY TRANSPLANT RECIPIENTS AS A PREDICTIVE MARKER FOR REDUCED GRAFT FUNCTION AND GRAFT SURVIVAL AFTER KIDNEY TRANSPLANTATION

Hristos Karakizlis*[1], Nadine Trudel[2], Alexander Brose[3], Alexander Reinisch-Liese[4], Martin Reichert[2], Andreas Hecker[2], Fabienne Bender[2], Ingolf Askevold[2], Lucy Rainer[1], Rolf Weimer[1], Gabriele Krombach[3], Winfried Padberg[2], Juliane Liese[2]

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Background: The association between sarcopenia of kidney transplant recipients and outcome after kidney transplantation (KT) has not yet been fully understood and is still considered controversial. The aim of our study was to analyse the impact of pre-transplant sarcopenia on graft function, postoperative complication rates, and survival of the patients after renal transplantation.
Methods: In this retrospective single-centre study, all patients who underwent KT (01/2013-12/2017) were included. Demographic data, rejection rates, delayed graft function, graft and patient survival rates were analysed. Sarcopenia was measured in computed tomography images by the sex-adjusted Hounsfield Units Average Calculation (HUAC).
Results: During the study period, 111 single KTs (38 women and 73 men) were performed. Living donor kidney transplants were performed in 48.6%. In total, 32.4% patients had sarcopenia. Sarcopenic patients were significantly older (59.6 years vs. 49.8 years; $p < 0.001$), had a higher body mass index (BMI = 27.6 kg/m^2 vs. 25.0 kg/m^2; $p = 0.002$) and were more likely to receive deceased donor kidneys (72.2 % vs. 41.3 %; p=0.002). Interestingly, 3 years after KT, the creatinine serum levels were significantly higher (2.0 mg/dl vs. 1.5 mg/dl; p=0.001), whereas eGFR (39.9 ml/min vs. 53.4 ml/min; p=0.001) and graft survival were significantly lower (p=0.004) in sarcopenic transplant recipients. Sarcopenic patients stayed in hospital significantly longer postoperatively than those who were non-sarcopenic.
Conclusions: At the time of kidney transplantation, sarcopenia was found to predict reduced long-term graft function and diminished graft survival after KT. The early identification of sarcopenic patients can not only enable an optimized selection of recipients, but also the initiation of pre-habilitation programs during the waiting period.

BOS9_13 EFFECTS OF SOCIAL DEPRIVATION ON REGISTRATION ON THE RENAL TRANSPLANTATION WAITING-LIST THROUGH MARKERS OF NEPHROLOGICAL CARE: A MEDIATION ANALYSIS

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Background: Reducing disparities in access to renal transplantation requires identification of factors involved in the association between socioeconomic status and registration on the renal transplantation waiting-list. This mediation analysis was conducted to estimate the effect of social deprivation on waitlisting and to identify modifiable mediators of this association.
Methods: From the Renal Epidemiology and Information Network, this retrospective observational multicenter study included all patients eligible for an evaluation for registration according to French recommendations who started dialysis between 1 January 2017 and 30 June 2018. Social deprivation was estimated by quintile 5 (Q5) of the European Deprivation Index (EDI). Registration was defined as being already listed at dialysis start or within the first 6 months. Mediation analysis was conducted to assess the direct effect of the EDI on registration and its indirect effect through markers of the nephrological follow-up, defined *a priori* in a directed acyclic graph.
Results: Among the 11655 patients included, 2410 were registered. Age, sex, comorbidities, dialysis modality and starting dialysis on a catheter or in emergency were associated with registration on the waiting-list. In the mediation analysis, Q5 had a direct effect on registration (OR 0.83 [0.81-0.85]) and an indirect effect mediated by emergency start dialysis (OR 0.97 [0.96-0.97]), hemoglobin < 11 g/dL and/or lack of EPO (OR 0.95 [0.95-0.96]) and albumin < 30 g/L (OR 0.98 [0.98-0.99]).
Conclusions: Social deprivation is directly associated with a lower chance of being registered on the renal transplantation waiting-list but its effect is also mediated by markers of the pre-dialysis care, suggesting that improving the follow-up of the most deprived patients should help to reduce disparities in access to renal transplantation.

BOS9_14 THE PATIENT'S WISH IS A MAJOR REASON FOR REMOVAL FROM THE EUROPEAN SENIOR PROGRAMME WAITING LIST

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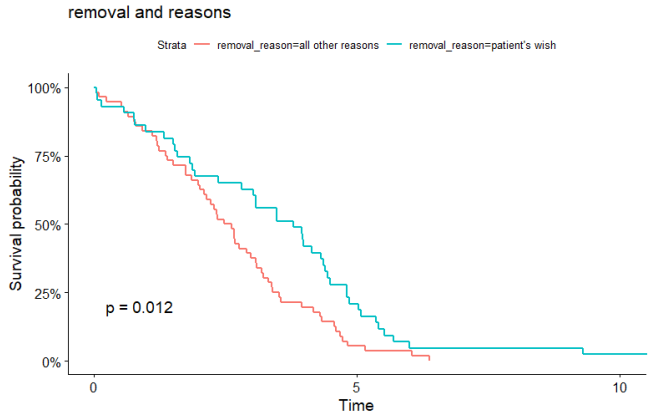
Background: In 1999, the Eurotransplant Senior Programme (ESP) was established to allocate local kidneys from donors ≥65 years to recipients ≥65 years. While ESP enhances transplant opportunities for older people, reasons to decide against transplantation are more. However, the reasons for permanent removal from the waiting list (WTL) in older people are unknown. We systematically analysed these reasons in a large local cohort of patients enrolled into ESP.
Methods: All patients with active status on the ESP-WTL at our centre between 1999 and 2019 were included into this analysis. The baseline marked either the 65th birthday (inclusion from regular allocation) or any other time point after the 65th birthday for primary ESP-allocation. Reasons for permanent removal were classified using the patients' electronic health record and the Eurotransplant Network Information System. The time of permanent delisting from baseline was analysed using Kaplan Meier.
Results: 820 patients were included: 530 transplanted, 191 WTL and 99 removed permanently. Removed patients had a shorter time on dialysis before listing and were older than transplanted or waitlisted patients (Table 1). Main reason for removal from the waitlist was the patient's wish (43.9%). Mean time of removal was 3 years after ESP-enlistment. Patients that were removed due to other reasons than the patient's wish were removed earlier than patients who wished to be removed (Figure 1).
Conclusions: Delisting due to the patient's wish is frequent in ESP patients. Especially after longer waiting time patients seem to prefer delisting than staying on the waiting list. This might reflect further health deterioration or feelings of uncertainty on the waiting list difficult to cope with.



Parameter	Removed	Transplanted	Waitlisted
N	98 (12%)	530 (65%)	191 (23%)
Male	61 (62%)	321 (61%)	126 (66%)
Time on dialysis before listing [years]	1.94 (1.04-3.25)	2.40 (1.40-4.67)	2.05 (1.11-4.44)
Age at listing [years]	68.6 (65.6-72.2)	66.4 (65.0-69.5)	66.7 (65.0-69.8)
Time of removal after listing [years]	2.90 (1.52-4.32)		
Reasons			
Patient's wish	43 (43.9%)		
Cardiac	12 (12.2%)		
Vascular	9 (9.2%)		
Cancer	7 (7.1%)		
Multiple comorbidities	5 (5.1%)		
Dementia	4 (4.1%)		
Infections	3 (3.1%)		
Restored renal function	3 (3.1%)		
Other medical reasons	9 (9.1%)		
Unknown	4 (4.1%)		

BRIEF ORALS

Cardiovascular and metabolic complications after kidney transplant

BOS10_1 IS A BLOOD PRESSURE BELOW 130/80 MM HG A UNIVERSAL GOAL FOR ALL RENAL TRANSPLANT RECIPIENTS? AN ANALYSIS OF THE COLLABORATIVE TRANSPLANT STUDY

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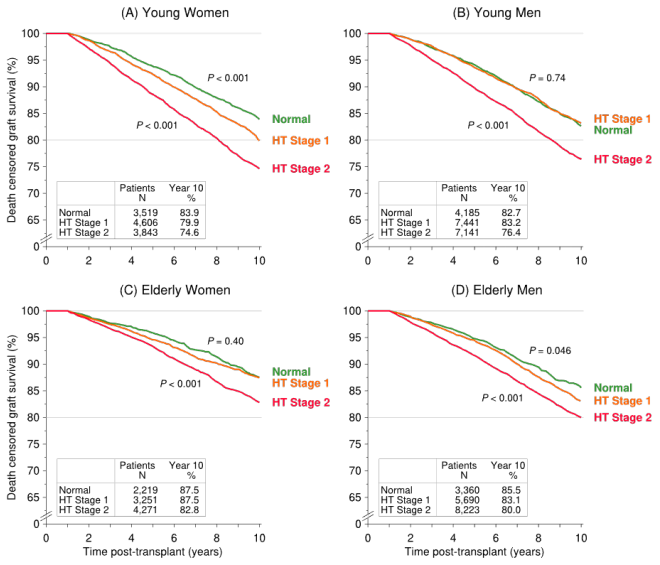
Background: In 2018, the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines published new categories for hypertensive blood pressure (BP) of adults, recommending a BP goal of less than 130/80 mm Hg. This goal was adopted in the 2021 KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease for adult kidney transplant recipients. Thanks to the contribution of many centers around the world over decades, the extensive database of the CTS could be used to verify whether this BP cut-off equally applies to different patient groups.
Methods: More than 57,000 adult patients who received kidney-only transplants since 2000, with a functioning graft one year after transplantation and for whom diastolic and systolic BP were available 1 year after transplantation, were analyzed in 3 categories: normal <130/80, hypertension stage 1 <140/90, and stage 2 ≥140/90 mm Hg. Multivariable Cox regression analyses that included 24 confounding factors were used to analyze the impact of 1-year BP on 10-year death-censored graft survival.
Results: Less than a quarter (23%) of patients had a normal BP below 130/80 mm Hg, with a strong dependence on patient age and sex. When all study patients were analyzed, patients with stage 1 hypertension had only a 7% higher death-censored graft failure rate than patients with normal BP (P=0.040), whereas the risk was increased by 35% in stage 2 patients (hazard rate HR=1.35, P<0.001). However, a stratification by recipient age and sex revealed remarkable differences (Figure 1). Cox regression of stage 1 and 2 vs. normal BP also showed strongly different risks with regard to graft number and 1-year serum creatinine; first transplants: HR 1.04 (P=0.27) for stage 1, HR 1.31 (P<0.001) for stage 2; retransplants: 1.23 (P=0.018), 1.60 (P<0.001); 1-year serum creatinine <130 µmol/l: 0.97 (P=0.66), 1.25 (P<0.001); ≥130 µmol/l: 1.14 (P=0.003), 1.42 (P<0.001).
Conclusions: Maintaining BP below 130/80 mm Hg is especially important for <50 year-old women, retransplanted patients, and recipients with impaired graft function.

Figure 1. Influence of hypertension (HT) stage on death-censored graft survival stratified by recipient age (<50, ≥50 y) and sex (pairwise P values vs. normal BP of Kaplan-Meier analyses are shown).



BOS10_2 COMPARISON OF OFFICE, HOME AND AMBULATORY BLOOD PRESSURE IN KIDNEY TRANSPLANT RECIPIENTS WITH AND WITHOUT TELEMEDICINE MONITORING

Georgios Eleftheriadis*[1], Marcel Naik[1], Bilgin Osmanodja[1], Klemens Budde[1]

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Background: Despite extensive cardiovascular screening before kidney transplantation, cardiovascular mortality among kidney transplant recipients (KTR) remains high. The aim of this study was to quantify hypertension control and evaluate concordance between available blood pressure modalities in a sample of KTR with and without telemedicine monitoring
Methods: For this cross-sectional study 80 KTR were recruited at the Charité Transplant Outpatient Clinic. Study participants had to be adults and transplanted at least 6 months prior to inclusion. Known arrhythmias, hemodialysis shunt on both arms as well as recent adjustment of antihypertensive drugs were defined as exclusion criteria. For each study participant office (OBP, automated office blood pressure “AOBP” and manual office blood pressure “MOBP), home (HBPM) and ambulatory blood pressure measurement (ABPM) were performed.
Results: Mean blood pressure for daytime-ABPM, HBPM, AOBP and MOBP was 130/82, 131/85, 126/71 and 129/73mmHg, respectively. The Bland-Altman plot showed the mean bias ± SD between systolic daytime ABPM and HBPM, AOBP, MOBP as -1±10mmHg, 4±13mmHg, 1±13mmHg with corresponding limits of agreement -21 and 18mmHg, -20 and 29mmHg, -24 and 26mmHg. Uncontrolled hypertension, as defined by 24h-ABPM, was present in 65% of trial participants. The evaluation of dipping status yielded a physiological dipping pattern in 12,5% of participants whereas 87,5% showed a non-physiological dipping pattern. Clinical features (i.a. edema, nocturia) did not correlate significantly with hypertension status, as defined by 24h-ABPM. Despite showing a tendency towards lower mean blood pressure by MOBP, AOBP and HBPM, the Telemedicine sample displayed no difference in ABPM measurements.
Conclusions: HBPM showed the narrowest limits of agreement compared to the gold standard ABPM. Nonetheless, HBPM showed a low negative predictive value with regards to daytime-ABPM. Furthermore we recorded a high prevalence of non-physiological dipping pattern among KTR. Despite the undebatable advantages of HBPM (tolerability, improved patient adherence and outcomes), systematic integration of ABPM into clinical practice, as proposed by recent hypertension guidelines, should not be withheld for the KTR population.

BOS10_3 PREDICTION OF MACE AND MORTALITY AMONG KIDNEY TRANSPLANT CANDIDATES USING RISK FACTORS, CORONARY ARTERY CALCIUM SCORE AND CORONARY CT ANGIOGRAPHY

Marie Nielsen*[1;2], Jonathan Dahl[3;4], Rasmus Laursen[5], Bente Jespersen[1;4], Per Ramløv Ivarsen[1;4], Simon Winther[3], Henrik Birn[1;2;4]

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Background: Kidney failure is associated with an increased risk of cardiovascular disease and death. The present study evaluated cardiovascular outcomes and all-cause mortality in asymptomatic kidney transplant candidates who were systematically referred to coronary artery calcium score (CACS) and coronary computed tomography angiography (CTA).
Methods: In a single-centre, observational study all potential kidney transplant candidates > 40 years, with diabetes or need for dialysis > 5 years were systematically referred to cardiac CT. All patients initiating cardiovascular screening prior to kidney transplantation between March 2014 and September 2019 were included. Data on clinical risk factors, major adverse cardiovascular events (MACE) and all-cause mortality was collected from patient records.
Results: A total of 529 kidney transplant candidates were included with a median follow-up of 4.7 years. CACS was evaluated in 437 patients and CTA was analyzed in 411. Both the presence of ≥ 3 risk factors, CACS ≥ 400 as well as multiple vessel stenoses or left main artery disease predicted MACE (HR 2.09 (95% CI 1.35-3.23); 4.65 (2.20-9.82); 3.70 (1.81-7.57); 4.90 (2.40-10.01)) and all-cause mortality (HR 4.44 (95% CI 2.54-7.76); 4.47 (2.22-9.02); 2.82 (1.34-5.94); 5.41 (2.81-10.41)) in univariate analyses. Among patients eligible for CACS and CTA (n = 376), only CACS and CTA were associated with both MACE and all-cause mortality.
Conclusions: Risk factors, CACS and CTA provides prognostic information in kidney transplant candidates. An additional value of CACS and CTA compared to risk factors was observed for prediction of MACE in a subpopulation undergoing both CACS and CTA.

Cardiovascular and metabolic complications after kidney transplant

BOS10_4 INFLUENCE OF LOW- AND HIGH-DENSITY LIPOPROTEIN CHOLESTEROL ON GRAFT FUNCTION IN RENAL TRANSPLANT RECIPIENTS - A COLLABORATIVE TRANSPLANT STUDY REPORT

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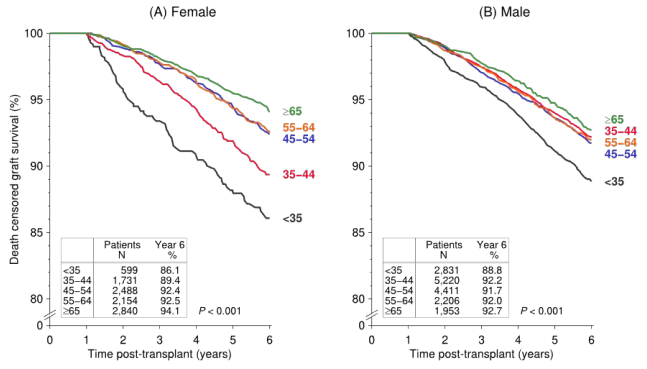
Background: Hypercholesterolemia is highly prevalent in renal transplant patients. Therefore, post-transplant screening of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol is routinely performed. When appropriate, post-transplant drug therapy is directed at lowering LDL cholesterol to reduce cardivascular risk. The extent to which LDL and HDL influence graft function has long been debated. Thanks to the contribution of many centers around the world, the large database of the CTS allows verification of the influence of LDL and HDL on graft outcome.
Methods: More than 26,000 adult patients who received kidney-only transplants since 2003, with a functioning graft one year after transplantation and for whom HDL and LDL levels were available one year after transplantation, were analyzed. Taking into account cholesterol-affecting characteristics such as recipient age, sex, and medication with statins, the influence of 1-year HDL and LDL on death-censored graft survival and the incidence of rejection treatment after the first post-transplant year was analyzed. Multivariable Cox regression analysis was used to adjust for additional confounding factors.
Results: Regardless of whether patients were treated with statins, transplanted women had approximately 10 mg/dl higher HDL levels than men. Increased LDL values in women were only found in recipients aged ≥50 years. For LDL, there was no significant trend for serum levels and death-censored graft survival. In contrast, patients with an HDL of less than 35 mg/dl had a strikingly increased risk of death-censored graft failure (P<0.001, Figure 1). Regarding the influence of HDL on death-censored graft survival, there were no significant differences with respect to recipient age or medication with statins; however, in female recipients a significantly higher risk was noted already at a cut-off of 45 mg/dl (P<0.001 vs. ≥45 mg/dl). The impact of HDL on the incidence of rejection treatment was similar during the second and third post-transplant years.
Conclusions: Low HDL serum cholesterol of <35 mg/dl in men and <45 mg/dl in women is a strong predictor of impending rejection or graft failure after kidney transplantation.

Figure 1. Influence of 1-year post-transplant HDL cholesterol (mg/dl) on subsequent death-censored graft survival.



BOS10_5 GLIFLOZIN IN RENAL TRANSPLANTATION: A MULTICENTER OBSERVATIONAL STUDY (GREAT-ASTRE)

Lucie Maigret*[1], Valérie Chatelet[2], Pierre-Guillaume Deliège[3], Peggy Perrin[4], Leonard Golbin[5], Laure Ecotiere[6], Cyril Garrouste[7], Martin Planchais[8], Coralie Poulain[9], Dany Anglicheau[10], Yannick Le Meur[11], Jean-Philippe Rerolle[12], Dominique Bertrand[13], Lucile Basle[3], Fabien Duthe[6], Philippe Gatault[1]

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Background: SGLT2 inhibitors (SGLT2i) decrease all-cause mortality, cardiovascular mortality and slow progression of kidney disease in patients with albuminuria. In agreement with the French marketing authorization, SGLT2i can be prescribed to kidney transplant recipients (KTR), although these patients were not included in large randomized clinical trials (DAPA-CKD, CREDENCE, EMPA-Kidney). GREAT-ASTRE is a real-life multicentric study of KTRs treated with SGLT2i.
Methods: We implemented an observational study of all KTRs followed in the 13 kidney transplant centres that collect transplantation-related data in ASTRE database (DR-2012-518). We added visits at initiation of SGLT2i, then at 3 and 6 months (M0, M3, M6). The aim was to identify all KTR receiving SGLT2i in order to describe the prescribing pattern and determine safety profile. We paid particular attention to urinary tract and genital infections, as well as treatment discontinuation.
Results: So far, 265 KTRs have been identified, 95% of them having received a prescription of dapagliflozin 10 mg/day. General characteristics of the patients at initiation are presented in the table. Most initiations took place between 1 and 10 years after transplantation (47.2%), only 10.9% in the first year of transplantation. HbA1c at initiation was < 7% in 33% and <8% in 67% of the 185 (69.8%) diabetic KTRs. Serum creatinine level increased following initiation of SGLT2i (M0 : 144±44 µmol/L, M3 : 156±55 µmol/L, p=0.0001), followed by a stabilization at M6 (160±60 µmol/L). A significant decrease in systolic blood pressure was observed between M0 and M3 (146±21 mmHg vs. 140±19 mmHg, p=0.036) with a further stabilization at M6 (142±19 mmHg). Similar results were observed with diastolic blood pressure. Safety data are currently adjudicated. Nevertheless, only 12 urinary tract and 2 genital infections were reported, without any ketoacidosis.
Conclusions: GREAT-ASTRE is the largest series of KTRs (diabetic or not) treated with SGLT2i. SGLT2i are frequently prescribed to KTRs, regardless of their diabetic status, without any safety alert in short-term follow-up. Complete follow-up data will be available soon.

ASTRA ZENECA funded ASTRE database to implement GREAT-ASTRE study.

	All (N = 265)
Age (years)	60.5 ± 11.9
Male sex, n (%)	204 (77)
Dapagliflozin, n (%)	250 (94)
Time from transplantation (years)	7.99 [2.79 - 11.92]
Diabetes mellitus, n (%)	185 (69.8)
BMI (kg/m²)	29.1 ± 5.3
Systolic blood pressure (mmHg)	144.6 ± 20.2
Diastolic blood pressure (mmHg)	80.9 ± 11.9
Serum creatinin level (µmol/L)	145.3 [112 - 168]

BRIEF ORALS

Cardiovascular and metabolic complications after kidney transplant

BOS10_6 RISK FACTORS OF DE NOVO POST TRANSPLANTATION DIABETES MELLITUS MORE THAN 8 WEEKS AFTER KIDNEY TRANSPLANTATION - A NATIONAL COHORT STUDY

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Background: Between 10 to 30% of kidney transplant recipients develop post-transplant diabetes mellitus (PTDM). PTDM is a major risk factor for cardiovascular events and death in kidney transplant recipients. In a retrospective single-center cohort study we investigated risk factors for development of *de novo* PTDM from eight weeks after kidney transplantation.
Methods: Inclusion criteria were kidney transplantation from 2015-2019, age > 18 years, no known diabetes prior to, or at the eight-week control after transplantation and with at least one year of follow up. At the eight-week control an oral glucose tolerance test (OGTT) was performed for PTDM diagnosis. *De novo* PTDM was defined as fasting glucose ≥ 7 mmol/L, 2-hours glucose ≥ 11.1 mmol/L at OGTT performed routinely at the one-year visit, or at least two registered dispensations of glucose lowering medication in the Norwegian Prescription Database (NorPD).
Results: In total 632 patients (median age 53 years, 62 % males) with a median follow-up of 2.7 years [1-4] were included of which 54 (8.5%) developed *de novo* PTDM (31 diagnosed by the OGTT at 1 year and 23 identified by glucose lowering dispensation). *De novo* PTDM patients were older than non-PTDM patients at transplantation (median age 63 vs 52 years), were more often males (81 % vs 61%), and had higher fasting blood glucose (mean 5.8 vs 5.3 mmol/L), 2-hour glucose (mean 8.3 vs 6.6 mmol/L) and HbA1c (median 38 vs 32 mmol/mol) at the eight-week post-transplantation control. In a multiple logistic regression analysis, significant associated factors of PTDM were age (years), OR 1.05 (CI 95%: 1.01;1.06), fasting triglycerides (mmol/L), OR 1.59 (CI 95%: 1.19;2.12) and tacrolimus (µg/L), OR 1.22 (CI 95%: 1.02;1.46) concentrations measured at the one-year control visits, accumulated methylprednisolone dose at rejections (g), OR 1.61 (CI 95%: 1.06;2.45) and CMV serostatus (positive donor to negative recipient), OR 2.12 (CI 95%: 1.02;4.38). Plasma magnesium, gender, BMI and plasma creatinine were not associated with development of PTDM.
Conclusions: In conclusion development of *de novo* PTDM later than eight weeks after kidney transplantation was associated with increased age, higher triglycerides, higher tacrolimus concentrations, accumulated methylprednisolone dose at rejections and D+/R- CMV-serostatus.

BOS10_7 POST-TRANSPLANT DIABETES MELLITUS IN DIFFERENT IMMUNOSUPPRESSION TREATMENTS: A META-ANALYSIS

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Background: Post-transplant diabetes mellitus (PTDM) is a frequent complication after kidney transplantation (KT). It increases the risk of cardiovascular disease, which is one of the main causes of death with functioning grafts. This systematic review aims to investigate the effect of different immunosuppressive regimens on PTDM incidence.
Methods: Relevant studies were obtained from a systematic literature search. We searched MEDLINE and CENTRAL (Cochrane Central Register of Controlled Trials) until 1st May 2022. We searched randomized controlled trials (RCT) including KT recipients receiving any immunosuppression and reporting PTDM outcomes. Meta-analysis was done by pooling data for calculating the relative risks (RR) of the outcome by comparing different immunosuppression strategies.
Results: We identified 1,848 reports. After removing duplicates and screening abstracts 156 full-text reports were assessed. We finally included 52 studies. Eight RCTs reported the outcome of PTDM using different induction therapies at ≤7 years after KT, including 1,495 recipients. The meta-analysis of all studies did not show differences in the risk of PTDM in any of the comparisons. 49 RCTs evaluated mTORi use: 32 at de novo KT and 17 long-term follow-up conversions. When comparing mTORi vs antimetabolite there was a higher risk of PTDM in the mTORi group at ≤5 years postKT (22 studies, 8,178 participants, RR 1.25, 95%CI [1.05-1.49], p=0.01). When comparing mTORi vs CNI there were no differences in PTDM risk at ≤5 years postKT (12 studies, 2,537 participants, RR 0.81, 95%CI [0.48-1.40], p=0.46). Conversions from CNI to mTORi at ≤2 years postKT showed an increased risk of PTDM (15 studies, 3,200 participants, RR 1.60, 95%CI [1.14-2.23] , p<0.01). We found 39 RCTs reporting PTDM with CNI. There was an increased risk of PTDM with tacrolimus compared to cyclosporine (26 studies, 5,635 patients, RR 1.71, 95%CI [1.38-2.11], p<0.01) after ≤5 years postKT. Belatacept compared to CNI showed a 38% reduction of PTDM at 1-year (6 studies, 2,100 participants, RR 0.62, 95% CI [0.42-0.91], p=0.02).
Conclusions: A higher risk of PTDM was observed in patients receiving TAC vs CsA, and mTORi inhibitors. Belatacept showed a 38% reduction in PTDM compared to CNI. However, the risk of PTDM should be balanced with the risk of rejection.

BRIEF ORALS

Cardiovascular and metabolic complications after kidney transplant

BOS10_8 DEVELOPMENT AND VALIDATION OF A NEW SCORE TO ASSESS THE RISK OF POST-TRANSPLANTATION DIABETES MELLITUS IN KIDNEY TRANSPLANT RECIPIENTS

Maria Carolina Isaza-Lopez[*1;2], Lina Maria Serna-Higuita[3], Gilma Hernández Herrera[4], Angelica Serna-Campuzano[5], John Nieto Rios[5], Nils Heyne[6], Peter Martus[3], Martina Guthoff[6]

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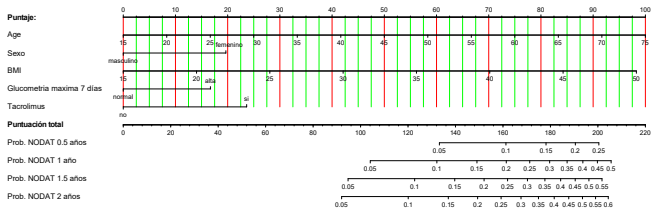
Background: Post-transplantation diabetes mellitus (PTDM) is a serious complication following solid organ transplantation. It is associated with major adverse cardiovascular events, which represent a leading cause of morbidity and mortality in transplanted patients. PTDM is also associated with reduced patient and graft survival The purpose of this study was to develop and validate a score for predicting the risk of PTDM in kidney transplant recipients
Methods: Single-center retrospective cohort study conducted in a tertiary care hospital, Medellin-Colombia from 2005 to 2019. Data from 727 kidney transplant recipients were used to develop a risk prediction model. Significant predictors were identified using time-dependent proportion hazard Cox regression models. To build the prediction model, the score for each variable was weighted by the regression coefficients calculated. External validation of the model was performed using independent external data including 198 kidney transplant recipients from the University Hospital of Tübingen
Results: Among 727 kidney transplant recipients, 122 of whom developed PTDM. The predictive model was based on 5 predictors (age, body mass index; gender, tacrolimus therapy, and hyperglycemia during the first week after kidney transplantation), and exhibited good predictive performance (C-Index: 0.9 [95% CI 0.65 – 0.76] in the development cohort. The risk score was then used in 198 kidney transplant recipients in the validation dataset, including 33 patients with PTDM. The results showed good discrimination (C-Index: 0.72 [95% CI 0.62 – 0.84]). The Brier calibration plot demonstrated an acceptable calibration capability in the external validation
Conclusions: We proposed and validated a prognostic model to predict the risk of PTDM. The model performed well in discrimination and calibration, being simple to use and implement. In addition, a nomogram based on the Cox model was established for clinical application

Figure 1. Nomogram of the probability of developing diabetes mellitus after kidney transplantation



BOS10_9 A PROSPECTIVE COHORT STUDY OF SODIUM/GLUCOSE COTRANSPORTER 2 INHIBITOR-TREATED DIABETIC KIDNEY TRANSPLANT PATIENTS

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Background: Diabetic kidney transplant(DKT) patients suffer from increased burden of cardiovascular(CV) disease. The graft outcome of these patients is not only determined by immunologic injury but also by diabetic kidney disease(DKD) of graft. The SODIUM/GLUCOSE COTRANSPORTER 2 INHIBITOR(SGLT2i) reduces CV events and delays the progression of DKD, and would favor the outcome of these patients. There are limited experiences of the use of SGLT2i on DKT patients.
Methods: One hundred and forty-nine DKT patients treated with dapagliflozin have been prospectively followed for more than 6 months(median 15.4 ±7.0 months) in our institute. Four patients had type 1 diabetes, 58 had type 2 diabetes, and 87 had posttransplant diabetes. Twenty-five patients were on insulin. Baseline serum creatinine was 1.3±0.4(0.6~2.4)mg/dl.
Results: Baseline HbA1c was 7.0±1.8%, which decreased significantly at 3 months(6.8±1.3%, p=0.01) and maintained stable thereafter. Body weight decreased significantly from 66.5±27.1 to 65.1±27.3kg(p=0.00) at 3 months and slightly more reduced until 12 months. Baseline urine albumin-creatinine ratio was 188.9±511.1 mg/g, which decreased significantly at 3 months(132.3±301.2 mg/g, p=0.03), reduced further until 6 months and maintained unchanged until 24 months. The slope of eGFR decline before and after the use of SGLT2i did not differ significantly. Eight patients stopped dapagliflozin due to acute cystitis in 3, weight loss in 2 and patient's preference in 3. There was no episode of acute kidney injury. Acute pyelonephritis was infrequent and did not appear to be increased with this drug.
Conclusions: SGLT2i reduced albuminuria and was well tolerated in DKT patients. The long-term benefit of patient and graft outcome would be worth to be evaluated by further follow up.

BOS10_10 FIRST USE OF DEEP LONG SHORT-TERM MEMORY NEURAL NETWORK IN PREDICTING KIDNEY GRAFT FUNCTION

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Background: Predicting kidney allograft function represents a major challenge in management of kidney transplant recipients. Currently there are many different models for predicting the risk of graft failure and patient survival, some of which are used for graft allocation and decision-making during kidney transplant procurement. All these models are based on mathematical algorithms and machine learning algorithms. Deep Long Short-Term Memory Neural Network (LSTM) is an artificial neural network (ANN) that can learn from entire sequences of measured data through prolonged periods of time, which makes it suitable for learning patterns and predicting final outcomes. Here we present for the first time the results of the use of Deep LSTM neural network in predicting graft function dynamics for future medical examinations.
Methods: A dataset was formed form characteristics of 922 kidney donors and their recipients that underwent a total of 6123 ambulatory controls during which creatinine, eGFR, proteinuria and GFR were measured. This dataset was split in two separate datasets, one was used for ANN model learning, the other for ANN model evaluation.
Results: Deep LSTM ANN learned to predict weather graft function (eGFR) on the next medical examination will be better or worse according to stages of chronic kidney disease (CKD). Better meaning one class better than current stage, the same (same CKD stage), worse (CKD stage class higher for one point than previous), or much worse (CKD stage higher for 2 points or more). It predicted a better CKD stage with an of accuracy 0.67, precision 0.92, specificity 0.88. The same CKD stage with accuracy 0.89, precision 0.7, specificity 0.97, worse CKD stage with accuracy 0.92, precision 0.83, specificity 0.98; and graft failure (much worse CKD) with accuracy 1.0, precision 1.0, specificity 1.0.
Conclusions: This study shows that a Deep LSTM neural network was able to learn and predict graft function on future medical examinations with high accuracy, precision and specificity. In the present era of a broad artificial intelligence application, we find that the next step in improving kidney transplant patients care will be the use of neural networks and their predicting abilities.

BRIEF ORALS

Cardiovascular and metabolic complications after kidney transplant

BOS10_12 ERECTILE DYSFUNCTION AFTER KIDNEY TRANSPLANTATION IN MALES WITH END-STAGE KIDNEY DISEASE: A META-ANALYSIS

Adelina Miron[*1;2], **Anca-Elena Stefan**[2;3], **Ionut Nistor**[2;3], **Andreea Covic**[2;3], **Corneliu Morosanu**[1;2], **Adrian Covic**[2;3]

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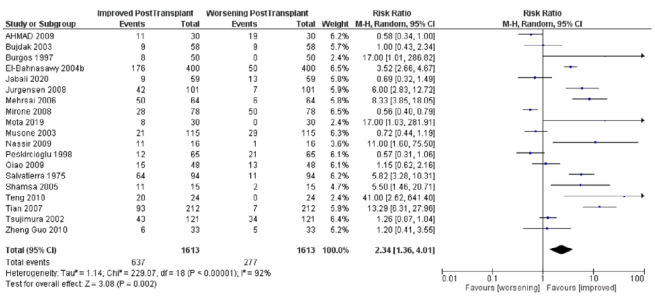
Background: Patients with end-stage kidney disease (ESKD) on dialysis have a constant uremic status and associated comorbidities, such as diabetes mellitus, peripheral, coronary artery disease, or hypertension, as well as complications related to dialysis. There is also a high prevalence (82%) of erectile dysfunction (ED) in males with chronic kidney disease (CKD). Data regarding erectile dysfunction and kidney transplantation (KT) are controversial, ranging from worsening to improvement of ED after KT. We aimed to evaluate the effect of KT on ED in males with ESKD.
Methods: Potentially relevant studies were searched in the following databases: MEDLINE (PubMed), SCOPUS, Embase and Cochrane library from inception until January 2023. Eligible studies compared the same population before and after KT. The primary outcome of our study was to assess the effect of KT on ED. We used a random-effects model for meta-analysis and expressed treatment effects as a risk ratio (RR) with 95% confidence intervals (CI). We used the I^2 statistic to assess for inconsistency. An I^2 > 50% indicated large inconsistency across studies not explained by chance. All statistical analyses were performed using Review Manager Version 5.2 (The Cochrane Collaboration 2012).
Results: 20 articles with a total population of 1681 patients were included, with most patients undergoing hemodialysis before KT. Most studies used the International Index of Erectile function (IIEF) questionnaire as the main method to assess sexual function. Our analysis shows that after kidney transplantation, there was an improvement in erectile dysfunction of 234% (RR 2.3) (95% CI 1,36, 4,01), as seen in Figure 1.
Conclusions: Our meta-analysis shows improvement of ED in males with ESKD after KT. Our study has a few strong points. First, there was a large study population. Second, we used studies that evaluated the same population before and after KT. However, there are a few limitations to our meta-analysis, such as the observational nature of the studies included. Our findings show a beneficial effect of KT on ED.

Figure 1 - Forest plot of the RR of patients with improved sexual function vs worsening sexual function post-KT



BOS10_13 OUTCOMES FOLLOWING ARTERIO-VENOUS FISTULA LIGATION FOLLOWING KIDNEY TRANSPLANTATION

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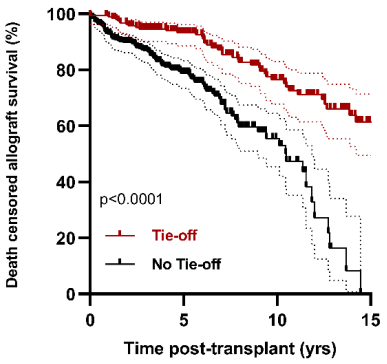
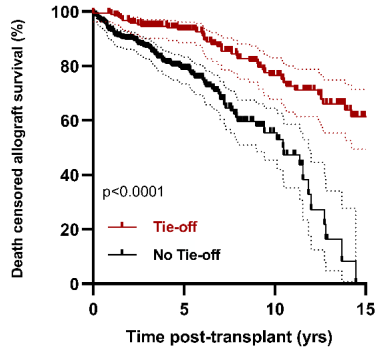
[1]Imperial College London, London, United Kingdom, [1]Imperial College London, London, United Kingdom

Background: Cardiovascular disease remains one of the leading cause of death post-kidney transplantation. Recent evidence suggests an improvement in functional cardiovascular tests following ligation of arterio-venous fistulae (AVF). Ligation of AVF post-successful transplant could improve outcomes; however, this needs to be balanced against removal of venous access, which may be needed should the transplant fail. This investigation aims to: 1. Describe the outcomes following AVF ligation in kidney transplant recipients (KTR), n=190. 2. Compare allograft outcomes against a control group of KTR without AVF ligated, n=380 (1:2 cases:controls) 3. Identify risk factors associated with return to dialysis following AVF tie-off
Methods: Patients and outcomes were identified from a prospectively maintained transplant database. Ligation episodes were captured from health records. All patients, irrespective of indication for ligation were included.
Results: 190 patients (70% males, median age 50 (40-59) years, 33% white, 76% receiving a deceased donor transplant and 19% with diabetes) underwent AVF ligation at a median time of 2.5 (2.0-3.3) years post-transplant. Median follow up was 6.4 (5.2-7.1) years post tie-off. 5-yr all-cause and death censored allograft survival was 71.9% and 81.8% respectively. Risk adjusted cox-proportional hazards regression for; a. all-cause allograft survival, showed fistula excision was independently associated with improved risk of all-cause allograft loss, HR 0.44 (0.2-0.61), p<0.0001 (*Figure 1*); b. death-censored allograft survival, showed fistula excision was independently associated with improved risk of death-censored allograft loss, HR 0.35 (0.23-0.53), p<0.0001 (*Figure 1*). A diagnosis of diabetes (HR 2.13 (1.23-3.369), p=0.007) and time to tie-off post-transplant (HR 1.09 (1.02-1.16), p=0.008), are associated with all-cause graft loss. Time to tie-off (HR: 1.19 (1.10-1.30), p=0.0001 and receipt of a living donor transplant (HR 0.33 (0.11-0.98), p=0.045) impacted on risk of death censored allograft loss.
Conclusions: AVF ligation post-transplant may have potential graft and patient benefits with careful timing and patient selection.

Figure 1.





BRIEF ORALS

Cardiovascular and metabolic complications after kidney transplant

BOS10_14 PROSPECTIVE RANDOMIZED CONTROLLED TRIAL ANALYZING THE EFFECTS OF DENOSUMAB ON BONE MINERAL DENSITY AND BONE METABOLISM IN RENAL ALLOGRAFT TRANSPLANTS

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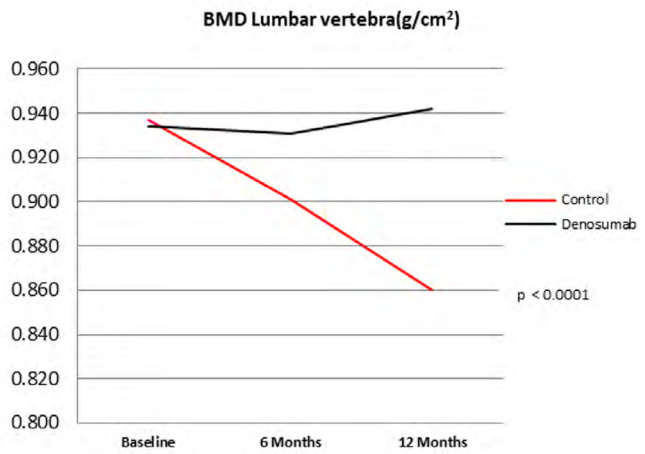
Background: The administration of denosumab decreases bone resorption and increases bone mineral density in osteoporosis in non-transplant settings. This study at our centre was done to study the potential benefits of denosumab in terms of bone health in renal transplant patients.
Methods: A single centre (PGIMER Chandigarh India) randomized control study to analyse the effects of denosumab on Bone Mineral Density(Measured by DEXA scan and HRPQCT Scan) and bone turnover markers(PINP , Beta CTX,BSAP) in denosumab group patients (Received Inj. denosumab 60 mg s.c two dose 6 months apart for 1 year, along with standard immunosuppression plus calcium 1 gram and vitamin D 500 IU daily) and control group patients (Do not received denosumab but received standard immunosuppression plus regular calcium 1 gram and vitamin D 500 IU daily).
Results: 30 were randomized into denosumab (n=15) and control (n=15) groups. Mean age in denosumab group was 32.36±8.77 years and 34.57±8.72 years in control group. Other baseline demographics were balanced between two groups. Six monthly DEXA Scans revealed significant fall in BMD at lumbar vertebra in control group (p =<0.0001) over 1 year. The denosumab significantly increased BMD at lumbar vertebra (p< 0.0001) (Two way repeated measure ANOVA) in denosumab group. In HRPQCT scan significant difference in tibial trabecular thickness (in mm) (p =0.045) was noticed at end of 1 year. Denosumab also resulted in significant fall in bone turnover markers (measured 6 monthly), PINP (P<0.03), Beta-CTX (p=0.001) and BSAP (p=0.006).Asymptomatic significant fall in serum calcium was noticed (p<0.001) after each denosumab dose but no clinical side effect noticed after denosumab use.
Conclusions: The bone mineral density at lumbar vertebra decreased significantly after renal allograft transplantation which may predispose the patient to risk of fractures in long term. The use of denosumab in two doses 6 month apart effectively countered the reduction and improved bone mineral density in lumbar vertebral region and tibia. Denosumab resulted in favourable reduction in bone turnover markers with no adverse side effect profile.

Serial Comparison of BMD at Lumbar vertebra between Denosumab and Control (Two-way Repeated Measure ANOVA)



Kidney rejection, function and survival

BOS11_1 LANDSCAPE OF T-CELL MEDIATED REJECTION RESPONSE TO TREATMENT AFTER KIDNEY TRANSPLANTATION

Gillian Divard*[1], Sofia Naser[1], Olivier Aubert[1], Marc Raynaud[1], Arnaud Delbello[2], Nassim Kamar[2], Carmen Lefaucheur[1], Alexandre Loupy[1]

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Background: In the current era of immunosuppression, T-cell mediated rejection (TCMR) seems to be less severe than antibody mediated rejection, however TCMR phenotype has become more complex and the response to therapy has not been investigated in large clinical trials. There is a need to better assess response to treatment in TCMR in order to optimize clinical trial and end points definition.
Methods: This multicenter prospective cohort study included patients who presented a first T-cell-mediated rejection between 2004 and 2021 in four French transplant centers. TCMR cases were reassessed using the latest Banff 2019 classification. Patients with features of concomitant antibody mediated rejection (AMR) were excluded. All clinical, immunological, histological and TCMR therapies were collected at time of rejection and during the follow-up. All patients received a standard of care treatment with 3 steroid pulse and steroid taper +/- anti thymocyte treatment. At 3 months after treatment, a kidney allograft reevaluation was performed including eGFR, proteinuria, DSA and graft biopsy assessment.
Results: A total of 550 patients were included. The TCMR occurred in a median time of 3.4 [1.1-12.3] months post-transplantation. Mean eGFR was 40.0 (20.3) mL/min/1.73m². The distribution of TCMR grade was 26.4% grade IA, 37.7% grade IB, 23.5% grade IIA, 8.3% grade IIB and 4.1% grade III. The median time between TCMR and kidney allograft reevaluation was 3.1 [1.8-7.7] months post-TCMR. At time of reevaluation, mean eGFR was 42.0 (18.5) mL/min/1.73m², 25.5% of patients had positive anti-HLA DSA. The main diagnoses at reevaluation after treatment were: 1) persisting TCMR 10.8%, 2) AMR 10.9%, and 3) borderline lesions 10,8%. After a mean follow-up time of 7.8 (5.3) years post TCMR, 169 (32.8%) patients experienced graft failure. Patients with persisting features of allograft activity, either TCMR and AMR has decreased graft survival compared with patients with TCMR histological resolution (p<0.05)
Conclusions: In the largest cohort of well phenotyped TCMR, response to treatment is suboptimal for almost 30% of patients and associated with worse prognosis. We provide here the basis for better assess response to treatment after TCMR to better individualize treatment strategies, clinical trials and improve patients outcomes.

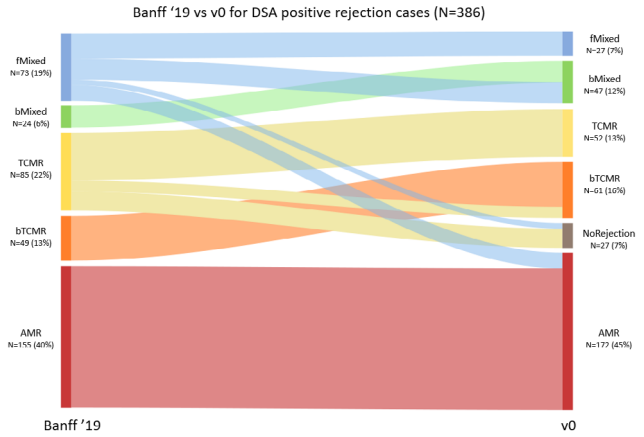
BOS11_2 OPERABILITY OF THE BANFF "V" LESION SCORE IN DSA POSITIVE MIXED REJECTION

Karolien Wellekens*[1], Priyanka Koshy[2], Tim Debyser[2], Evert Cleenders[1], Marie-Paule Emonds[2], Dirk Kuypers[1], Aleksandar Senev[1], Elisabet Van Loon[1], Maarten Coemans[1], Maarten Naesens[1]

[1]KU Leuven , Department of Microbiology, Immunology and Transplantation, Leuven, Belgium, [2]KU Leuven , Leuven, Belgium

Background: According to the Banff Classification of Allograft Pathology, the "v" lesion score appraises the degree of intimal arteritis by the presence of inflammatory cells in the subendothelial space. This lesion score remarkably contributes to the diagnosis of antibody-mediated rejection (AMR) as well as T cell-mediated rejection (TCMR); high "v" scores alone can give rise to TCMR diagnosis independently of other main TCMR features. Here, we aim to investigate the operability of this lesion score in rejection diagnosis.
Methods: In this single-center observational study, we made use of a retrospective cohort database consisting of kidney biopsy samples (=7601) from all adult patients (n=1868) who received a kidney transplant between March 2004 and May 2021. We retrospectively defined TCMR and AMR by the histological Banff'19 criteria and related the histological phenotype to DSA status and C4d staining results in peritubular capillaries.
Results: 386 out of 1020 DSA positive biopsies showed acute rejection subtypes (38%): 155 AMR (40%), 85 TCMR (22%), 49 borderline TCMR (13%), 73 full mixed (AMR-TCMR, 19%), and 24 borderline mixed rejection (AMR-borderline TCMR, 6%). A large number of mixed rejections was however explained by the "v" lesion as a criterion for TCMR. When the "v" lesion was not considered for TMCR, we scored 27 full mixed rejection (7%) cases (Figure 1). Yet, the proportion of borderline mixed and AMR cases increased with 6% and 5% respectively. In total, we reclassified 35% of the phenotypes (P<0.001).
Conclusions: A significant proportion of DSA positive mixed rejection biopsies meet the TCMR criteria by the "v" lesion, indicating the need to review the sensitivity and specificity of this lesion, and thus its operability in rejection diagnosis in general. Our data suggest not using the "v" lesion to classify rejection phenotypes, but rather applying it as a 'risk estimator' as it is proven to be a negative prognostic factor for kidney allograft survival.

Figure 1: Reclassification of DSA positive mixed rejection phenotypes when not considering the "v" lesion score for TCMR. fMixed: full mixed rejection (AMR-TCMR), bMixed: borderline mixed rejection (AMR-borderline TCMR), bTCMR: borderline TCMR.



BOS11_3 CALLING INTO QUESTION THE ADDED VALUE OF THE 'PTC RULE' IN CLASSIFYING KIDNEY TRANSPLANT REJECTION

Karolien Wellekens*[1], Priyanka Koshy[2], Tim Debyser[2], Marie-Paule Emonds[2], Dirk Kuypers[1], Aleksandar Senev[2], Elisabet Van Loon[1], Maarten Coemans[1], Maarten Naesens[1]

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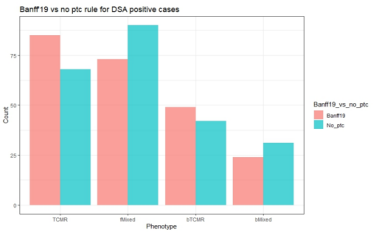
Background: To establish antibody-mediated rejection (AMR) diagnosis in the presence of (borderline) T cell-mediated rejection (TCMR), peritubular capillaritis ("ptc") alone is not sufficient and glomerulitis ("g") must be present. We aim to study the importance of peritubular capillaritis as an exclusion criterion to classify rejection phenotypes in accordance with the Banff Classification of Allograft Pathology.
Methods: In this single-center observational study, we made use of a cohort database consisting of kidney biopsy samples (=7601) from all adult patients (n=1868) who received a kidney transplant between March 2004 and May 2021. We retrospectively defined TCMR and AMR by the histological Banff'19 criteria and reclassified these phenotypes not taking into account the 'ptc rule' ("ptc" or "g" ≥2 / "ptc" or "g" ≥1 in case of C4d positivity).
Results: 386 out of 1020 (38%) DSA+ and 1060 out of 5316 (20%) DSA- biopsies showed acute rejection phenotypes. In DSA+ cases, we scored 155 AMR (40%), 85 TCMR (22%), 49 borderline TCMR (13%), 73 mixed (AMR-TCMR, 19%), and 24 borderline mixed rejection (AMR-borderline TCMR, 6%) phenotypes. 187 AMR (18%), 392 TCMR (37%), 333 borderline TCMR (31%), 112 mixed (11%) and 36 borderline mixed (3%) phenotypes were identified in DSA- cases. When the 'ptc rule' was not taken into account for DSA+ cases, we reclassified only 4% of TCMR to mixed and 2% of borderline TCMR to borderline mixed rejection phenotypes; both changes did not reach statistical significance(Figure 1). For DSA- cases, 6% of TCMR and 3% of borderline TCMR phenotypes were reclassified to mixed and borderline mixed rejection respectively (P<0.01).
Conclusions: Omitting the 'ptc rule' has a minor impact on final rejection phenotype classification for DSA+ cases. In DSA- cases, further research on how phenotype reclassification is related to outcome and immunological risk factors such as non-HLA antibodies and missing self is ongoing to define whether elimination of the 'ptc rule' in DSA- cases indeed alters the accuracy of the classification. These findings will likewise contribute in determining if we could fully align the histological definition of DSA+ and DSA- microvascular inflammation.

Figure 1: Reclassification of phenotypes according to the Banff'19 consensus vs when not taking into account the 'ptc rule'.

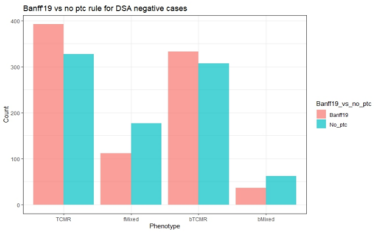
Phenotype classification according to Banff'19 versus no ptc rule (Chi2 P=0.1652)

DSA+ phenotype	Banff'19 (n)	No ptc rule (n)
TCMR	85	68
Borderline TCMR	49	42
Borderline mixed	24	31
Full mixed	73	90



Phenotype classification according to Banff'19 versus no ptc rule (Chi2 P<0.01)

DSA- phenotype	Banff'19 (n)	No ptc rule (n)
TCMR	392	327
Borderline TCMR	333	307
Borderline mixed	36	62
Full mixed	112	177



BOS11_4 COMPARISON OF CLINICAL AND PATHOLOGICAL FEATURES OF REJECTION IN ABO-IMCOMPATIBLE AND ABO-COMPATIBLE KIDNEY TRANSPLANTATION

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Background: ABO-incompatible(ABOi) living donor kidney transplantation(LDKT) is gradually being implemented to overcome the shortage of donor kidneys. Since ABOi LDKT began in 2007 in Korea, there have not been yet sufficient reports regarding the post-transplant long term outcomes including the incidence of rejection of ABOi LDKT. We analyzed the decade of our experiences of ABOi LDKT with comparing ABO-compatible(ABOc) LDKT from the standpoint of rejection and de novo DSA.
Methods: We retrospectively analyzed 1190 living donor kidney transplant recipients between July 2010 and December 2020 at the Severance Hospital. We compared clinical outcomes and rejection type of ABOi LDKT (n = 246) with those of ABOc LDKT (n = 749).
Results: No significant difference in death-censored graft survival was observed between ABOi KT and ABOc KT (P = 0.217). Patient survival after ABOi KT was similar to that after ABOc KT (95.0% vs. 97.3%, respectively, p= 0.108). The prevalence of de novo DSA production and biopsy-proven acute T-cell mediated rejection(TCMR) and chronic antibody–mediated rejection(ABMR) were comparable between the two groups. The incidence of biopsy-proven active ABMR was significantly higher ABOi KT than ABOc KT (9.8% [24/246] vs. 5.5% [41/749], respectively p = 0.018). In addition, biopsy–proven acute rejection(BPAR) free survival rate was lower in ABOi KT than ABOc KT (71.8% vs. 76.4%, respectively P = 0.024) Multivariable cox regression confirmed that DR and DQ –associated de novo DSA was independently associated BAPR but ABO incompatibility was not a significant risk factor of BAPR after adjustment with covariates.
Conclusions: ABOi LDKT was not inferior to ABOc LDKT for patient survival and graft survival. However, ABO incompatibility was associated with the increased incidence of active ABMR.

BOS11_5 ACUTE REJECTION AFTER CONVERSION TO BELATACEPT IN KIDNEY TRANSPLANTATION

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Background: After kidney transplantation, conversion to belatacept is an interesting alternative in patients with poor graft function or intolerance to calcineurin inhibitors (CNI). The occurrence of acute rejection has been widely described and studied during de novo use, but much less so in conversion conditions.
Methods: We present here a retrospective multicenter study investigating the occurrence of acute rejection after conversion to belatacept.
Results: Between 2011 and 2021, 901 patients were switched to belatacept after transplantation and 54 of them experienced a biopsy-proven acute rejection, i.e. 6% of the cohort. Among the 54 patients, 47 (87%) developed a T cell mediated rejection rejection (5 borderline, 9 grade Ia, 9 grade Ib, 7 grade IIa, 11 grade IIb, 6 grade III). This rejection episode occurred after a median of 2.6 months (IQR: 2.1-2.6) after switch. In all cases, rejection therapy was offered (high dose steroids in 91.5% of cases) and belatacept treatment was discontinued in 51.2% of cases. Renal function improved in 56.4% of patients. We recorded 18 graft losses (38.9%) within a median of 7.2 months (IQR: 1.4-10.1) after rejection and 8 patients died after rejection. We compared these 47 patients to a multicenter historical cohort (2011-2017) of 262 patients switched to belatacept who did not develop rejection at follow-up, to determine clinico-biological predictors of acute rejection. After multivariate analysis, the only factors associated with the occurrence of rejection after switch were the use of thymoglobulins as induction (HR: 0.46, 95% CI: 0.21-0.99, p=0.05), tacrolimus treatment before switch (HR: 2.97, 95% CI: 1.23-7.14 p=0.01) and late switch > 6 months after transplant (HR: 0.46, 95% CI: 0.23-0.92 p=0.03).
Conclusions: The occurrence of acute rejection after switching to belatacept appears to be less frequent than with de novo use. Nevertheless, the risk of graft loss or deterioration of renal function after rejection is significant in patients with already poor renal function.

BOS11_6 SUBCLINICAL ANTIBODY-MEDIATED REJECTION DETECTED BY EARLY (TWO WEEKS) PROTOCOL BIOPSIES IN HIGHLY IMMUNIZED TRANSPLANT RECIPIENTS

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Background: Renal graft recipients with donor-specific anti-HLA antibodies show an increased risk of antibody-mediated rejection (ABMR). Protocol biopsies may help detect subclinical rejection. The aim of this research was to describe the prevalence, severity and outcomes of patients with high immunological risk who underwent early protocol biopsy
Methods: Renal transplant (RT) recipients with pre-transplant calculated cPRA≥90% who received a cadaveric donor kidney graft between 2015 and 2022 were evaluated. Patients with protocol biopsy within the first two weeks post transplantation were included. Baseline characteristics, immunological parameters, immunosuppressive treatment, presence of delayed graft function and serum creatinine levels throughout follow-up were reported. The prevalence of ABMR was analyzed by early protocol biopsy in the study group.
Results: Out of 155 patients, a total of 128 early protocol biopsies were performed. Thirty-eight patients (29.5%) had at least one episode of rejection excluding borderline during follow-up: 23 (60.5%) corresponded to active ABMR, of which 17 were diagnosed early (<90 days post-TR), and 6 late. Among patients with early ABMR 11 (64.7%) were diagnosed by protocol biopsies within 2 weeks post-TR (early ABMR). No significant differences in pre-TR immunological data or donor clinical characteristics were observed, except for a higher percentage of uncontrolled asystole in the rejection group. At 1-year follow-up the patients with early ABMR rejection: 2 had graft dysfunction, 2 developed ABMR chronic-active and differences were observed in eGFR: 32±7 vs 48±2 p=0.038 compared to those without early biopsy rejection.
Conclusions: 64.7% of early ABMR were detected by early protocol biopsy in a population at high immunological risk (cPRA≥90%), information not previously reported in this population.

BOS11_7 A NOVEL TWO STAGE REJECTION PREDICTION MODEL IN KIDNEY ALLOGRAFT USING SERIAL GENE EXPRESSION PROFILE AND DONOR-DERIVED CELL-FREE DNA

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Background: Non-invasive blood biomarkers for rejection have gained significant attention as an alternative to invasive kidney biopsies. We aimed to develop predictive models using serial samples gene expression profile (GEP) and donor-derived cell-free DNA (dd-cfDNA) up to 2-year post kidney transplantation (KT).
Methods: We used data from a previously reported prospective multicenter observational study. For 1-year post KT prediction model, we analyzed 212 subjects with 1 year-post KT biopsies and at least one serial samples of GEP and dd-cfDNA. We also developed a 2-year post KT prediction model using 166 subjects with 2-year post KT biopsies and serial samples. A microarray GEP method and fraction of dd-cfDNA over total cell free DNA were used. Two stage model fitting was performed. The first stage was to fit two linear mixed effect model to calculate random intercept and random slope followed by the second stage logistic regression model.
Results: For 1-year post-KT rejection model, 792 GEP and 1375 dd-cfDNA samples were analyzed. The area under the receiver operating characteristic curve (AUC) of 1-year post KT rejection model was 0.80 (Table 1). A total of 921 GEP and 1,666 dd-cfDNA samples from 166 subjects were used for the 2 year-KT rejection model (Table2). As more serial samples were incorporated into the model, the AUC improved to 0.84 at 24 months (Table 2).
Conclusions: Accumulation of data from multiple serial GEP and dd-cfDNA samples improved 2-year post KT rejection prediction with AUC 0.84. Further study will be needed to validate this novel rejection prediction model and incorporate additional data elements.

Table 1) The summary of 1-year post KT rejection prediction model

	Number of subjects	Number of GEP	Number of dd-cfDNA	Number of rejections	AUC
Up to 3 months	120	211	294	40	0.65
Up to 1-year	212	792	1375	68	0.80

Table 2) The summary of 2-year post KT rejection prediction model

	Patient numbers	Number of GEP	Number of dd-cfDNA	Rejection episodes	AUC
Up to 15 months	166	692	1208	51	0.74
Up to 17 months	166	703	1299	51	0.75
Up to 24 months	166	921	1666	51	0.84

BOS11_8 SURVIVAL OUTCOMES COMPARING OLDER LIVING DONOR VERSUS STANDARD CRITERIA DONOR KIDNEY TRANSPLANTATION VERSUS NOT BEING TRANSPLANTED

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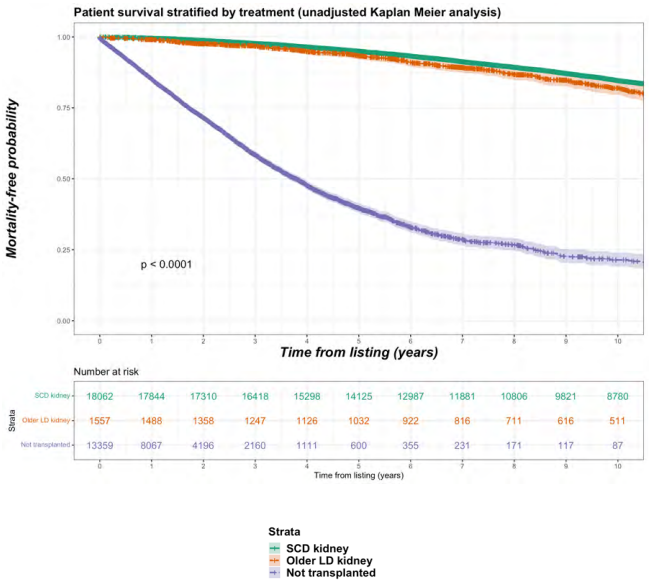
Background: The literature regarding mortality outcomes for kidney transplant candidates receiving older living donor kidneys versus receiving a younger standard criteria donor (SCD) kidney or remaining on dialysis has not been explored. The aim of this analysis was to explore this using UK transplant registry data, with older living donors defined as a donor aged 60 years and above.
Methods: A retrospective cohort study was undertaken of prospectively collected registry data of all waitlisted kidney failure patients receiving dialysis in the United Kingdom. From January 1, 2000 until September 30, 2019 inclusive, all patients listed for their first single kidney transplant were included. The primary outcome was mortality, with survival analysis conducted according to the intention-to-treat principle. Time-to-death from listing was analysed using nonproportional hazard Cox regression models with transplantation handled as a time-dependent covariate. All analyses were done using R statistical software (version 4.2.2).
Results: A total of 32,978 waitlisted kidney failure patients formed the primary study cohort, of whom 18,796 (58.5%) received a kidney transplant (1,557 older living donor kidneys and 18,062 SCD kidneys). Older living donor kidney transplantation constituted only 17.0% of all living donor kidney transplant activity (overall living kidney donor cohort; n=9,140). Recipients of older living donor kidneys had reduced all-cause mortality compared to receiving SCD kidneys (HR 0.904, 95% CI 0.845-0.967, p=0.003) and much lower all-cause mortality versus remaining on the waiting list (HR 0.160, 95% CI 0.149-0.172, p<0.001).
Conclusions: Waitlisted kidney transplant candidates who proceed with living donor kidney transplantation from donors aged 60 years and over have similar all-cause mortality versus waiting for any SCD kidney transplant or remaining waitlisted. Older living kidney donors should be actively explored to expand the living donor kidney pool and are an excellent treatment option for waitlisted kidney transplant candidates.



BOS11_9 PREDICTION OF GRAFT SURVIVAL PRIOR TO ACCEPTING AN OFFER FOR LIVING DONOR KIDNEY TRANSPLANT: AN ARTIFICIAL INTELLIGENCE APPROACH

Hatem Ali*[1], Mahmoud Mohamed[2], Bernard Burke[3], David Briggs[4], Nithya Krishnan[5]

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Background: The current available models for evaluation of outcomes of living donor kidney transplant before accepting an offer are poorly developed, and validated. Aim: We aim to use Artificial Intelligence to build a model that can accurately predict death censored graft survival for living donor kidney transplant prior to accepting an offer.
Methods: All living kidney transplant patients who were: registered in the UNOS database between 1/1/2007 and 1/6/2021, maintained on TAC/MMF immunotherapy were included in our analysis. We excluded patients with age<18 years old and ABO incompatible transplant. We divided the data randomly into training and testing dataset with ratio 80:20. We performed recursive feature elimination to select the important ones for prediction. Features were selected based on their Gini impurity scores. We performed Artificial Neural Network analysis (ANN). We evaluated the model using Harrell Concordance-time-dependent score (for discrimination), and Integrated Brier score (for calibration). We also assessed dynamic AUC for model performance.
Results: 54,110 living donor kidney transplant patients were included in the study. Harrell C-Statistic scores were 0.70 at 5 years post-transplant, 0.68 at 10 years post-transplant and 0.68 at 13 years post-transplant, indicating very high discrimination power. Integrated Brier Score was 0.08, indicating very high calibration score for our model. Dynamic AUC scores were 0.71 at 5 years post-transplant and 0.68 at 10 and 13 years post-transplant, indicating adequate performance for our model. The key players in our model were recipient age (variable importance=0.26), donor age (variable importance=0.17), donor ethnicity (variable importance=0.90), followed by dialysis vintage pre-transplantation.
Conclusions: The ANN model had high discrimination, calibration, and performance indices for predicting death censored graft survival prior to transplant. It can aid the clinical decision for management of the transplant patients. We are currently developing a user-friendly web application that can be used to apply the ANN model for prediction. Our model can help ranking potential living kidney donors based on graft outcomes. Therefore, our model can help improve current outcomes of kidney paired exchange schemes.

BOS11_10 PREDICTION OF KIDNEY FAILURE AND DEVELOPMENT OF HYPERTENSION AMONG POTENTIAL LIVING DONORS: AN ARTIFICIAL INTELLEGENCE APPROACH

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Background: Our aim is to predict occurrence of lifetime kidney failure and development of hypertension among living donors prior to donation.
Methods: All living kidney transplant donors registered in the UNOS database from 1994 till 2020 were retrospectively reviewed. Kidney failure was defined as the need for maintenance dialysis post-donation or being added to the transplant waiting list. The outcome of kidney failure was followed-up for lifetime per donor. Development of hypertension was defined as "requiring long-term medication for treatment of hypertension post-donation". The data was divided into training and test dataset with ratio 70:30 in order to train the model and then evaluate its performance on the unseen data. Decision based models for survival analysis were used (decision tree, Random Forest and XGBOOST). Class weights were used to encounter for class imbalance. Evaluation criteria were Area under the curve (AUC) and accuracy to evaluate model performance for discrimination between the class outcomes. Sensitivity and specificity for identifying each outcome were evaluated.
Results: 159,617 patients were included in our study. For the predicting kidney failure, the xgboost model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.77, sensitivity=0.78 and specificity=0.77. The key-players with the highest weights for predicting kidney failure were "history of cigarette smoking" (weight =0.35), "biological relationship with the recipient" (weight=0.15), followed by "donor ethnicity" (weight=0.12). For the predicting development of hypertension, the random forest classifier model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.76, sensitivity=0.76 and specificity=0.76. The key-players with the highest weights for predicting the development of hypertension were "history of cigarette smoking" (weight =0.13), "duration of abstinence" (weight=0.09), followed by "donor ethnicity" (weight=0.08).
Conclusions: Decision based models can aid in predicting kidney failure and development of hypertension among potential living donors. user-friendly web app can be developed using our model. Key players in prediction for kidney failure and hypertension were cigarette smoking, biological relationship with the recipient and donor ethnicity.

BOS11_12 IMPACT OF INDIVIDUAL EPLETS TO ACUTE REJECTION STUDIED BY MACHINE LEARNING METHOD: ANALYSIS OF KOREAN ORGAN TRANSPLANTATION REGISTRY

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Background: Epitope matching has been shown to predict allograft survival and development of de novo donor-specific antibodies. However, statistical superiority of eplet mismatch to predict rejection outcome than that of HLA genotype mismatch were not thoroughly investigated.
Methods: Patients included in the Korean Organ Transplantation Registry(KOTRY) were used. Kidney transplant recipients who received transplants from 2014 to 2021 were enrolled. HLA four-digit genotypes were imputed by matching to the four-digit haplotype distribution as our previous method. The primary outcome measurement was acute rejection, biopsy-proven acute rejection (BPAR), T-cell mediated rejection (TCMR) and B-cell mediated rejection (BCMR) within 1 year. Ten fold cross-validated Extreme Gradient Boost (XGBoost) model and logistic regression were used as statistical method and cross-validated receiver operating characteristics (ROC) curves were compared.
Results: Among 9,150 donor-recipient pairs, four digits HLA estimation were successful in 7,607 pairs. Exact 1:1 matching of HLA haplotype were successful in 1,980 pairs (call 4 digits group). Mean class I and class II eplet mismatches were 10.6±7.1 and 17.8±12.4 respectively. As depicted in Table, area under curve (AUC) of individual eplets are not better than HLA mismatch numbers in total population (0.549 vs. 0.576 by XGBoost and 0.562 vs 0.568 by logistic regression). In call 4 digits group, individual eplets using XGBoost better predict acute rejection (0.585 vs 0.575), BPAR (0.536 vs 0.500), TCMR (0.535 vs 0.500) than HLA mismatch numbers. Sum of eplet mismatch by logistic regression did not show any better predictability to rejection episode than HLA mismatch numbers.
Conclusions: In this Korean population study, individual eplet mismatches predicted acute rejection better than HLA mismatches in the subpopulation who had accurate 4 digits matched subpopulation. Sum of eplet mismatch number did not show better predictability than HLA mismatch numbers.

10 folds Cross-validated AUC		Total population				Call 4 digits				Estimated 4 digits			
		AR	BPAR	TCMR	BCMR	AR	BPAR	TCMR	BCMR	AR	BPAR	TCMR	BCMR
XG Boost	Individual Eplets	0.549	0.500	0.500	0.500	0.585	0.536	0.535	NaN	0.552	0.562	0.500	0.559
	Clinical	0.566	0.500	0.587	0.500	0.560	0.500	0.500	NaN	0.564	0.500	0.579	0.500
	HLA mismatch no.	0.576	0.586	0.500	0.500	0.575	0.500	0.500	NaN	0.563	0.500	0.500	0.500
Logistic Regression	Eplet mismatch no.	0.562	0.571	0.551	0.595	0.579	0.575	0.549	0.616	0.567	0.573	0.554	0.598
	Clinical	0.572	0.557	0.604	0.551	0.578	0.587	0.590	0.623	0.568	0.554	0.604	0.543
	HLA mismatch no.	0.568	0.582	0.569	0.578	0.589	0.580	0.545	0.635	0.564	0.580	0.575	0.588

BOS11_13 CLINICAL EVOLUTION OF PATIENTS WITH DE NOVO DONOR-SPECIFIC HLA ANTIBODIES AFTER KIDNEY TRANSPLANTATION

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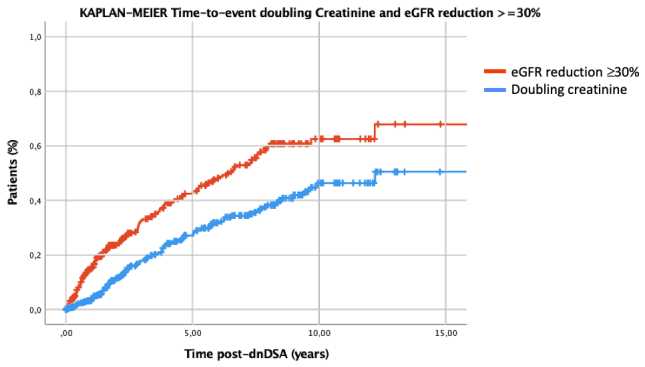
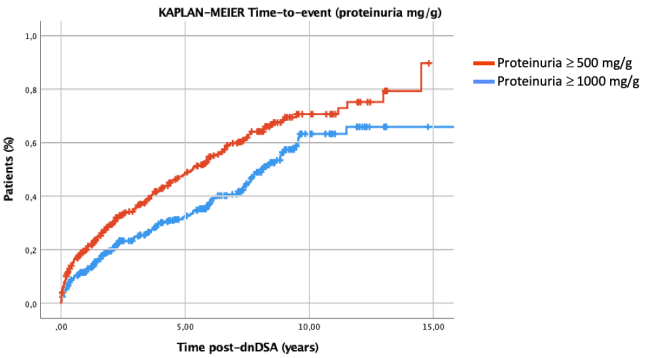
Background: *De novo* donor-specific antibodies (dnDSA) may cause antibody-mediated rejection (ABMR) and graft dysfunction. In this study we aimed to assess the value of estimated glomerular filtration rate (eGFR) and proteinuria to predict graft loss in patients with dnDSA and their potential utility as surrogate endpoints for clinical trials.
Methods: All 400 kidney transplant recipients at our center with dnDSA against the last graft (01/03/2000-31/05/2021) were included in this retrospective study. The dates of doubling creatinine, ≥30% eGFR decline and proteinuria ≥500 mg/g and ≥1000 mg/g in at least two consecutive determinations and before graft failure were registered from day of first dnDSA occurrence. Patients were classified as 'completely stable' (no graft loss, no ≥30% eGFR reduction, no proteinuria ≥500 mg/g) at 5 years after first occurrence of dnDSA.
Results: During 8.3 years of follow-up, graft loss occurred in 33.3% of patients. Creatinine doubled after a median of 2.8 years from dnDSA appearance, and the time from doubling creatinine to graft failure was 1.0 years. Analyzing a ≥30% decline in eGFR, the time from dnDSA occurrence to this event was 2.0 years, with a positive predictive value of 47.3% to predict graft failure, which occurred after 1.9 years. The median time from proteinuria ≥500mg/g and ≥1000mg/g to graft failure was identical (1.8 years). The 5-year incidence of renal outcomes is shown in figure 1. Interestingly, 5 years after first occurrence of dnDSA, 113/400 (28.2%) patients were 'completely stable'.
Conclusions: A relevant (28.2%) proportion of patients has a 'completely stable' clinical course after 5 years post-dnDSA. A ≥ 30% decline in eGFR is a more conservative endpoint that appears earlier after dnDSA and is associated with graft failure. Similarly, proteinuria ≥ 500mg/g is a marker of progression in this high-risk population.

Figure 1. Time-to-event renal outcomes: A) By survival analysis, the 5-year incidence of doubling creatinine and ≥30% eGFR decline was 27.2% (± 2.7%) and 42.9% (±3.1%), respectively. B) At 5 years post-dnDSA, 48.5% (± 2.9%) of patients had proteinuria ≥500 mg/g and 32.7% (± 2.7%) had proteinuria ≥1000 mg/g.

A)



B)



BOS11_14 USE OF TOCILIZUMAB IN CHRONIC ACTIVE ANTIBODY-MEDIATED REJECTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

Maria Sangermano[*1], Susanna Negrisolo[2], Benedetta Antoniello[3], Andrea Carraro[3], Marta Vadori[4], Elisa Cuciz[4], Germana Longo[1], Enrico Vidal[1], Davide Meneghesso[1], Mattia Parolin[1], Emanuele Cozzi[4], Elisa Benetti[1]

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Background: Chronic active antibody-mediated rejection (caAMR) has a deleterious impact on allograft survival. Current evidence for treatment of caAMR is limited, especially in children. Tociluzumab (TCZ) is a potential therapeutic option thanks to its action against IL-6-mediated inflammation and humoral immunity. We describe the effects of TCZ therapy in pediatric kidney transplant (pKT) recipients with caAMR.
Methods: We retrospectively analyzed the outcomes (renal function and histological lesions) of a 6-months TCZ therapy in 6 pKT recipients treated between November 2021 and December 2022. All patients had caAMR according to the Banff classification 2018 (category 2) and all received intravenous TCZ (8mg/kg/month for 6 months). Collected data included creatinine, eGFR, proteinuria, HLA and non-HLA antibodies at baseline, month +3 (M3) and month +6 (M6) after TCZ initiation. For each patient, a follow-up biopsy was scheduled at the end of the treatment.
Results: Six patients (average age 15 years, 4 male) were included. Immunosuppression at the time of caAMR included tacrolimus with MMF (4 patients, 66.6%) or mTOR inhibitor (2 patients, 33.3%), and daily prednisone. AntiHLA antibodies (DSA) were detected in 3 patients and nonHLA antibodies (AT1R and ETAR) in 2. caAMR diagnostic was based on histological findings in the 3 patients without DSA. Mean time to caAMR was 4 years after transplantation. At the time of caAMR diagnosis, mean eGFR was 40.6±12.8 mL/min/1.73 m². In one patient, TCZ treatment was discontinued after 3 doses due to graft failure. Another patient performed follow up biopsy, which showed persistent caAMR with worsened histological lesions, and subsequently lost his graft. Two patients showed a stable renal function, but histological lesions had worsened (ct1, ci3, IFTA2). In one patient, with worsened renal function, follow up biopsy was not performed due to intrarenal arteriovenous fistula. In the last patient, the biopsy is yet to be performed. Globally, mean eGFR worsened to 31.4±15.3 mL/min/1.73 m² at M3 and remained stable at M6. Proteinuria, antiHLA and nonHLA antibodies remained stable.
Conclusions: In our experience, TCZ therapy did not appear to be significantly effective in modifying the natural history of caAMR. However, more studies are needed to clarify the role of TCZ in caABMR.

BOS12_1 SPLIT-LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS IS ASSOCIATED WITH REDUCED GRAFT SURVIVAL DUE TO HEPATIC ARTERY THROMBOSIS

Daniel Cox[*1;2], Dora Huang[2], Ruelan Furtado[2], Eunice Lee[1;2], Bz Wang[2], Graham Starkey[2], Marcos Perini[1;2], Robert Jones[1;2], Michael Fink[1;2]

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Background: Primary sclerosing cholangitis (PSC) is a common indication for liver transplantation (LT). In the context of chronic shortages, split-liver transplantation (SLT) has the potential to increase the pool of donor organs. Biliary complications occur with increased frequency following LT for PSC, and in SLT. The aim of this study was to compare graft survival in SLT and whole liver transplantation (WLT) for patients with PSC.
Methods: Outcome data for 2656 adult liver transplant recipients were analysed from the Australia-New Zealand Liver and Intestinal Transplant Registry, 2011-2020. Patients were categorised into 4 groups: PSC with SLT (PSC-SLT), PSC with WLT (PSC-WLT), non-PSC with SLT (non-PSC-SLT) and non-PSC with WLT (non-PSC-WLT). Graft and patient survival were analysed using Kaplan-Meier graphs with log-rank tests. Univariate Cox proportional hazards testing, followed by multivariate proportional hazards regression were used to identify variables independently associated with graft loss. Re-transplantation rates for any cause were compared between groups using chi-square.
Results: The cohort included 261 PSC patients (PSC-SLT n=26). 5-year graft survival was significantly reduced following PSC-SLT (57.9%), compared to the other groups (*see* Table). Reduced graft survival post PSC-SLT was significant when compared with PSC-WLT (p=0.002) and non-PSC-SLT (p=0.006). On multivariate analysis, PSC-SLT was the strongest, *independent* risk factor for graft loss (HR 3.24, 95% CI 1.77-5.92, p<0.001). There were no significant differences in *patient* survival (p=0.62) or biliary complications leading to graft loss (p=0.061) between groups. Graft loss in PSC-SLT was strongly linked to an increased incidence of hepatic artery thrombosis [HAT] leading to graft failure (PSC-SLT 15.4% *vs* non-PSC-SLT 2.4%; PSC-WLT 0.4%; non-PSC-WLT 0.7%; p<0.001).
Conclusions: PSC-SLT is associated with significantly reduced graft survival compared with PSC-WLT and non-PSC-SLT, and should be avoided where possible. SLT is generally associated with an increased risk of HAT, but this may be further compounded by a hypercoagulable state in PSC. Patients undergoing PSC-SLT may benefit from perioperative anticoagulation and enhanced vascular monitoring protocols to mitigate increased risks of graft loss.

Group	Primary Outcome: Graft survival					
	1-year	3-year	5-year	10-year	p value	
PSC-WLT	91.1%	83.7%	77.8%	55.3%	0.002	0.006
PSC-SLT	73.1%	57.9%	57.9%	Not reached		
Non-PSC-SLT	88.3%	82.4%	78.8%	63.0%	0.412	
Non-PSC-WLT	91.6%	86.0%	81.9%	70.2%		
		p value	0.001			

BOS12_2 IDENTIFICATION OF NOVEL LIVER TRANSPLANT BIOPSIES PHENOTYPES ASSOCIATED WITH DISTINCT BIOLOGICAL PROFILES AND ALLOGRAFT SURVIVAL

Zeynep Demir[*1], Olivier Aubert[1], Mylene Sebagh[2], Jean-Paul Duong van Huyen[3], Dominique Debray[4], Valerie Paradis[5], Cyrille Feray[2], Francois Durand[6], Eric Vibert[2], Christophe Chardot[7], Claire Francoz[5], Carmen Lefaucheur[1], Alexandre Loupy[1]

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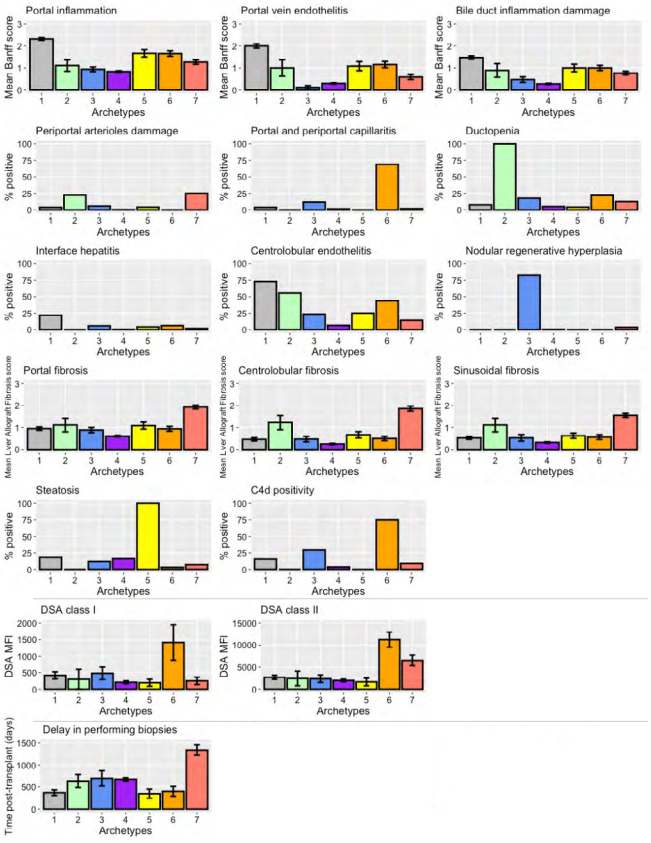
Background: The heterogeneity of histological lesions in liver transplant (LT) biopsies has not been precisely characterized nor classified so far; especially those associated with circulating anti-HLA DSA. We hypothesized that a probabilistic unsupervised approach applied in a large comprehensive and well annotated prospective LT cohort could bring new insights of liver allograft phenotypes.
Methods: We evaluated LT biopsies with concomitant investigation of anti-HLA DSA from pediatric and adult recipients transplanted between 2010 and 2020 in 3 French centers. Using a comprehensive cohort of LT including clinical, immuno-histological and outcome data, unsupervised archetypical analysis was done integrating the 27 clinical, histological and immunological parameters assessed for each biopsy. The association between the archetypes identified and liver function tests and allograft survival were investigated. The primary outcome was liver allograft failure while the secondary outcome was the occurrence of biliary strictures.
Results: A total of 490 LT biopsies provided by 325 patients were evaluated. The median time from LT to biopsy was 426.5 days (IQR:137-871). Liver allograft survival rates after biopsy were 89.1% and 80.2% at 5 and, 10 years, respectively. The unsupervised archetypical analysis identified 7 archetypes characterized by distinct clinical, immunological and pathological features (Figure). The characteristics defining the archetypes were similar and conserved across pediatric and adult cohorts. The 7 archetypes displayed distinct biological profiles and allograft outcomes: 1) with allograft survival rates ranging from 92.8% to 50% between archetypes 3 years after biopsy (log rank p value<0.001); 2) and biliary strictures free rates: 100% to 66.7% at 3 years after biopsy (log rank p value=0.002). The allograft outcomes were mainly determined by the severity of histological bile duct lesions and/or presence of circulating anti-HLA DSA.
Conclusions: Based on an unsupervised analysis, we identified clinically meaningful phenotypes with distinct biological profiles and outcomes, allowing to quantify and refine the currently unclassified liver-graft histological lesions.

Figure. Summary of clinical and immuno-histological features characterizing the 7 archetypes



BOS12_3 MACHINE PERFUSION TECHNIQUES FOR LIVER TRANSPLANTATION - A META-ANALYSIS OF THE FIRST SEVEN RANDOMIZED CONTROLLED TRIALS

Janina Eden*[1], Alessandro Parente[2], Fabio Tirotta[3], Alessia Pini[4], Daniele Dondossola[5], Tommaso Manzia[2], Philipp Dutkowski[1], Andrea Schlegel[1;5]

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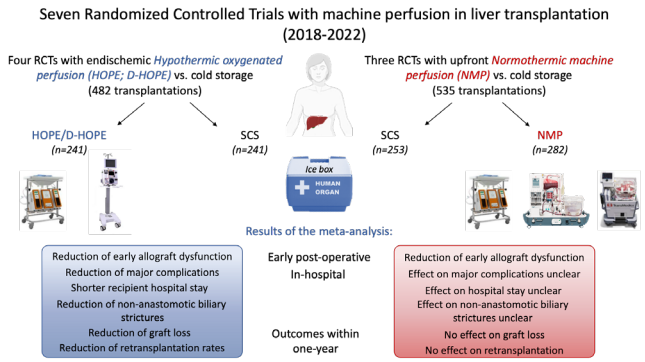
Background: To assess the role of machine perfusion on outcomes after liver transplantation compared to static cold storage (SCS).
Methods: A MEDLINE and EMBASE database search was performed to identify randomized controlled trials (RCTs) reporting the outcomes after transplantation of machine perfused livers compared to SCS. Data were pooled using random effect models. Risk ratios (RR) were calculated for clinically relevant outcomes including early allograft dysfunction (EAD), complications, graft loss and retransplantation within the first year after liver transplantation.
Results: Seven RCTs were identified for endischemic hypothermic oxygenated (HOPE, n=4) and upfront normothermic machine perfusion (NMP, n=3), including a total number of 1017 patients (241 HOPE vs. 241 SCS; 282 NMP vs. 253 SCS). While both NMP and HOPE were associated with significantly lower EAD rates (NMP: RR: 0.50, $CI_{95\%}$: 0.30-0.86, p=0.01, I^2: 39%; HOPE: RR: 0.48, $CI_{95\%}$: 0.35-0.65, p<0.00001, I^2: 5%) compared to SCS, only the HOPE-approach, despite performed after cold storage, showed impact on other clinically relevant outcomes. The duration of hospital stay was shortened (Mean Difference: -4.26, $CI_{95\%}$: -7.98-0.55, p=0.02, I^2: 95%), and the number of patients with major complications (Clavien Grade ≥IIIb) was reduced by HOPE (RR: 0.79, $CI_{95\%}$: 0.62-0.99, p=0.04, I^2: 0%), together with lower rates of non-anastomotic biliary strictures (RR: 0.43, $CI_{95\%}$: 0.20-0.93, p=0.03; I^2: 0%) and re-transplantation (RR: 0.21, $CI_{95\%}$: 0.04-0.96, p=0.04; I^2: 0%) with subsequently significantly better graft survival rates (RR: 0.40, $CI_{95\%}$: 0.17-0.95, p=0.04; I^2: 0%).
Conclusions: This study provides the highest (level 1) evidence on the role of machine perfusion in liver transplantation. The HOPE-technique was found to best protect liver recipients from clinically relevant posttransplant complications and should therefore be routinely considered in clinical practice.

Figure: graphical presentation of the metanalysis results for the first seven randomized controlled trials on ex-situ machine perfusion in liver transplantation.



BOS12_4 ABSORBABLE SELF-EXPANDABLE BILIARY STENT AS APREVENTIVE TREATMENT OF BILIARY COMPLICATIONS IN LIVER TRANSPLANT

Victor López-López*[1], Christoph Kuemmerli[2], Alberto Hiciano[1], Pedro Cascales Campos[1], Alberto Baroja-Mazo[1], Kohei Miura[3], José Antonio Pons[1], Laura Martínez-Alarcón[1], Francisco Sanchez-Bueno[1], Pablo Ramírez Romero[1], Ricardo Robles-Campos[1]

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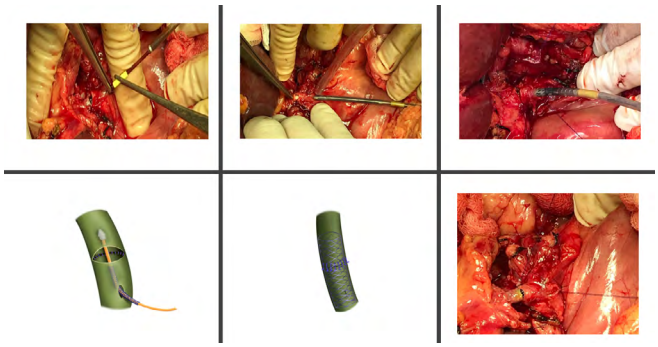
Background: Complications related to the biliary anastomosis in liver transplant (LT) have been reduced in recent years but remain a weak spot of the procedure. In this study, we analysed the use of a self-expandable absorbable stent to support the biliary anastomosis in LT.
Methods: Between July 2019 and September 2022,patients who had LT with duct-to-duct biliary anastomoses were analyzed. The primary endpoint was to assess the technical details and complications of a self-expandable absorbable biliary stent. We also compared biliary complications associated in patients with absorbable stent, T-tube, and no stent. A cost analysis was also performed.
Results: A total of120 patients were included(47withoutstent, 54withabsorbablestent, and 19withT-tube).Overall biliary complications were significantly lower in the absorbable stent group compared to T-tube and no stent groups(p<0.001).Ninety-days biliary complications were significantly lower in the absorbable stent group (1.9%)compared to the T-tube (21.1%, p=0.020) and no stent (29.8%,p<0.001) groups. Hospital stay related to biliary complications after LT was significantly shorter in the absorbable stent group(16[12-21]) compared to no-stent(19[15-24]) and T-tube(22[18-31])groups. In the absorbable stent group, the mean cost and the excess cost calculated according to the cost prediction calculator and the hospital stay related to biliary complications, were significantly lower compared to non-absorbable stent groups(p=0.004and p=0.006, respectively).
Conclusions: Placement of a self-expandable absorbable biliary stent during biliary anastomosis in LT is a feasible and safe technique. Our study suggests that its use may reduce the rate of early and late biliary complications with a reduction in the costs associated with its management.



BOS12_5 THE ITALIAN EXPERIENCE ON LIVER TRANSPLANTATION FOR UNRESECTABLE PERI-HILAR CHOLANGIOCARCINOMA: A NATIONAL SURVEY AND FUTURE PERSPECTIVES

Alessandro Furlanetto[*1], Jacopo Lanari[1], Ilaria Billato[1], Luciano De Carlis[2], Vincenzo Mazzaferro[3], Renato Romagnoli[4], Matteo Cescon[5], Marco Vivarelli[6], Paolo De Simone[7], Francesco Enrico D'amico[1], Salvatore Gruttadauria[8], Massimo Cardillo[9], Ugo Boggi[10], Umberto Cillo[1], Enrico Gringeri[1]

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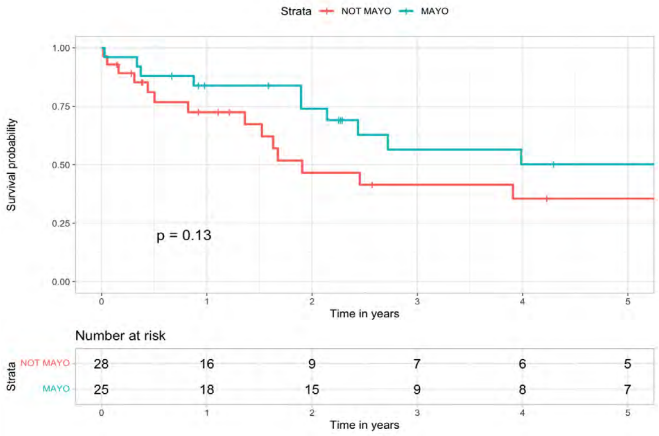
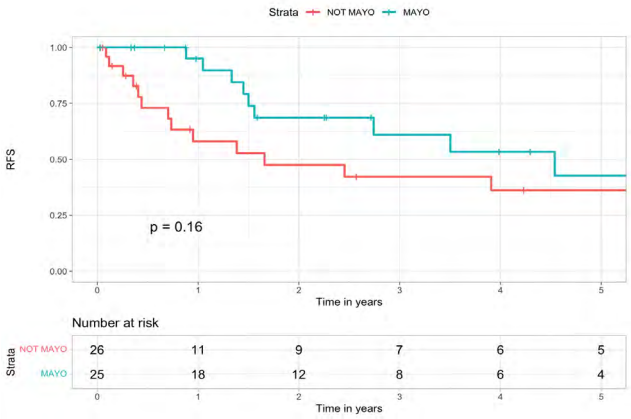
Background: Perihilar Cholangiocarcinoma (pCCA) is a rare tumor of the liver, associated with poor prognosis even for patients amenable to radical surgery. Since the introduction of the Mayo Clinic protocol, with strict inclusion and exclusion criteria and an extensive preoperative chemo and radiotherapy treatment, liver transplantation (LT) is becoming an innovative therapeutic option.
Methods: All 22 Italian LT Centers were asked to participate in a national survey. From 1984 to 2021, 53 LT for pCCA were performed in 8 Italian centers (Table). Patients were stratified according to whether they were subjected to full neoadjuvant radio-chemotherapy (Group 1, n 25) or not (Group 2, n 28), and whether transplantation occurred before (n 26) or after 2015 (n 27).
Results: Eighteen patients (18/53, 34%) died because of recurrence of disease, 14/28 in Group 2 (, 50%) and 4/25 in Group 1 (16%). Nine patients died of unrelated causes, 6 in Group 1 (6/25, 24 %) and 3 in Group 2 (3/28, 11%). Three patients received early re-transplantation for technical complications, such as portal vein thrombosis (n. 1) or biliary necrosis (n.1), or for primary non function (n. 1). Overall survival at 1y, 3y and 5y was 78,2%, 49,3% and 43,1% (median 57 months); in Group 1 was 83,8%, 56,6% and 50,6%, while in Group 2 was 72,4%, 41,4% and 35,5% respectively (p = 0.13). Recurrence-free survival at 1y, 3y and 5y was 76,9%, 51,7% and 40,3%, (time to recurrence 16,6 months); in Group 1 was 91,2%, 61,1% and 47,2%, while in Group 2 was 58,2%, 42,2% and 36,1% respectively (p 0.16) (Figure) Competing risk regression analysis showed a 5-year risk of cancer-related death of 19% for patients in Group 1, against 62.3% in Group 2 (hazard ratio 0.31, 95% CI 0.10-0.98, p 0,047).
Conclusions: The preliminary data from this survey can be the basis for a nationwide discussion about the obstacles to a more widespread implementation of the protocol and its possible evolution.

	n° LT (53)	Neoadjuvant RT-CT (Group 1)	No Neoadjuvant RT-CT (Group 2)	Before 2015	After 2015
ANCONA	2	1 / 2 (50%)	1 / 2 (50%)	0	2
BOLOGNA	12	7 / 12 (58%)	5 / 12 (42%)	2	10
PADOVA	10	7 / 10 (70%)	3 / 10 (30%)	3	7
MILANO - TUMORI	8	8 / 8 (100%)	0 / 8 (0%)	5	3
PISA	4	0 / 4 (0%)	4 / 4 (100%)	1	3
MODENA	2	2 / 2 (100%)	0 / 2 (0%)	0	2
TORINO	5	0 / 5 (0%)	5 / 5 (100%)	5	0
MILANO NIGUARDA	10	0 / 10 (0%)	10 / 10 (100%)	9	1





BOS12_6 EARLY DIAGNOSIS OF LIVER GRAFT FIBROSIS AND STEATOSIS: ARE NON-INVASIVE TESTS THE ANSWER?

Colin Dumont*[1], Samuele Iesari[2;3], Pamela Baldin[4], Selda Aydin[4], Guillaume Henin[1;5], Marie Philippart[1], Eliano Bonaccorsi Riani[6], Olga Ciccarelli[6], Laurent Coubeau[3;6], Hubert Piessevaux[1], Nicolas Lanthier[1;5], Géraldine Dahlqvist[1]

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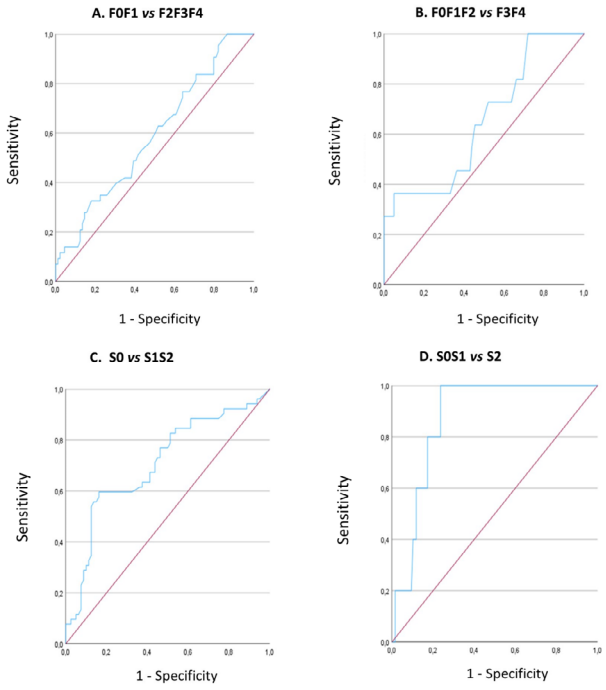
Background: Detection of graft fibrosis and steatosis is a new challenge to avoid graft loss after liver transplantation (LT). The role of liver biopsy (LB) after LT is changing with the emergence of non-invasive tests, including transient elastography (TE) with controlled attenuation parameter (CAP) and liver stiffness measurement (LSM). Our aim is to evaluate the accuracy of TE in predicting fibrosis and steatosis in post LT.
Methods: This prospective analysis was performed on 158 LT patients undergoing protocolar LB, from February 2021 to September 2022. Fibrosis was classified according to Metavir score and steatosis was classified in 3 categories (S0: <3%, S1: 3-33%, S2: > 33%). LSM and CAP were carried out using Fibroscan® prior to LB. We performed univariate analysis of factors associated with fibrosis and steatosis. We built ROC curves to evaluate the predictive performance of TE. Based on these results, to dichotomize LSM, we chose a cut-off associated at least 0.80 specificity. The Spearman's rho was used to evaluate the correlation between Metavir and AST to platelet ratio index (APRI) or fibrosis-4 index (FIB-4).
Results: 60% of the patients were male, median age was 59. Median BMI was 25 kg/m2. Median time since LT was 5 years. Median stiffness, CAP values and IQR/med were 6.00 kPa, 222 dB/m and 14% respectively. Factors associated with fibrosis were pre-LT autoimmune liver diseases (p = 0.05), arterial hypertension (p = 0.024), and low lipids levels (p < 0.001). Factors associated with steatosis were pre-LT non-alcoholic steatohepatitis (p = 0.033) and current body mass index (p < 0.01). Using LSM, AUROC were 0.59 (CI = 0.49-0.68, p = 0.101) and 0.65 (CI = 0.48-082, p = 0.099) for the diagnosis of graft fibrosis ≥ F2 and F3-F4 respectively. Using CAP, AUROC were 0.87 (CI = 0.79-0.95, p = 0.005) and 0.71 (CI = 0.61-0.80, p < 0.001) for the diagnosis of graft steatosis > S2 and > S1 respectively. Cut-offs for LSM were 7.95 for ≥ F2 and 9.25 for ≥ F3. Cut-offs for CAP were 198 dB/m for S1 and 276 dB/m for S2. We found no correlation between Metavir and APRI or FIB-4.
Conclusions: Compared to other non-invasive tests, evaluation using TE with CAP may be useful for the screening of advanced fibrosis, and interestingly for steatosis after LT. It could become a tool to track graft metabolic dysfunction and to propose lifestyle interventions.



BOS12_7 IMPROVEMENT OF THE OUTCOMES OF LIVER TRANSPLANTATION AFTER THE COVID-19 ERA: THE POSITIVE PROACTIVE EFFECT OF SARS-COV-2

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Background: The ongoing IMPROVEMENT project aims to develop predictive models of 90-day and 1-year allograft failure after liver transplantation (LT). A descriptive *ad interim* data analysis was performed to assess the effect of COVID-19 pandemic on complication rate and both graft and patient survival.
Methods: We currently evaluated data of 1970 deceased donor adult LTs from 21 LT centres worldwide. Centre- and patients-specific inclusion criteria are detailed elsewhere (https://gemelligenerator.it/projects/the-improvement-study-2/) and on https://ClinicalTrials.gov (Ref. NCT05289609). The study sample was stratified in pre-COVID (Jan 2016-Feb 2020; 1444 cases) and post-COVID period (July 2022-Jan 2023; 526 patients) and the 2 groups were compared. A composite endpoint (Clavien complications and survival rates) was further considered.
Results: Donors' median age was higher in the post-COVID (58 vs 53.5 yrs.; p=0.02), Table 1. The retrieval location has different prevalence according to the pre/post COVID period (p<0.01). In post-COVID were more often local (46.6% vs 35.5%) and less regional (30.6% vs 41.6%). In the post-COVID, DCDs (22.1% vs 14.9%) and ECDs (34.6% vs 27.6%) were more frequent. Perfusion Machines (PM) were more often used. In the post-COVID more women received a LT (32.1% vs 18.6%; p=0.04), and diagnosis of viral liver disease decreased as compared to pre-COVID (16% vs 28.3%; p=0.004), with a relative increase in metabolic aetiology (15.4% vs 10.4%; p=0.03), while HCC rate remained stable (32.1% vs 30.6%; p=0.6). LTs in the post-COVID disclosed a different pattern of complication grade rates (p<0.001). More minor (Clavien IIIa-b grade 31% vs 24.4%) but fewer major (Clavien IVa-b grade 14.4% vs 24.7%) complications were observed (Figure 1a). Furthermore, CCI was stable in both study periods (39.6 vs 36.2; p=0.07). As for graft survival, this was higher in the post-COVID, though without reaching the statistical significance (Figure 1b).
Conclusions: Preliminary IMPROVEMENT data show a clear evolution in the profile of LT. After the pandemic, a higher-risk donor and/or recipient profile was accepted. Technical innovations, such as PM, were more commonly implemented. The COVID-19 pandemic stimulated transplant surgeons to revise local protocols and management practices.

Table 1. Demographic and clinical characteristics of the patients

	PRE-COVID PERIOD (2018-2019) (n = 1444) MEDIAN (IQR) N (%)	POST-COVID PERIOD (July 2022-January 2023) (n = 526) MEDIAN (IQR) N (%)	p value
DONOR			
Age, median (IQR)	58 (44 - 71)	53,5 (45 - 69)	0.02
Gender female, n (%)	560 (38,8)	216 (41,1)	0.07
BMI, median (IQR)	25,7 (23,4 - 28,3)	25 (23,9 – 28,0)	0.8
Cause of death, n (%)			
Trauma	343 (23,8)	123 (23,4)	0.7
Cerebrovascular accident	791 (54,8)	273 (51,9)	0.2
Other	310 (21.5)	130 (24.7)	0.1
DRI, median (IQR)	1,9 (1,5 - 2,2)	1,8 (1,3 - 2,2)	0.9
Location of retrieval, n (%)			
Local	512 (35,5)	242 (46,4)	0.005
Regional	601 (41,6)	163 (30,6)	0.02
Extra-regional	331 (22,9)	121 (23,0)	0.6
Type donor, n (%)			
- DBD	1229 (85,1)	410 (77,9)	0.02
- DCD	215 (14,9)	116 (22,1)	
- ECD	398 (27,6)	182 (34,6)	0.01
- Standard	1046 (72.4)	344 (65.4)	0.09
Machine Perfusion, n (%)			
- HOPE	39 (2.7)	11 (2.1)	0.1
- D-HOPE	7 (0.5)	29 (5.5)	0.05
- NMP	6 (0.4)	6 (1.14)	0.07
- A-NRP	65 (4.5)	21 (4)	0.1
RECIPIENT			
Age, median (IQR)	58 (52 - 64)	61 (52 - 67)	0.4
Gender female, n (%)	268 (18,6)	169 (32,1)	0.04
BMI, median (IQR)	26,2 (23,6 - 29,5)	25,6 (21,7 - 29,4)	0.08
Type of cirrhosis, n (%)			
Alcohol	368 (25,5)	132 (25,1)	0.7
Viral	408 (28,3)	84 (16)	0.004
Metabolic	150 (10,4)	81 (15,4)	0.03
Cholestatic	44 (3)	77 (14,6)	0.002
HCC	463 (32,1)	161 (30,6)	0.6
Other	148 (10,2)	38 (7,2)	0.1
MELD at transplant, median (IQR)	14 (10 - 21)	17 (11 - 22)	0.2
MELDNa at transplant	15 (10 – 23)	19 (12 – 21)	0.1
MELD 3.0	12 (3 – 21)	12 (1 – 28)	0.8
Portal thrombosis, n (%)	136 (9,4)	42 (8)	0.4
- Yerdel I	73 (5.1)	19 (3.6)	0.06
- Yerdel II	44 (3.1)	9 (1.7)	0.07
- Yerdel III	11 (0.8)	9 (1.7)	0.6
- Yerdel IV	8 (0.6)	5 (1)	0.5
CAD-LT, median (IQR)	8 (6 - 10)	8 (6 - 10)	0.7
Clavien-Dindo grade, n (%)			
- I - II	566 (39,2)	222 (42,2)	0.6
- IIIa - IIIb	352 (24,4)	163 (31)	0.03
- IVa – IVb	357 (24,7)	76 (14,4)	0.02
- V	151 (10,5)	46 (8,7)	0.2
Comprehensive CI, median (IQR)	36.2 (20.9 – 54.9)	39.6 (22.6 – 52.7)	0.3
CONUT Score, median (IQR)	4 (2 - 6)	3 (0 - 5)	0.4
EASE Score, median (%)	-3,4 (-4,5 - -2,1)	-3,2 (-4,4 - -2,5)	0.8
L-GrAFT 7, median (IQR)	-3,1 (-3,7 - -2,2)	-3 (-3,6 - -2,4)	0.7
L-GrAFT 10, median (IQR)	-3,3 (-4 - -2,3)	-3,2 (-3,8 - -1,5)	0.8

Figure 1a. Comparison of the Clavien-Dindo complications

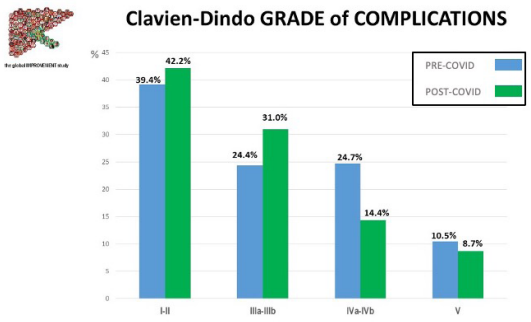
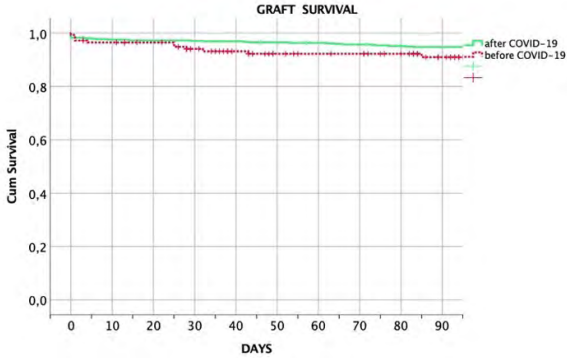


Figure 1b. Kaplan-Meier curve for graft survival



BOS12_8 RADIOLOGICAL CLASSIFICATION OF ISCHEMIC CHOLANGIOPATHY AFTER DECEASED-DONOR LIVER TRANSPLANTATION

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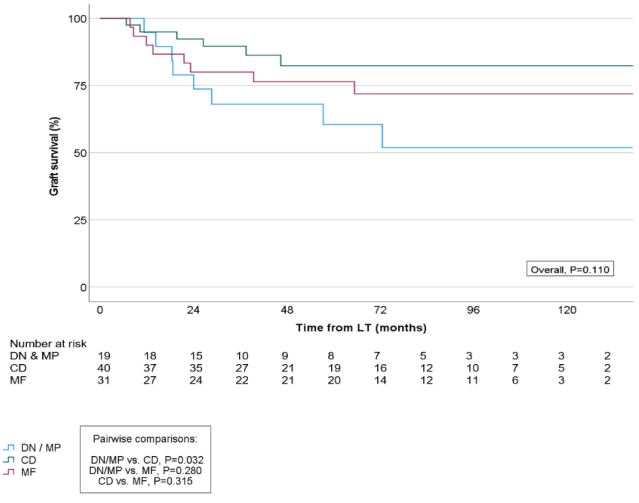
Background: Ischemic cholangiopathy (IC) is a feared complication after liver transplantation (LT). There is growing evidence that, rather than being a single entity, IC represents a spectrum with distinct radiological patterns and clinical courses. This study aimed to investigate whether IC classified by these radiological patterns can predict the clinical outcomes, in both DCD and DBD-LT.
Methods: All adult patients with symptomatic IC after first-time deceased-donor LT between 2011 and 2020 were included. Symptomatic IC was defined as any narrowing of the donor bile ducts documented by MRCP, accompanied by clinical signs or laboratory findings suggestive of cholestasis, in the presence of a patent hepatic artery. An expert radiologist created 4 groups according to a recently described classification of IC after DCD-LT by Croome et al.: diffuse necrosis (DN), multifocal progressive (MP), confluence dominant (CD) and minor form (MF). Graft survival (primary outcome) was assessed by Kaplan-Meier analysis and compared between groups by the Log-rank test. Secondary outcomes were related to the clinical course of IC.
Results: 90 patients (16.8% of total LT) developed symptomatic IC (48 DCD [23.9% of total DCD] and 42 DBD patients [12.6% of total DBD]), of whom DN in 2, MP in 17, CD in 40 and MF in 31 patients. Due to the low number of DN, DN and MP patients were analyzed together (n=19). Graft survival was significantly different between DN/MP and CD patients (P=0.032, figure). Graft survival at 1 and 5 years was 94.7% and 59.8% for DN/MP; 94.9% and 82.3% for CD and 90.2% and 76.5% for MF patients. Graft survival was also significantly different per IC class in DCD (P=0.013) but not in DBD patients. In total, 17 patients (18.9%) were relisted and 12 (13.3%) were retransplanted (26.3% of DN/MP, 7.5% of CD and 12.9% of MF patients). After DCD-LT, MF patients had the shortest cumulative in-hospital length of stay and CD patients had the longest duration of stent therapy. After DBD-LT however, clinical courses of IC classes were less distinct.
Conclusions: IC after DCD-LT can be classified into subtypes with distinct clinical outcomes. Severity and location of IC after DCD-LT are indicative of the risk of graft loss and the need for hospitalization and stent therapy. However in DBD patients, this classification does not have prognostic value.



BOS12_9 ADD-ON CONTRAST-ENHANCED US WITH DOPPLER US ON POD#1 CAN REDUCE FALSE POSITIVES OF VASCULAR COMPLICATION AFTER LIVER TRANSPLANTATION

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Background: To investigate advantages of the add-on contrast-enhanced ultrasound (CEUS) on the first post-operative day (POD#1) after liver transplantation (LT) for detection of immediate vascular complications such as hepatic arterial complications (HAC) and acute bleeding
Methods: A total of 913 patients who underwent LT and a routine ultrasound (US) examination on the POD#1 were enrolled in the retrospective study. The protocol of the routine US examination consists of Doppler US followed by CEUS using sulfur hexafluoride microbubbles. An experienced radiologist performed Doppler US with measuring hepatic arterial resistive index (HARI). If HARI was lower than 0.5 or hepatic artery was not detected, it was defined as suspicious HAC. And then, CEUS was followed. If microbubbles arrived in the hepatic artery within 15 sec after injection, hepatic artery was considered normal; however, they didn't arrive in the hepatic artery, it was defined highly suspicious HAC, and CT angiography was recommended. We compared the diagnostic performance between Doppler US and add-on CEUS study. Gold standard is follow-up CT or angiography. In addition, microbubble extravasation into the perihepatic space was investigated after vascular evaluation to detect active bleeding. For statistical analysis, McNemar test was performed to compare the diagnostic performances between Doppler US only and add-on CEUS.
Results: Patients with suspicious HAC on Doppler US only were 6.7% of the subject (62/913), and those with highly suspicious HAC on add-on CEUS were 3.9% (36/913). The false positive rate of Doppler only was 2.2%, but that of add-on CEUS was 0.3% (p = 0.0002). However, two cases with abnormal CEUS findings but intact Doppler US were proven as unremarkable (2/913). In terms of acute bleeding, 18 patients (18/913) had active bleeding on CEUS, and 10 patients (10/18) underwent surgical removal of hematoma, and the rest was conservative management.
Conclusions: CEUS as an add-on test was useful to find acute complication of LT. Especially, it can decrease false positive of hepatic arterial complications on Doppler US presenting decreased HARI.

BOS12_10 SURVIVAL OUTCOMES OF SALVAGE VS PRIMARY LIVER TRANSPLANTATION FOR EARLY-STAGE HEPATOCELLULAR CANCERS: SYSTEMATIC REVIEW AND META-ANALYSIS

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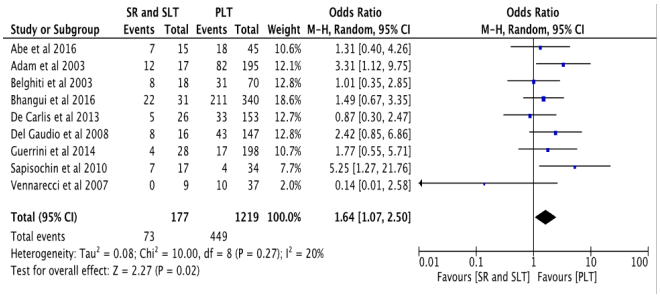
Background: Salvage liver transplantation (SLT) after surgical resection (SR) or locoregional ablative therapies (LRAT) is utilised in hepatocellular carcinoma (HCC) patients with very early/early-stage and preserved liver functions. However, recurrence and survival outcomes of SLT when compared to primary liver transplantation (PLT) are disputed by several studies. This systematic review and meta-analysis compared the clinical outcomes of SLT after SR or LRAT with PLT.
Method: MEDLINE, EMBASE, CENTRAL and Web of Science databases were searched to identify studies comparing risk estimates of mortality and recurrence for SLT (after SR or LRAT) vs PLT. Selection was based on inclusion criteria to include studies comparing patients with HCC classified as very early/early-stage as per EASL practice guidelines 2022. Risk of bias was reviewed using the Newcastle-Ottawa Scale. A random effects model assessed primary endpoints based on evaluation of heterogeneity.
Results: 5734 patients from 16 studies were included. For SLT after SR, the odds ratio of mortality at 1-,3-and 5-years were comparable to PLT. However, the odds of HCC recurrence at 1-,3- and 5-years were higher when SLT after SR was compared to PLT, particularly at 5 years (OR [95%] =1.64 [1.07 - 2.50]), as shown in Figure 1. For SLT after LRAT vs PLT, the odds ratios of mortality HCC recurrence and mortality showed no statistically significant difference compared to PLT, but interpretations are limited by high heterogeneity of included studies.
Conclusions: Very early/early-stage HCC patients who underwent SLT after SR had higher risk of long-term of recurrence when compared with PLT, which could be explained by increased risk of surgical challenges when SLT is performed. The use of LRAT with SLT showed comparable outcomes to PLT, limited by the heterogeneity and small number of studies included.



BOS12_12 SALVAGE LIVER TRANSPLANTATION FOLLOWING RESECTION OF COMBINED HEPATOCELLULAR-CHOLANGIOCARCINOMA

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Background: Between November 2000 and November 2019, all consecutive patients submitted to HR for HCC-CC were included. SLT was considered after HR in patients with underlying liver cirrhosis, ≤ 65 years old and without recurrence of disease for at least 6 months after HR. No evidence of extra-hepatic disease, including lymphatic metastases was required at listing.
Methods: Between November 2000 and November 2019, all consecutive patients submitted to HR for HCC-CC were included. SLT was considered after HR in patients with underlying liver cirrhosis, ≤ 65 years old and without recurrence of disease for at least 6 months after HR. No evidence of extra-hepatic disease, including lymphatic metastases was required at listing.
Results: During the study period, 44 patients were included. Among them, 6 patients (13.6%) were submitted to SLT. In median, SLT was performed 596 days (range 249-4613) after HR. Overall survival was significantly higher in SLT group compared to those who were not transplanted (131 mo vs. 17.7 mo, p=0.017). Disease-free survival was higher in SLT group but without reaching statistical significance (39.8 vs. 8.3 mo, p=0.122). According to COX-regression multivariate analysis, SLT was significantly associated to OS (p=0.048). With regard to DFS, low-grade HCC-CC, positive lymphnodes, extra-hepatic disease as well as portal vein tumoral thrombosis were independent predictors of recurrence after HR.
Conclusions: SLT may be considered as a therapeutic option for patients with HCC-CC and cirrhosis after HR if no recurrence occurs. Biology as well as tumor differentiation should be added to the current criteria to better select those patients.

Figure 1. Odds ratio of HCC recurrence at 5 years comparing SLT after SR vs PLT.

BRIEF ORALS

Transplantation outcomes and complications

BOS12_14 MODIFYING TACROLIMUS RELATED TOXICITY AFTER LIVER TRANSPLANTATION COMPARING ENVARSUS® AND ADVAGRAF®: A MULTICENTER RANDOMIZED, CONTROLLED TRIAL

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Background: The hypothesis of this study was that meltdose tacrolimus (Envarsus®) compared to extended-release tacrolimus (Advagraf®) will result in less chronic kidney disease (CKD), new-onset diabetes after transplantation (NODAT) and new-onset hypertension.
Methods: In this multicenter RCT, patients were randomized at discharge after liver transplantation (LT) in a 1:1 ratio to 1) Advagraf® (control group) or 2) Envarsus® (interventional group). The primary endpoint was a composite endpoint of any of three events at 12 months: CKD defined as eGFR <60 ml/minute/1.73 m2 for >3 months, sustained (>3 months post LT) NODAT or new-onset hypertension. Secondary endpoints included: safety, quality of life, neurotoxicity (tremors), graft and patient survival, rejection, liver steatosis and fibrosis, pharmacokinetics and –dynamics.
Results: A total of 106 patients were included and baseline characteristics were comparable for both groups. In the intention-to-treat analysis, significantly less LT recipients reached the primary endpoint at 12 months in the interventional group compared to the control group (50.9% and 71.2%, p = 0.005). No significant difference was shown between interventional group and control group in the percentage of LT recipients developing NODAT (15.1% and 21.2%, p=0.35) or new-onset hypertension (30.2% and 36.5%, p=0.42). Significantly less LT recipients developed CKD in the interventional group compared to the control group (26.4% and 42.3%, p=0.03). The per protocol analysis showed comparable results and in addition significantly less LT recipients developed new-onset hypertension in the interventional group compared to the control group (27.6% and 42.9%, p=0.04). In total, 95.3% (101/106) of the LT recipients developed serious adverse events (SAEs, n=156). SAEs most frequently reported: fever (23.7%), infections (10.3%) and cholangitis and bile duct obstruction (10.3%).
Conclusions: After 1 year, meltdose tacrolimus (Envarsus®) results in a significant reduction in the prevalence of the composite endpoint and a significant reduction of CKD compared to extended-release tacrolimus (Advagraf®)

Organ preservation and ischemia reperfusion

BOS13_1 REMOVAL OF CHROMATIN-ASSOCIATED-MOLECULAR-PATTERNS (CAMPS) REDUCES EX-SITU REPERFUSION INJURY IN PORCINE DCD LIVERS PRESERVED WITH NMP

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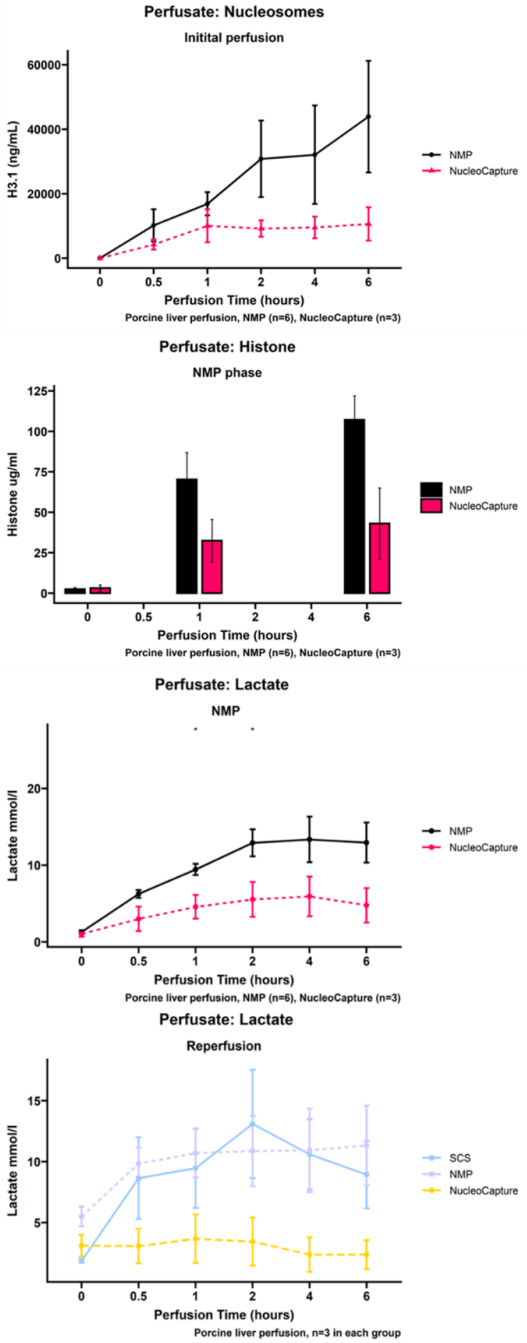
Background: DCD and extended-criteria donor livers are highly susceptible to reperfusion injury, even when occurring ex-situ in the context of normothermic machine perfusion (NMP) during organ preservation. This 'ex-situ reperfusion injury' (ERI), is driven by the release of endogenous alarmins and damage signal molecules, in particular chromatin-associated molecular patterns (CAMPs) such as histones, nucleosomes and cell free DNA (cfDNA). CAMPs released into the circuit upon reperfusion propagate inflammation and injury which can result in poor function ex-situ, resulting in subsequent organ discard. We aimed to assess the impact of removing circulating CAMPs during NMP, on ex-situ function and subsequent reperfusion in a large animal DCD liver perfusion model
Methods: 12 DCD pig livers were included in the study. CAMPs were removed from the circulating perfusate using the NucleoCapture column that was integrated into the perfusion circuit and these livers were compared to NMP controls. Perfusate Nucleosomes/NETs, free histone and cfDNA was measured sequentially during perfusion (including pre and post-column). Perfusion parameters, functional assessment of the livers and histological features were assessed between groups. Statical analysis was performed using repeated measures ANOVA and t-test/Wilcoxons-test.
Results: NucleoCapture significantly reduced early circulating CAMPs across the column: cfDNA p=0.009(1hr), Histone p=0.009(1hr) and Nucleosomes p=0.033(2hr). This also corresponded with a significant improvement in early lactate clearance (0.5hrs p= 0.033, 1hr p=0.013, 2hr p=0.043) supported by improved haemodynamic perfusion metrics and less neutrophil infiltration on histological assessment. Warm and cold ischaemic times were comparable between groups. All livers produced bile and metabolised glucose.
Conclusions: NucleoCapture effectively removes circulating CAMPs from the perfusate during NMP, improving graft function and mitigating ERI. Application of this technology during NMP of DCD and extended-criteria donor livers could reduce organ discard due to poor function ex-situ and be pivotal in organ optimisation for transplantation.

Fig. 1: (Top) Perfusate levels of CAMPs during perfusion. (Bottom) NucleoCapture significantly improved lactate clearance



BOS13_2 IN SITU AND EX SITU DYNAMIC PRESERVATION VERSUS COLD STORAGE IN LIVER TRANSPLANTATION FROM OLDER DONATION AFTER CIRCULATORY DEATH DONORS

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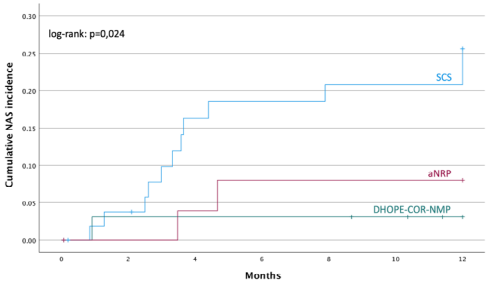
Introduction: Dynamic preservation strategies were shown to significantly reduce non-anastomotic biliary strictures (NAS) after liver transplantation (LT) using selected, controlled donation after circulatory death (DCD) livers. Whether this also applies to DCD livers from older donors is unknown.
Methods: In this retrospective, multicenter study, we compared outcomes after transplanting livers procured from DCD donors older than 60 years that were preserved either with static cold storage (SCS), sequential dual-hypothermic perfusion, controlled oxygenated rewarming, and normothermic perfusion (DHOPE-COR-NMP), or abdominal normothermic regional perfusion (aNRP) between 2016 and 2022. Incidence of NAS at 1-year, post-transplant peak aspartate transaminase (AST), early allograft dysfunction (EAD), and 1-year patient/graft survival were compared. Kaplan-Meier curves with log-rank test, Kruskal-Wallis and Fisher's exact test were used. Median [IQR] or percentage are given, unadjusted p-values are reported.
Results: 56 LT were included in the SCS group, 33 in the DHOPE-COR-NMP group, and 27 in the aNRP group. Donor warm ischemia time was shorter in the SCS group (20 [16-24] minutes) compared to DHOPE-COR-NMP (32 [26-35] minutes, p<0.001) and aNRP (36 [31-40] minutes, p<0.001) (DHOPE-COR-NMP vs. aNRP: p=0.58). Cold ischemia times were similar in all groups (SCS 306 [270-344] minutes, DHOPE-COR-NMP 319 [278-352] minutes and aNRP 339 [287-389] minutes, all p>0.2). Kaplan-Meier curves show a significant difference in NAS incidence between groups (p=0.02) (Figure). Incidence of NAS at 1-year was lower in the DHOPE-COR-NMP group compared to the SCS group (3% vs 21%, p=0.03). Two patients (7%) in the aNRP group suffered NAS, which was not significantly different from other groups (p=0.13 vs. SCS, p=0.58 vs. DHOPE-COR-NMP) (Table). Peak AST was lower in DHOPE-COR-NMP compared to SCS (p=0.02). There were no differences in EAD and 1-year patient/graft survival.
Conclusion: Our data suggest that dynamic preservation strategies enable safe transplantation of livers from donors older than 60 years. Especially, the risk of NAS is significantly lower after DHOPE-COR-NMP, compared to SCS, despite longer donor warm ischemia time.

Figure Kaplan Meier Hazard plot of 1-year NAS incidence



SCS	56	52	45	44	43	43	43
DHOPE-COR-NMP	33	32	32	32	32	31	29
aNRP	27	27	26	25	24	24	24

Table Post-transplant outcome

	SCS (n=56)	DHOPE-COR-NMP (n=33)	aNRP (n=27)	P_1	P_2	P_3
1y NAS	12 (21%)	1 (3%)	2 (7%)	**0.027**	0.13	0.58
Peak AST (U/L)	759 (536-1222)	510 (333-844)	682 (483-1153)	**0.022**	0.92	0.064
EAD	9 (16%)	7 (21%)	5 (19%)	0.58	0.76	>0.99
1y patient survival	52 (93%)	32 (97%)	26 (96%)	0.65	>0.99	>0.99
1y graft survival	52 (93%)	30 (91%)	25 (93%)	>0.99	>0.99	>0.99

P_1: SCS vs. DHOPE-COR-NMP; P_2: SCS vs. aNRP; P_3: DHOPE-COR-NMP vs. aNRP

BOS13_3 MAXIMUM LIVER FUNCTION CAPACITY TEST (LIMAX) DURING ABDOMINAL NORMOTHERMIC REGIONAL PERFUSION AS PREDICTOR OF GRAFT FUNCTION AFTER TRANSPLANTATION

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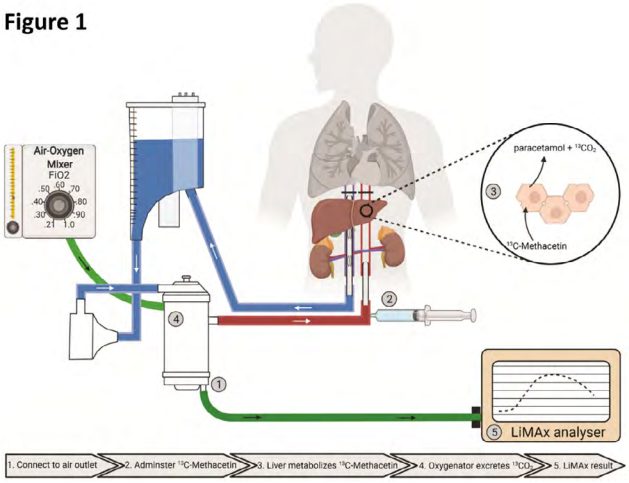
Background: Abdominal normothermic regional perfusion (aNRP) enables assessment of donor liver viability during donation after circulatory death (DCD). However, a gold standard for adequate liver function is lacking, and livers are usually subjectively assessed, with the risk of under-utilization. We aimed to assess the maximum liver function capacity (LiMAx) test to objectively grade liver function during aNRP.
Methods: aNRP was performed for salvage of extended criteria DCD liver grafts in 18 consecutive donors and grafts were transplanted after positive evaluation criteria (n=13). After one hour of aNRP, the LiMAx test was performed, using the aNRP circuit (Figure 1). LiMAx scores were compared to aNRP variables and post-transplantation outcomes.
Results: The LiMAx test was performed successfully in 17 aNRPs donors (94%). LiMAx scores ranged between 35 and 510 µg/kg/h. During aNRP, LiMAx scores of livers with good lactate clearance were significantly higher compared to livers with impaired lactate clearance (396 (IQR:301-451) versus 105 (IQR:70-158) µg/kg/h; P=0.006). Furthermore, livers that demonstrated a stress hyperglycemia peak (>20mmol/l glucose) had a higher LiMAx score compared to grafts with no glucose peak (P=0.032). LiMAx scores significantly correlated with ALT (R=-0.755; P<0.001) and AST (R=-0.800; P<0.001) levels at the end-aNRP. The LiMAx scores of the 13 transplanted grafts were significantly higher compared to the 4 non-transplanted grafts (397 (IQR:346-453) versus 154 (IQR:87-206) µg/kg/h; P<0.001). The LiMAx score during aNRP did not correlate with post-transplantation hepatic injury markers (ALT and AST) but it was significantly correlated to lactate levels at 24 hours (R=-0.585; P=0.045).
Conclusions: We demonstrated that LiMAx testing is feasible during aNRP. The LiMAx test is the first objective method that can reliably assess liver-specific function during aNRP. We propose a LiMAx score of >240 µg/kg/h during aNRP as a safe cut-off for use of extended criteria donor livers.

Figure 1



BOS13_5 OUTCOMES OF LIVERS WITH PROLONGED DURATION OF EX SITU NORMOTHERMIC PERFUSION: CAN LIVER TRANSPLANTATION BE A DAYTIME ACTIVITY?

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Background: Normothermic ex-situ liver perfusion (NESLiP) gives the opportunity to assess and modify marginal livers. Additionally, it also helps overcoming the time barriers by increasing the preservation time. NESLiP can be employed from the donor hospital until implantation or once the liver arrives at the recipient centre in a cold box. In this study, we discuss our experience of liver grafts subjected to prolonged NESLiP.
Methods: Retrospective analysis of livers undergoing NESLiP at our institute from May 2017 till January 2022. Patients were divided into two groups based on the duration of NESLiP (<10 hours and >10 hours) and outcomes compared. All livers underwent blood-based perfusate.
Results: There were 203 (DBD 80; DCD 123) livers undergoing NESLiP during the study duration resulting in 154 (76%) liver transplants. Thirty-five (30%) out of these were perfused for more than 10 hours before implant with median 20.2 hours of total preservation. There was no difference in early graft function or renal function.
Conclusions: This experience suggests that prolonged NESLiP is safe. It is useful in manging logistics with increased preservation time.

Parameters	NESLiP <10 hrs (n=119)	NESLiP >10 hrs (n=35)	p-value
DCD (%)	60 (50)	24 (69)	0.082
DRI (Feng et al, AJT2006)	2.0 (1.6 – 2.4)	2.2 (1.9 – 2.7)	0.035
UK DLI	1.4 (1.0 – 1.8)	1.6 (1.2 – 1.9)	0.21
Total preservation duration, hrs	15.4 (13.7 - 17.1)	20.2 (18.1 - 23.0)	<0.0001
NESLiP duration, hrs	7.2 (5.7 - 8.5)	12.0 (10.8 - 13.7)	<0.0001
UKELD	54 (51 – 59)	54 (50 – 58)	0.66
Peak ALT in first week	429 (207 – 771)	384 (200 – 669)	0.546
MEAF score	3.8 (2.5 – 5.4)	3.8 (2.8 – 5.5)	0.816
AKI (%)	35 (29)	11 (31)	0.836

Values are medians (interquartile range) or number (percentage)
Donor risk index (DRI); Alanine transaminase (ALT); Model for early allograft function (MEAF); Ischaemia type biliary lesion (ITBL)

BOS13_6 GRAFT VIABILITY AND LIVER TRANSPLANT RECOVERY ASSESSMENT USING INDOCYANINE GREEN CLEARANCE TEST: PRELIMINARY ANALYSIS OF A PROSPECTIVE STUDY

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Background: Indocyanine green clearance test (retention rate, RR15) is a prognostic marker for advanced cirrhosis and liver resection. RR15 has not been prospectively evaluated in liver transplantation (LT). Whether grafts from deceased donors with higher RR15 values are less likely to be utilized for LT is the objective of this study. Secondly, the relation between the change in RR15 after LT and function recovery is investigated.
Methods: This is a preliminary analysis from a single-center prospective study on consecutive LT donors and recipients. RR15 was calculated before procurement, at the end of LT, and on day one, three and seven after LT using the pulsidensitometric method. The procurement surgeon was blinded to the results of the test.
Results: Of 39 prospectively evaluated donors during the period April-December 2022, 30 grafts were deemed viable for LT. Grafts were discarded due to liver-related causes (n=8) or liver-unrelated causes (n=1; tumor): biopsy-proven necrosis >10% (n=3), macro-steatosis >60% (n=1), and fibrosis F3-4 (n=4). Using a RR15 cut-off of 13.5, no differences in donor characteristics were observed between the lower-RR15 (n=28) and higher-RR15 (n=10) groups. At c-statistics, RR15 cut-off value of 13.5 had a sensitivity of 75% and a specificity of 87% (diagnostic odds ratio, DOR=20) to identify grafts to discard due to liver-related causes, with an AUC=82% (95.0% CI=67.2-97.0%; p 0.006). Thirty-three LT recipients were prospectively evaluated using a RR15 cut-off of 13.5 on post-LT day 7. Compared to patients with lower (n=20) RR15, patients with higher (n=11) RR15 registered higher transaminase on days 1-3 post-LT (p 0.043-0.049), and total bilirubin (p < 0.0001) and "International Normalized Ratio" (p 0.002) on day 7. On post-LT day 7, RR15 <13.5 identified early allograft dysfunction (EAD) with a sensitivity of 87.5% and a specificity of 80% (DOR=28), with an AUC=97% (95.0% CI=91.4-100%; p<0.0001).
Conclusions: Donors with impaired indocyanine green clearance have lower chances of being viable for LT. Similarly in LT recipients, impaired clearance on day 7 correlates with EAD, aiding early diagnosis and resource allocation.

BOS13_7 OBSERVATIONS DURING IMPLEMENTATION OF AN EX-SITU NORMOTHERMIC LIVER MACHINE PERFUSION PROGRAMME

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Background: The use of ex situ normothermic machine perfusion may increase organ utilisation through better functional assessment and by improving transplant logistics. We aim to assess the impact of implementing a liver NMP programme on the transplant activity and clinical outcomes in a multi-organ transplant centre that already had access to novel perfusion technologies.
Methods: All DBD donor livers undergoing ex situ NMP were included in the analysis. All DCD cases underwent NRP and sequential ex situ NMP and therefore were excluded from the analysis. A propensity score matching was undertaking comparing patients receiving DBD livers with and without NMP. Patients were matched using optimal full matching where all patients were matched to at least one patient in the opposite group, using a probit link.
Results: Since 2020, 47 ex situ NMP perfusions were undertaken. 9 DCD and 23 DBD livers were transplanted. The indication for ex situ NMP was logistics (19), additional assessment (2) and recipient related (2). NMP for logistics facilitated the transplant of 9 additional organs (liver, pancreas or kidney) that would have otherwise been discarded. During the study period 19% of the DBD livers underwent ex situ NMP. There were no significant differences in the length if ICU and hospital stay nor the readmission post-transplant rates according to the use of NMP. Graft survival and the incidence of allograft dysfunction as determined by the EAD or MEAF scores were comparable between grafts with and without use of ex situ NMP.
Conclusions: The use of ex situ NMP allowed for a significant expansion of the DBD liver transplant programme and facilitated an increased utilisation of other organs in a multi-organ transplant centre with no detrimental impact on the liver transplant outcomes

	Ex situ NMP (n=23)	No NMP (n=95)
ICU stay (days) (median / IQR)	2.3 (0.4 - 4.4)	2.0 (1.4 - 3.3)
Length of index admission (days) (median / IQR)	20.0 (14.1 - 26.5)	16.6 (12.8 - 28.1)
Readmission within six months (%)	10 (45.5%)	51 (58%)
Total days in hospital readmissions (median / IQR)	23.4 (17.9 - 38.8)	21.8 (15.1 - 37.1)
Death within six months (%)	1 (4.3%)	7 (7.4%)

BOS13_8 MARKERS OF COAGULATION AND FIBRINOLYSIS DURING NORMOTHERMIC LIVER PERFUSION MIGHT REFLECT ON VASCULAR INTEGRITY AND PRESERVATION INJURY

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Background: During normothermic machine perfusion (NMP), thrombocytes and coagulation factors are exclusively derived from the perfused graft. As some factors are synthesized by the liver and the endothelial cells themselves, these dynamics might reflect on their condition. Further, vascular dysfunction and formation of microthrombi are known pathomechanisms in IRI and ischemic cholangiopathy. Our aim was to investigate factor composition during NMP and their association with liver function and post-transplant outcomes.
Methods: During NMP of 27 livers, including 21 from extended criteria donors, D-dimer, thrombocytes, van Willebrand factor activity (vWF), factor V activity (FV) and factor XIII activity (FXIII) in perfusate were assessed. Liver and bile duct biopsies were taken before and after perfusion.
Results: Out of 27 grafts that underwent NMP, 18 livers met viability criteria and were transplanted. Median peak perfusate levels were D-Dimer 3,39 µg/mL (IQR: 2,83-3,38), vWF 6 % (IQR: 5-8), thrombocytes 14 G/L (IQR: 13-27), FV 17 % (IQR:6-26), FXIII 32 % (IQR:20-39) and bilirubin 0,85 ng/dL (IQR: 0,66-3,31). Thrombocytes, bilirubin and FV increased steadily, FXIII and D-Dimer peaked and decreased afterwards. There were 11 cases with irregular parameters, 6 livers were declined for failure to produce bile or clear lactate. The 5 transplanted livers passed our standard viability criteria. Three recipients had an uneventful follow-up until now. One transplanted liver (5,81µg/mL D-Dimer, 96G/L thrombocytes, bilirubin 5,81 ng/dL, vWF 18 %) performed well on the machine but histology analysis afterwards resulted in fibrotic bile ducts in the back-table biopsy, the recipient later developed a biliary leak and biliary CAST syndrome. Another patient with FXIII of 175 % developed a bile duct necrosis. Median follow-up after transplantation was 12 months (IQR: 12-19)
Conclusions: Vascular integrity and thromboembolic events during preservation might be reflected by composition of pro- and anticoagulatory factors. Further, grafts with pathological biopsies presented with high D-Dimer levels during perfusion. Thus, viability testing during NMP might be complemented by dynamic changes in coagulation markers. Prospective studies are warranted to validate these initial findings.

BOS13_9 PILOT, RANDOMIZED TRIAL FOR THE COMPARISON OF HYPOTHERMIC VERSUS NORMOTHERMIC EX-SITU LIVER PRESERVATION IN DCD LIVER TRANSPLANTATION (DCDNET TRIAL)

Francesco Torri[1], Emanuele Balzano[1], Daniele Dondossola[2], Paolo De Simone[1], Davide Ghinolfi*[1]

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Background: In Italy, 20 minutes of continuous, flat-line electrocardiogram are required for death declaration, which significantly increase the risks of complications after DCD liver transplantation. Despite prolonged warm ischemia time, Italian centers reported good outcomes in DCD liver transplantation by combining normothermic regional (NRP) and end-ischemic machine perfusion. However, there are no studies comparing the two main ex-situ preservation techniques: dual-hypothermic oxygenated machine perfusion (D-HOPE) versus normothermic machine perfusion (NMP).
Methods: This is the first multicenter, prospective, randomized study comparing clinical outcomes of sequential NRP and end-ischemic D-HOPE versus sequential NRP and end-ischemic NMP in DCD liver transplantation. Graft eligibility to transplantation was assessed on NRP parameters.
Results: Between January 2021 to August 2022, 24 liver grafts were procured and transplanted, being 12 assigned to DHOPE and 12 to NMP group. Median donor age was 69 and 73 years (p=0.66) in D-HOPE and NMP group, respectively, being 9 (37%) grafts older than 80 years. 90-day graft survival was 83% versus 100% (p=0.20) in D-HOPE and NMP group respectively No differences in terms of post-reperfusion syndrome rate (25% versus 22%, p=0.88), early allograft dysfunction rate (42% versus 22%, p=0.35), ICU stay (3.5 versus 4 days, p=0.27), hospital stay (17 versus 13 days, p=0.23), and comprehensive complications index (31.6 versus 20.9, p=0.34) were noted in the D-HOPE and NMP group, respectively. There were 3 cases of biliary complications in NMP group (1 ischemic cholangiopathy, 2 leakages) versus 0 (0%) in D-HOPE group (p=0.06).
Conclusions: The sequential use of NRP and end-ischemic machine perfusion is a safe method to perform DCD liver transplants with extended warm ischemia time without donor age limits. No major differences between D-HOPE and NMP have been showed. Further data are needed to draw definitive conclusions.

BOS13_10 NORMOTHERMIC MECHANICAL PERFUSION (NMP) REDUCES THE RISK OF ISCHEMIC CHOLANGIOPATHY IN RECIPIENTS OF DCD LIVER TRANSPLANTS

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Background: We aimed to report the impact of instituting a normothermic mechanical liver perfusion (NMP) program using an FDA-approved device (Transmedics™ Liver OCS) on the rates of IC in recipients of DCD liver grafts.
Methods: We performed a single center cohort study of all DCD LTs performed between January 1, 2020 - November 20, 2022. IC was defined as intrahepatic biliary strictures without arterial insufficiency. We calculated differences in IC between NMP- DCD LT and static cold storage DCD LT (SCS- DCD LT) using univariate statistical methods.
Results: A total of 616 LT were performed during the study period. This included 292 DCD LT's (93 NMP-DCD LT (33.3%) and 199 SCS-DCD LT (66.7%). Table-1 outlines donor and recipient characteristics. Mean donor age for NMP-DCD LT was 52 years ± 9 and 47 years ±8 for SCS -DCD LT. Median allocation MELD at transplant was 20 for NMP group and 21 for SCS groups. NMP was associated with longer preservation time (12.5h NMP vs 5.5h SCS). UK DCD risk score was >10 in 53% NMP vs 44% SCS. IC was observed in 40/199 (20%) of SCS-LT patients, and 9/40 required retransplantation. All IC cases were diagnosed within the first 12 weeks post LT. Zero patients with NMP LT developed IC with median follow up of 16 weeks. Unadjusted actuarial 1-year graft survival was significantly higher in the NMP-LT (96%) compared to SCS-LT (88%)
Conclusions: NMP utilization in a high-volume DCD LT center confirms a significant reduction in the rates of IC despite expanding donor selection with 53% of grafts with UK DCD score >10. Broader use of NMP in DCD LT should be encouraged to improve outcomes and liver utilization.

Table 1: Patient characteristics

	NMP-LT (n=93)	SCS-LT (n=199)	p-value
Median Recipient age (yrs)	63	61	NS
Median Donor age (yrs)	52	47	NS
Median Preservation time (hrs)	12.5	5.5	<0.05
Meadian warm ischemia time (mins)	26	30	
Median Allocation MELD	20	21	NS
Ischemic Cholangiopathy	1%	20%	<0.05
UK DCD risk score <5 5-10 >10	 3% 44% 53%	 16% 48% 36%	
1 yr actuarial patient survival	97%	90%	
1 yr actuarial graft survival	96%	88%	<0.05

BOS13_11 THE ROLE OF COLD ISCHEMIA TIME AND HYPOTHERMIC PERFUSION IN PREDICTING EARLY HEPATOCELLULAR CARCINOMA RECURRENCES AFTER LIVER TRANSPLANTATION

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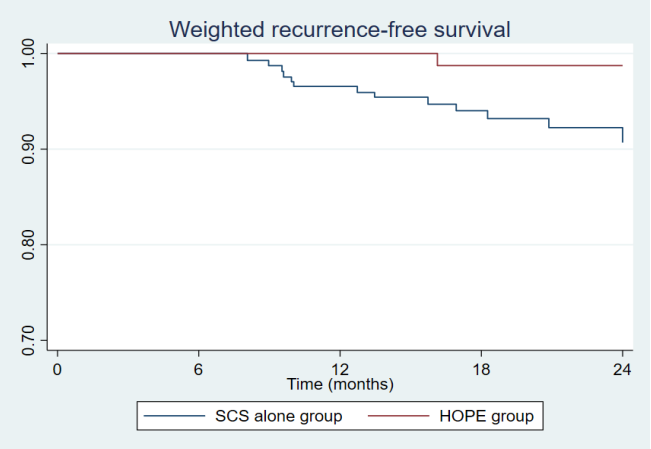
Background: Liver transplantation (LT) is the treatment of choice in eligible patients with hepatocellular carcinoma (HCC). Despite the use of validated eligibility criteria, HCC recurrences develop in up to 20% of the cases and are associated with poor survival. The aim of the study was to identify clinical predictors of early tumor recurrence in patients with hepatocellular carcinoma after liver transplantation.
Methods: Retrospective cohort study in consecutive liver recipients with HCC between 2016 and 2021. Multivariate logistic analysis was performed to identify clinical predictors of early HCC recurrences. The impact of hypo-oxygenated perfusion (HOPE) on outcome was analyzed after propensity score weighting.
Results: A total of 237 patients were included in this study with an early HCC recurrence rate of 6%. Microvascular invasion (OR 3.737, 95% CI 1.246 – 11.206, p=0.019) and cold ischemia time (OR 1.002, 95% CI 1.000 – 1.005, p=0.049) were independently associated with a lower risk of HCC recurrences (Table 1). After balancing for age, sex, MELD score, donor risk index and Milan Criteria status at listing, patients in the HOPE group had lower rates of tumor recurrence (weighted OR 0.126, 95% CI 0.016 – 0.989, p=0.049) and higher recurrence free survival (weighted HR 0.132, 95% CI 0.017 – 0.999, p=0.050) (Figure 1).
Conclusions: Reducing cold ischemia time and graft perfusion with HOPE can lead to lower rates of early HCC recurrences and higher recurrence-free survival after liver transplantation.

Table 1 Univariate and multivariate stepwise logistic analysis for predictors of early HCC recurrences

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	OR (95% CI)	P value
Age (years)	0.99 (0.92 – 1.05)	0.7	-	
Male gender	0.67 (0.18 – 2.52)	0.6	-	
MELD-Na score	0.98 (0.90 – 1.06)	0.6	-	
HCC at listing				
Outside Milan Criteria	2.31 (0.80 – 6.64)	0.1	-	
Number of HCC nodules	0.91 (0.57 – 1.44)	0.7	-	
Diameter of largest HCC nodule (cm)	1.027 (0.998 – 1.057)	0.070	-	
AFP levels (mg/dL)	1.00 (0.99 – 1.01)	0.7	-	
HCC at last evaluation before LT				
Outside Milan Criteria	0.65 (0.08 – 5.17)	0.7	-	
Number of HCC nodules	1.14 (0.85 – 1.53)	0.4	-	
Diameter of largest HCC nodule (cm)	1.02 (0.98 – 1.06)	0.4	-	
AFP levels (mg/dL)	1.005 (1.002 – 1.009)	0.005	-	
Donor age (years)	1.01 (0.98 – 1.05)	0.5	-	
Graft fibrosis grade ≥2 (METAVIR)	1.10 (0.13 – 9.49)	0.9	-	
Donor Risk Index	1.41 (0.41 – 4.79)	0.6	-	
Cold Ischemia Time (min)	1.003 (0.999 – 1.005)	0.080	1.002 (1.000 – 1.005)	0.049
Graft perfusion with HOPE	0.20 (0.03 – 1.53)	0.1	-	
Histological exam after explant				
Presence of HCC	1.63 (0.45 – 5.97)	0.5	-	
Number of HCC nodules	1.311 (1.024 – 1.678)	0.031	-	
Diameter of largest HCC nodule (cm)	1.025 (0.997 – 1.055)	0.085	-	
Satellite nodules	0.96 (0.20 – 4.55)	0.9	-	
Microvascular invasion	3.425 (1.172 – 10.008)	0.024	3.737 (1.246 – 11.206)	0.019
Macrovascular invasion	5.182 (1.261 – 21.294)	0.023	-	
Histological grade ≥3	4.000 (1.098 – 14.567)	0.036	-	
Peak ALT at 7th POD (U/L)	1.00 (0.99 – 1.01)	0.5	-	
Peak AST at 7th POD (U/L)	1.00 (0.99 – 1.01)	0.9	-	
Early Allograft Dysfunction	2.21 (0.72 – 6.80)	0.2	-	

Figure 1 – Kaplan-Meier curves for weighted recurrence-free survival in the HOPE group and Static Cold Storage (SCS) alone group



BOS13_12 THE EFFECT OF CONTINUOUS LIVER NORMOTHERMIC MACHINE PERFUSION ON THE SEVERITY OF HISTOLOGICAL BILE DUCT INJURY

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Background: Ischemic Cholangiopathy (IC) is a feared complication after Liver Transplantation (LT). Static Cold Storage (SCS) results in histological injury to the bile duct (BD). Normothermic Machine Perfusion (NMP) preserves the liver better than SCS, but its effect on the severity of BD injury is unknown. In a sub-study of the COPE randomized controlled trial on liver NMP, we investigated if the type of preservation influences the severity of the histological Bile Duct Injury Score (BDIS).
Methods: LT included in the COPE NMP trial (06/2014-03/2016) with at least one BD biopsy available either at the end of preservation or 1h post-LT and consisting of at least ½ circumference of BD were considered. The total BDIS was calculated in blinded fashion as the sum of the scores for peribiliary glands injury, stromal and mural loss, haemorrhage, and thrombosis. A bivariate linear model estimated and compared BDIS between SCS and NMP (Table 1). Median (IQR) or estimate (CI) are given.
Results: 65 out of 222 LT included in the trial met the inclusion criteria and 85 BD biopsies were analysed. 23 grafts were preserved with SCS and 42 with NMP. Baseline characteristics were comparable, except for a lower donor peak of sodium and shorter cold ischemic time in the NMP group. Post-LT peak AST was significantly lower in the NMP [381 (196-906) IU/dL] than in the SCS group [741 (474-2221) IU/dL, p=0.01]. The BDIS increased over time regardless of preservation type (p=0.04). The overall estimated BDIS was higher with NMP [8.02 (CI 7.40-8.65)] than with SCS [5.39 (CI 4.52-6.26), p<0.0001], and remained higher at both timepoints considered. BDIS changes in time did not differ according to preservation type (interaction effect). One patient in each group developed IC, with a BDIS at 1h post-LT of 6 for the NMP preserved liver. Six other NMP grafts had a BDIS at 1h post-LT between 7-12 but did not develop IC.
Conclusions: BDIS increases over time (upon reperfusion) regardless of preservation type. Although liver NMP was associated with more severe BD histological injury, there was no significant increase in the incidence of IC. BDIS may overestimate the risk of IC after liver NMP and its role as a surrogate endpoint to define viability criteria should be re-evaluated.

Table 1. Bivariate linear model comparing BDIS of livers preserved with SCS or continuous NMP.

	SCS (n=23)	NMP (n=42)		
BDIS	**Estimate (CI)**	**Estimate (CI)**	**P-value**	**Bonferroni-Holm**
Main effect preservation†	5.39 (4.52;6.26)	8.02 (7.40;8.65)	**<.0001**	.
End preservation	5.17 (3.96;6.39)	7.25 (6.44;8.06)	**0.0060**	**0.006**
1h post-transplant	5.61 (4.49;6.73)	8.80 (7.94;9.66)	**<.0001**	**<.0001**
Main effect time*				**0.04**
Interaction effect#				0.25

†Main effect preservation: does the type of preservation influence BDIS, regardless of time?
*Main effect time: is there any change in BDIS over time, regardless of the type of preservation?
Interaction effect: do BDIS change over time differs between preservation types?
"Estimate" indicate the mean from a multivariate regression model for longitudinal measures.
BDIS, bile duct injury score; CI, confidence interval; NMP, normothermic machine perfusion; SCS, static cold storage.

BRIEF ORALS

Organ preservation and ischemia reperfusion

BOS13_13 THE IMPACT OF DONOR TIME TO DEATH AND FUNCTIONAL WARM ISCHAEMIA TIME ON RECIPIENT OUTCOME FOLLOWING DCD LIVER TRANSPLANTATION

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Background: UK practice is to abandon donor hepatectomy if functional warm ischaemia time (FWIT) exceeds 30 minutes in donors after circulatory death (DCD). During this agonal phase, beginning from treatment withdrawal, donor blood pressure and oxygen saturations are expected to drop, reducing flow of oxygenated blood to the liver graft causing ischaemic injury. We assessed what impact donor time to death (TTD) and FWIT had on recipient outcomes following DCD liver transplantation.
Methods: Data were extracted from the NHS Blood and Transplant registry on all DCD liver graft recipients from 2006 to 2021. TTD was defined as the time from withdrawal of life sustaining treatment to asystole, and FWIT was the time from systolic BP and/or SpO2 falling below 50mmHg and 70%, respectively, to aortic perfusion. The primary endpoint was 1-year graft survival. Potential predictors were fitted into separate hierarchical Cox proportional hazards regression models for TTD and FWIT to avoid collinearity, with multiple imputation for missing data.
Results: 1558 recipients of DCD liver grafts were included. Median TTD was 13 minutes (IQR 9-17 minutes); TTD occurred between 0-10 minutes in 347 (33.9%), 10-16 minutes in 382 (37.3%), and >16 minutes in 296 (28.9%) recipients. TTD exceeded 30 minutes in 43 donors (2.8%). TTD was not available in 533 donors (34.2%). The incidence of primary non-function did not differ across the 3 TTD categories (6.6% vs. 3.7% vs. 5.1%, p=0.193). TTD (HR 0.82, 95% CI 0.61-1.11, p=0.2) and FWIT (HR 1.00, 95% CI 0.44-2.27, p>0.9) did not predict 1-year graft loss. On sensitivity analysis TTD >30 minutes did not predict 1-year graft loss. Prolonged donor hepatectomy time was significantly associated with 1-year graft loss in the TTD (HR 1.87, 95% CI 1.23-2.83, p=0.003) and the FWIT models (HR 1.89, 95% CI 1.25-2.87, p=0.003). In separate modelling donor TTD, FWIT and hepatectomy time were not predictive of 1-year recipient mortality (all p>0.05).
Conclusions: Prolonged hepatectomy time, but not TTD or FWIT, was associated with worse graft survival. Expanding the 30-minute FWIT limit may increase the number of DCD liver grafts retrieved without harming recipient outcomes if hepatectomy time is kept short. Further prospective evaluation of recipient risk from grafts retrieved outside current criteria is warranted.

BOS13_14 HOPE REDUCES DURATION OF GLYCOCALYX SHEDDING – ITS DAMAGE MARKER SYNDECAN-1 CAN PREDICT EARLY ALLOGRAFT DYSFUNCTION

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Background: During liver transplantation, the graft has to endure an ischemic phase and additional injury after reperfusion (IRI), especially mediated by reactive oxygen species (ROS). The endothelial glycocalyx covers the luminal side of the vascular endothelium and regulates vascular permeability, modulates adhesion of leucocytes onto the vascular wall and transduces mechanical shear stress. It is very sensitive to ROS and therefore degraded during graft preservation and reperfusion. Hypothermic oxygenated machine perfusion (HOPE) is a preservation strategy that can reduce IRI-inflicted graft injury compared to static cold storage (SCS). We aimed to measure glycocalyx degradation after HOPE or SCS alone, to evaluate its viability-assessment potential for liver transplantation.
Methods: We measured glycocalyx degradation via ELISA for its main component Syndecan-1, in samples from 77 liver transplant patients. 37 grafts were directly transplanted after SCS, 40 grafts additionally underwent HOPE with the Organ Assist® perfusion system, prior to liver transplantation.
Results: Sdc-1 concentrations in the graft effluent are significantly lower after HOPE [466 (350-1073)] compared to SCS alone [4011 (3382-4683)] (p<.001). Further, Sdc-1 concentrations regenerate faster towards baseline levels on postoperative day 1 [HOPE: 362 (232-880) vs. SCS: 1017 (637-1900) p<.001], indicating a shorter glycocalyx shedding period. Regarding viability assessment, Sdc-1 concentrations in the perfusate were elevated in EAD patients after 60 minutes of HOPE compared to non-EAD patients [429 (260-556) vs. 896 (419-1681) p=.018]. Additionally ROC-analysis indicated a significant discriminatory value of Sdc-1 concentration after 60 minutes of HOPE regarding the occurrence of EAD with an AUC of 74% (p=.018, sensitivity 66.7% and specificity 84.6%).
Conclusions: HOPE reduces the duration of glycocalyx shedding, evident by Sdc-1 release in recipient serum after liver transplantation. Sdc-1 concentration during HOPE can predict early allograft dysfunction. Therefore, Sdcc-1 could be a potential viability assessment marker in liver transplantation.

Safety and quality at the core of donation and transplantation

BOS14_1 SETTING EUROPEAN QUALITY AND SAFETY STANDARDS FOR ORGAN DONATION AND TRANSPLANTATION

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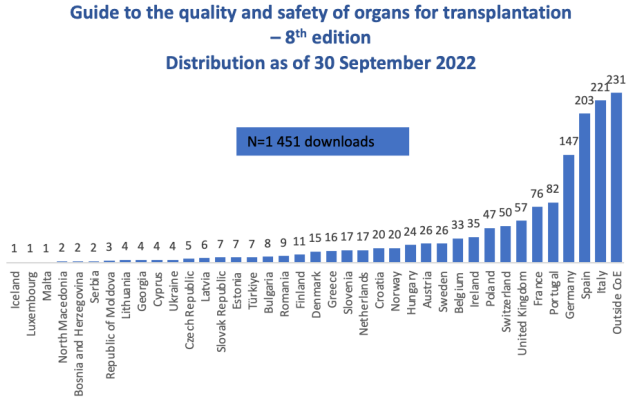
Background: Organ transplantation has progressed in recent decades, yet demand for organs exceeds supply. As all substances of human origin, organs entail a risk of disease transmission. It is thus needed to set European quality and safety standards for organ donation and transplantation.
Methods: A group of 40 experts nominated by member states of the Council of Europe drafted and agreed on European standards based on a previous edition. In addition, 48 worldwide experts were involved in the revision of certain topics. Standards were revised according to the state of the art, and new and important items were added. Once the text was final, it underwent a stake-holder consultation. 301 comments were received, which were carefully revised, 82% leading to changes in the final text.
Results: The result has been the 8th edition of the Guide to the quality and safety of organs for transplantation (contents shown in table 1), published in July 2022.
Conclusions: The Guide has demonstrated to be a unique tool for co-ordinators, those responsible for the clinical use of organs, quality managers and health authorities. Its goal is to improve successful and safe transplantation rates.

Table 1: Contents of the 8th edition of the Guide to the quality and safety of organs for transplantation

Chapter	
1	Introduction
2	Identification and referral of possible deceased organ donors
3	Determination of brain death by neurologic criteria
4	Family approach and consent/authorisation for post-mortem organ donation
5	Management of the potential donor
6	General donor characterisation, assessment and selection criteria
7	Specific organ characterisation, assessment and selection criteria
8	Risk of transmission of infectious diseases
9	**Risk of transmission of cancer**
10	**Risks related to the use of organs from donors with other conditions and diseases**
11	**Organ procurement, preservation and transportation**
12	**Donation after the circulatory determination of death**
13	**Living donation**
14	**Paediatric donation**
15	**Donation of vascularised composite allografts**
16	**Biovigilance and surveillance**
17	**Achieving and measuring quality in organ donation and transplantation**
18	**Measuring outcomes in transplantation**
19	Communication of risk and shared decision-making

Guide was widely used (see figure 1).
Figure 1: Downloads of the Guide as of 30 September *2022*



BOS14_3 DONOR-TRANSMITTED CANCER IN ORGAN DONATION AND SOLID ORGAN TRANSPLANTATION IN GERMANY FROM 2016-2022

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Background: Analyzing reported serious adverse events (SAE) and serious adverse reactions (SAR) is an essential part of an effective vigilance and surveillance system in organ donation and transplantation. The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is assigned by the German Federal Ministry of Health to manage and monitor SAE and SAR. Donor-transmitted cancer (DTC) can pose an additional risk to the recipients with significant morbidity and mortality.
Methods: All incoming SAE and SAR reported from January 1st 2016 to December 31st 2022 related to a potential malignant disease were analyzed. A DTC was defined as a malignancy already present within the organ at the time of transplantation. The assessment of imputability as proven or probable (P/P) transmission was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC).
Results: 145 reports were analyzed. In 104 reports the final histopathological analyses showed a malignant tumour (104/145; 72%). 16 reports were classified as P/P DTC from the donor to one or more recipients. These 16 cases involved 22 recipients resulting in 11 attributable deaths (11/22; 50 %). These cases included three adenocarcinomas, two lymphomas, two melanomas, two renal cell carcinomas, two urothelial carcinomas, two neuroendocrine lung cancer, one pleural mesothelioma, one squamous cell carcinoma and one angiosarcoma. 0,19 % of the 8519 donors (16/8519; 0,19 %) transmitted a P/P cancer to 0,11 % of all recipients (22/20315; 0,11 %).
Conclusions: Donor-Transmitted cancer is a rare event, but when it occurs can lead to significant morbidity and mortality of the recipients.

Malignancy Type/ Location	Donors reported	P/P donors	Total recipients From P/P donors	Total recipients with transmission from P/P donors*	Total deaths from cancer transmission**
Renal	43	2	5	2 (40%)	0 (0%)
Adenocarcinoma	11	3	8	4 (50%)	3 (75%)
Hematological	9	2	5	4 (80%)	2 (50%)
Lung	8	2	6	2 (33%)	1 (50%)
Melanoma	2	2	4	4 (100%)	2 (50%)
Other Malignancy	31	5	16	6 (37,5%)	3 (50%)
Total	104	16	44	22 (50%)	11 (50%)

*% = recipients with transmission/recipients from P/P donors. **% = deaths from cancer transmission /total recipients with cancer transmission

BOS14_4 NO SURVIVAL BENEFIT IN KIDNEY TRANSPLANT RECIPIENTS IN THE EUROPEAN SENIOR PROGRAM

Marcel Naik*[1], Mareen Pigorsch[2], Elke Schaeffner[3], Vivien Greese[1], Kai-Uwe Eckardt[1], Michael Kammer[4;5], Ulrich Frei[1], Mira Choi[1], Lutz Liefeldt[1], Robert Öllinger[6], Frank Friedersdorff[7], Klemens Budde[1], Fabian Halleck[1]
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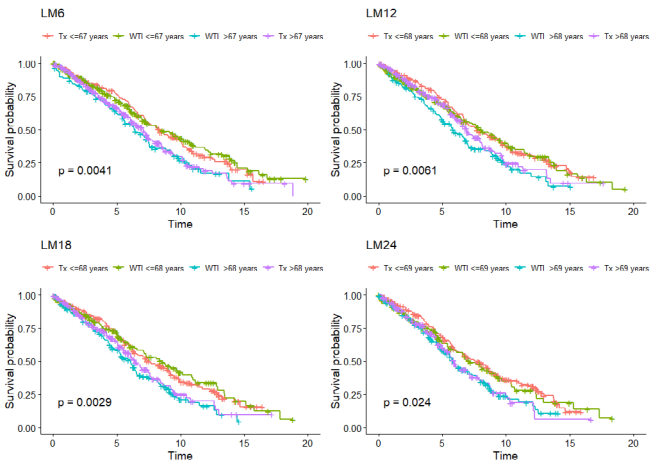
Background: In the European Senior Program (ESP) recipients ≥65 years are waitlisted to receive local kidneys from cadaveric donors ≥65 years without HLA-matching. We compare patient survival of waitlisted (WTL) with survival of transplant (TX) patients in the ESP over 20 years at our center.
Methods: All patients waitlisted with active status in the ESP in our centre between 1999-2019 were included into this survival analysis. The baseline marked either the 65th birthday (inclusion from regular allocation) or any time point thereafter (primary ESP-allocation). To investigate patient survival, landmark analyses were performed at 6, 12, 18 and 24 months after baseline. Patients were analysed in WTL- or TX-group depending on their status at the respective landmark. Survival was estimated using Kaplan Meier analysis. In the age-dependent survival analyses, the median at the respective landmark was used for stratification.
Results: 820 patients were included into the cohort (median age at baseline 67.8 years, 62% male). Landmark analyses at 6, 12, 18 and 24 months including 780, 744, 710 and 662 patients, respectively, showed a survival until landmark of 35%, 32%, 29%, and 31% for TX and 36%, 33%, 33% and 29% for WTL at 10 years, respectively. Age-dependent landmark analyses at 6, 12, 18 and 24 months (Figure 1) stratified by median age at each landmark showed better survival in younger patients below median irrespective of transplant status. Sensitivity analysis in 570 patients who were first listed into the ESP after their 65th birthday (median age 69.9 years) did not show any survival benefit for transplanted patients either.
Conclusions: Our results demonstrate in a large monocentric cohort that kidney transplant recipients ≥65 years receiving an organ from a donor ≥65 years have no survival benefit compared to waitlisted dialysis patients of the same age. A deeper analysis considering major covariates like comorbidities at time of listing and time on dialysis is needed to further validate this finding. A major limitation of our study is that the patients' quality of life was not recorded.



BRIEF ORALS

Safety and quality at the core of donation and transplantation

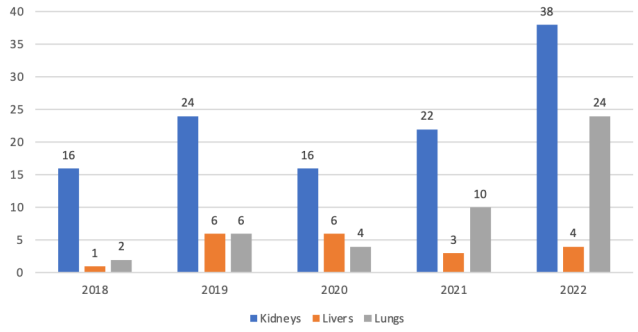
BOS14_5 DONATION AFTER MEDICAL ASSISTANCE IN DYING IN QUÉBEC – THE FIRST FIVE YEARS

Matthew Weiss[*1;2;3], **Mathilde Dupras-Langlais**[1], **Marie-Josée Lavigne**[1], **Annie-Carole Martel**[1], **Sylvain Lavigne**[1], **Prosanto Chaudhury**[1;4]

[1]Transplant Québec, Montréal, Canada, [2]Canadian Donation and Transplant Research Program, Edmonton, Canada, [3]CHUL et Centre Mère-Enfant Soleil, Pediatric Intensive Care, Québec, Canada, [4]MUHC - McGill University Health Centre (Glen Site), Multi-organ Transplant Program, Montréal, Canada

Background: Since the 2015 passage of a law allowing medical assistance in dying (MAID), Québec became one of few jurisdictions where deceased organ donation after MAID was possible.
Methods: We reviewed all cases referred for donation after MAID from January 2018 to December 2022, the first five full years of our program. As a retrospective, anonymized report, we did not seek ethics approval. All data is presented descriptively with no comparison statistics.
Results: We received 240 referrals for donation after MAID. We retained and confirmed initial consent for 81 of these references (81/240, 34%). 130/159 non-retained references had a recorded reason: 75/130 (58%) were for medical unsuitability (age, medical history, etc.), 30/130 (23%) were due to patient refusal, and 12/130 (9%) patients withdrew from the MAID process entirely. Seventeen of the 81 retained cases were canceled later in the process, almost all (16/17, 94%) due to medical contraindication discovered during the donation evaluation. One patient died before MAID was realized. The most common underlying diagnostic group was neurodegenerative disorders (85%), followed by cardiopulmonary disorders (6%), or other (9%). The average time from administration of the MAID agents to determination of death was 12.6 minutes (3-28 min); the average WIT was 26.6 minutes (16-43 min). A total of 182 organs (116 kidneys, 20 livers, 46 lungs) were transplanted. Table 1 details the transplanted organs per year. Sixty-four patients became actual donors after MAID increasing from 8 in 2018 to 24 in 2022. The total conversion rate was 26% (64/240) of all referrals and 79% (64/81) of referrals retained after initial evaluation. MAID donors represented 8% (64/803) of total deceased donors during the study period, increasing from 5% (8/164) in 2018 to 14% (24/173) in 2022.
Conclusions: These data describe the substantial increase in deceased donation after MAID in the first 5 years of implementation in Québec and show that ODOs can establish a system that honors the wishes of patients pursuing MAID to donate their organs after their death. Future study will focus on how to optimize these systems to ensure these requests are treated in the most ethically and medically effective way possible.

Table 1. Transplanted organs from MAID donor in Quebec



BOS14_6 THE SCARCITY OF ORGAN DONORS IN CHILE IS NOT EXPLAINED BY FAMILIAL REFUSAL, BUT BY UNPREPARED ER AND ICU PROFESSIONALS

Francisca Gonzalez Cohens[*1], **Felipe Vera Cid**[1], **Rosa Alcayaga Droguett**[1], **Fernando Gonzalez Fuenzalida**[2;3]

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Background: Despite appropriate legislation and adequate financial coverage, organ donation rates (ODR) in Chile remain low. Experts blame high familial refusal rates, while dismissing the effect of procurement process inefficiencies in hospitals. Our objective is to study some of those inefficiencies that may lead to the scarce ODR.
Methods: Using a two-step approach, we started by obtaining two datasets, hospital discharges and organ procurements between years 2013-2017. We considered all patients that entered the system with a critical neurological condition according to ICD10, and exited dead; and all possible organ donors (PD) who entered procurement follow-up. We used descriptive statistics to merge and analyze both datasets. Second, we applied a survey on healthcare professionals (HCP, physicians and registered nurses) in ER and ICU of 3 large hospitals in the capital, which aimed at describing procurement process knowledge and behavior. We used descriptive statistics for analysis.
Results: At the first analysis we found that 87% of patients qualifying as PD never entered procurement follow-up and, as 50% of families refused to donate, 6% of all PD became effective organ donors. The survey was answered by 88 HCP. 50% physicians, 70% from ER. 51% declared they've actively detected a PD but 43% referred them to the Procurement Unit (PU), thus 22% detected and referred a PD (78% don't). 10% of the surveyed population was not sure about the validity of brain death diagnosis, and 52% never received formal training on any organ donation topic while studying. 73% thought procurement activity as important, but 40% declared not knowing enough about it. ICU HCP was more knowledgeable than ER (81% vs 23% declared more than sufficient knowledge, $p<0.001$).
Conclusions: The insufficient knowledge of procurement activity and concepts, especially from ER HCP may explain the lack of PD detection and referral found at a national level. It is also interesting that the HPC% who don't refer PDs is like PD% lost nationally. Although the small sample may not be fully representative of the target population, the findings provide the insight that the efforts to increase Chilean DDR should be put in educating HCP that participate in the procurement process, or even automating and standardizing the process to stop relying on people's knowledge

BOS14_7 CITIZENSHIP STATUS AND KIDNEY FUNCTION OF LIVING KIDNEY DONORS IN THE UNITED STATES

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Background: Kidney disease is perceived to greater affect non-citizens residing in countries with a variety of populations like the United States. Whether this disparity exists in living kidney donors (LKD) in the United States is unknown. We aim to evaluate the association between U.S. citizenship status and kidney function after a living kidney donation.
Methods: A retrospective cohort study using OPTN/SRTR database includes LKD undergoing living kidney donation between June 1972 and September 2022. Time-to-event of >35% rising post-donation serum creatinine (SCr) from pre-donation SCr between U.S. and non-U.S. citizens was examined by multiple Cox proportional hazard regression analyses.
Results: Of 136,814 LKD, the mean±SD age was 42±12 years and 61% were female. The majority were U.S. citizens (95%). Over a median time to follow-up of 6.27 months (IQR 4.07, 8.67), 103,938 LKD had post-donation SCr data and 75% (78,344) of these LKD had the event. The incidence rate of the event was 0.092 person-months. SCr during the pre-donation period was 0.85±0.19 mg/dL and post-donation SCr during routine follow-up visits at 6, 12, and 24 months were 1.22±0.30, 1.194±0.30, and 1.16±0.27 mg/dL, respectively (Figure 1A). There was a graded increase in the mean percentage of elevated SCr from pre-donation SCr at 6, 12, and 24 months post-donation of 46, 43, and 41%, respectively (Figure 1B). Compared to the non-U.S. citizen, the U.S. citizen had a non-significantly higher risk of increased post-donation SCr >35% (HR 1.02, 95%CI 0.99, 1.06, P 0.151). After adjusting for age, gender, race/ethnicity, education level, pre-donation BMI, history of hypertension, SBP, DBP, SCr, and post-donation proteinuria, the U.S. citizen became at greater risk for the event (HR 1.12, 95%CI 1.050, 1.204, P 0.001; Figure 2). There was no effect modification of the adjusted variables in the multivariable Cox regression model.
Conclusions: U.S. citizens are at higher risk of increased post-donation SCr >35% compared to non-U.S. citizens independent of pre- and post-donation factors. While non-U.S. citizen is the minority in the country, exploring factors contributing to this finding from qualitative studies as a mixed method design should explain the mechanism and mitigate the risk of worsening post-donation kidney function among U.S. citizens.

Figure 1: Distribution of pre-donation serum creatinine and serum creatinine at 6, 12, and 24 months post-donation (A) and mean percentage of rising serum creatinine from the pre-donation serum creatinine at 6, 12, and 24 months post-donation (B) SCr, serum creatinine

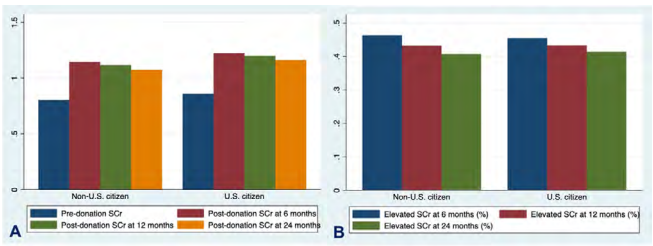
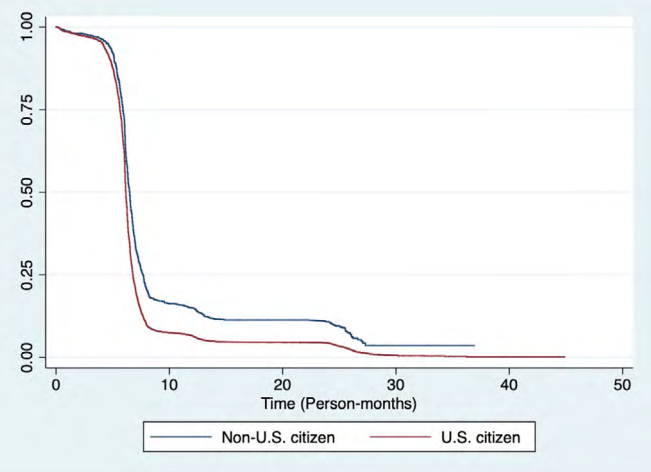


Figure 2: Kaplan-Meier cumulative hazard estimates of rising postdonation serum creatinine >35% from pre-donation serum creatinine



BOS14_8 KIDNEY FUNCTION DECLINE PREDICTING FACTORS IN LIVING KIDNEY TRANSPLANTATION DONORS

Zaklina Sterjova*[1], Lada Trajceska[1], Irena Rambabova Bushljetikj[1], Goce Spasovski[1], Stefan Filipovski[1], Galina Severova- Andreevska[1], Igor Nikolov[1], Mimoza Milenkova[1], Aleksandra Canevska Taneska[1], Adrijana Spasovska[1]

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Background: After nephrectomy kidney transplant donors lose 50% of their renal mass. Shortage of donors and long waiting list for deceased donor transplantation expanded the living donor criteria. The aim of this study to identify pretransplant donor related factors associated with renal function decline.
Methods: We retrospectively studied LDKT donors from one transplant center in the period 2013-2022. Data was retrieved from medical history charts and national electronic database system. Demographic characteristics as age, gender and relation to the recipient, patients preference to donate the kidney with higher measured split GFR, the presence of diabetes, hypertension, hyperlipidemia and BMI >30kg/m^2 were analysed. Estimated GFR by CKD EPI was notified prior donation, one and two years afterwards. In a multivariate regression analysis the reduction ratio of CKD EPI was explored as dependent variable.
Results: We studied 121 donors. The average age at time of transplant was 59.18 ± 10.99 years. Donors' average eGFR was 91.53 ± 18.62 mL/min. Donor's age and eGFR were significantly correlated (p < 0.0001, r=-0.529). Male donors were 37 (30%), 11 (9%) were unrelated to recipients, 9(7%) had BMI>30, 17 (14%) diabetes, 53 (44%) hypertension 5 (4% hyperlipidemia), and 65 (52%) had more than one comorbidity combined. Eight of donors (7%) decided to donate the better kidney. CKD EPI declined to 68.17±18.62ml/min at first and 66.01±21.29ml/min at the second year. The RR of 24.53 ± 20.60 % and 27.62±18.76% raised on yearly bases, respectively. In the univariate analysis of the GFR declination at the first year BMI>30kg/m^2 was associated with higher reduction of GFR (β=0.318, p=0.003). At the second year the presence of diabetes emerged as worsening factor of GFR (β=0.227, p=0.034) and BMI>30kg/m^2 kept its significance (β=0.426, p=0.000). All the other parameters showed no significant associations to the GFR decline. In the multivariate analysis BMI>30kg/m^2 remained as most powerful predictor at 12 months reduction of eGFR.
Conclusions: Patients with diabetes and especially with obesity are at higher risk of rapid decline in kidney function after kidney donation. Careful assessment prior kidney donation should weight the risks.

BOS14_10 / P766 CHARACTERISTICS OF PROSPECTIVE AND EFFECTIVE LIVING DONORS FOR RENAL TRANSPLANTATION: A CROSS-SECTIONAL STUDY

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Background: Living donor kidney transplantation accounts for 23% of transplants in the country, and most postulated donors do not complete the process. Therefore, the objective of this study was to describe the process of an effective donation, characterizing the potential and effective living kidney donors evaluated in a transplant centre.
Methods: In a cross-sectional study, we retrospectively reviewed the medical records of 1488 potential donors, evaluated between 2008 and 2019. A descriptive analysis of donor characteristics was performed. The characteristics of potential and effective donors were compared. And described the living donation process and reasons for non-donation in its distinct phases.
Results: Only 36.9% were effective donors, while 63% were disqualified. Of potential donors, 15.4% were not approved of by mental health, 31.8% were contraindicated by nephrology or surgery, the medical board did not authorize 11%, and 4.7% of donors were approved but did not complete the process. The most frequent reasons for non-donation due to medical contraindication were arterial hypertension, anatomic anomaly, and proteinuria greater than 300. Effective donors were younger, with lower body mass index and higher frequency of first-degree relationships.
Conclusions: Only one-third of potential donors become effective donors. The main reasons for non-donation are clinical, but a critical percentage is disqualified for mental health reasons and for dropping out of the process.

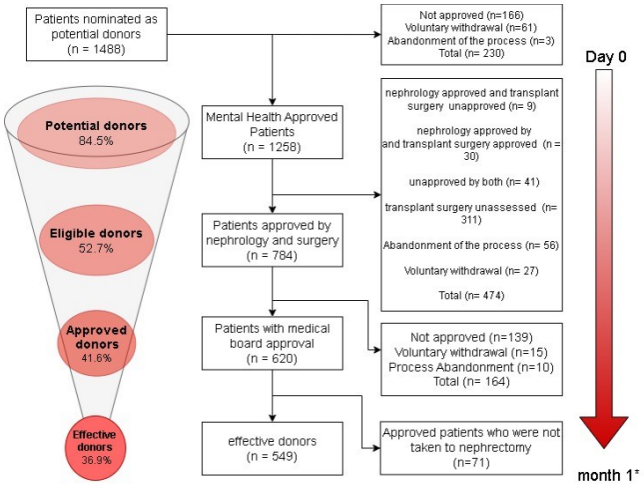

Figure 1. Approval flowchart from donor nomination to nephrectomy and transplantation. *Median follow-up time from donor application to nephrectomy.

Unapproved donors	(n=868)
Contraindication rationale for mental health	166 (19.1%)
Ethical	94 (56.6%)
Ethical and psychological	35 (21.1%)
Ethical and psychological	19 (11.4%)
Psychological	13 (7.8%)
Legal	3 (1.8%)
Legal, ethical, and psychological	2 (1.2%)
Rationale for clinical non-donation	513 (59.1%)
Arterial hypertension	136 (26.5%)
Anatomical abnormality	61 (11.9%)
Proteinuria greater than 300	53 (10.3%)
Others	44 (8.6%)
Other disease	39 (7.6%)
Group incompatibility	39 (7.6%)
Positive crossmatch	31 (6%)
Creatinine clearance less than 80	30 (5.8%)
Obesity	27 (5.3%)
Hyperglycaemia or diabetes	17 (3.3%)
Haematuria	16 (3.1%)
Nephrolithiasis	9 (1.8%)
Family background	4 (0.8%)
Renal asymmetry or atrophy	4 (0.8%)
Others related to the receiver	3 (0.6%)
Voluntary withdrawal	116 (13.3%)
Process Abandonment	73 (8.4%)

BOS14_11 AI MEASURED PREOPERATIVE RENAL VOLUME AND RISK FACTORS ASSOCIATED WITH CHRONIC KIDNEY DISEASE POST DONOR NEPHRECTOMY IN THE ELDERLY

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Background: After the age of 60, functional nephron loss occurs due to decreases in the number of glomeruli and increases in the number of sclerosed glomeruli per kidney. Kidney volume is a useful predictor to measure such kidney functions. The aim of this study was to assess whether old age kidney donors have lower remnant kidney volumes and have higher risks for developing chronic kidney disease (CKD) after donor nephrectomy.
Methods: A retrospective analysis of 1020 living kidney donors was performed at our centre. The remnant kidney whole volume and cortex volume were measured using preoperative computed tomography (CT) and a fully autosegmented program developed at our centre. Univariate and multivariate analysis for risk factors associated with chronic kidney disease (CKD) post donor nephrectomy was performed using preoperative factors including baseline characteristics, laboratory results, and remnant kidney volume.
Results: Compared to young donors (<=60 years), old age donors (>60 years) developed CKD more frequently during the cumulative 3-year follow-up period (43.0% (n=49/114) vs 13.2% (n=120/905); p<0.001). Preoperative kidney whole volume was smaller in old donors than young donors (159.5 ± 28.9 mL vs. 165.0 ± 27.8 mL; p=0.048). The cortex to whole volume ratio was also lower in old donors (0.60±0.08 vs. 0.62±0.07; p=0.004). Multivariate analysis results showed that old age >60 years (OR 2.37, 95% CI 1.21-4.66; p=0.012), male sex (OR 4.20, 95% CI, 2.59-7.04; p<0.001), BMI (OR 1.09, 95% CI 1.02-1.17; p=0.015), dyslipidemia (OR 1.5, 95% CI 1.01-2.50; p=0.012), remnant kidney volume to BSA ratio (OR 0.97, 95% CI 0.95-0.99; p<0.001), baseline eGFR (OR 0.85, 95% CI 0.82-0.88; p<0.001), and total protein (OR 0.55, 95% CI 0.34-0.90; p=0.017) were all significant risk factors for the development of CKD post-nephrectomy. Remnant kidney volume to BSA ratio of greater than 104.7 mL/m2 was found to be a protective factor with an odds ratio of 0.343 (95% CI 0.81-0.65; p=0.001).
Conclusions: Old donors have smaller kidney volume compared to young donors and this may result in increased risks for developing chronic kidney disease post nephrectomy.

BOS14_12 HIGHER ABDOMINAL FAT AREA ASSOCIATES WITH LOWER RENAL FUNCTION BEFORE AND AFTER LIVING KIDNEY DONATION

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Background: Central body fat distribution affects renal function. Abdominal fat measurements using computed tomography (CT) may prove superior in assessing body composition related renal risk in living kidney donors. This study aimed to determine the association between abdominal fat areas and renal function before and (long term) after donor nephrectomy, using CT imaging at L3 vertebral level.
Methods: Between 2002 and 2019, 570 living kidney donors were included in this study. CT-derived abdominal fat areas were determined at vertebral level L3 and indexed for height. Donors underwent glomerular filtration rate measurements (^{125}I-Iothalamate) before (n=568) and 5 years after donation (n=212). Linear regression analyses with crude mGFR and mGFR indexed for body surface area were performed to assess the association of tomographic fat measurements with renal function.
Results: Multivariable linear regression analyses in both male and female donors showed higher levels of total abdominal, visceral, subcutaneous, and intramuscular adipose tissue index were significantly associated with lower crude and body surface area indexed measured glomerular filtration rate levels before donation (body surface area indexed measured glomerular filtration rate: male donors: visceral adipose tissue index: B=-0.06, p=0.002, subcutaneous: B=-0.08, p<0.001, intramuscular: B=-0.65, p=0.003, total abdominal: B=-0.04, p<0.001; female donors: visceral adipose tissue index: B=-0.10, p<0.001, subcutaneous: B=-0.07, p<0.001, intramuscular: B=-0.75, p=0.002, total abdominal: B=-0.05, p<0.001). Long-term after donation, tomographic abdominal fat measurements remained inversely associated with mGFR indexed for body surface area in male donors.
Conclusions: This study shows that abdominal fat area, measured by CT analysis, is associated with renal function at time of screening and (in male donors) long-term after living kidney donation. Comprehending the renal outcomes of living kidney donation and accurately identifying their body composition related risk factors can aid clinicians in decision-making and donor counselling during screening for donation.

BOS14_13 BODY MASS INDEX (BMI), OBESITY AND URIC ACID: PRIOR TO DONOR NEPHRECTOMY AND OVER A 15-YEAR FOLLOW-UP PERIOD, EXPERIENCE OF OUR CENTER

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Background: Obesity is the most important metabolic factor for predicting a delayed recovery of renal function in living kidney donors. It was noticed that 26% of the examined donors in the the second part of the 20th century had a BMI ≥ 30 kg/m² compared to 8% in the period from 1963 to 1974. Some of these "obese" donors were accepted after a careful evaluation, due to the absence of other unfavorable metabolic conditions, or the fact that they were muscular prior to donation, which was the reason for the higher body mass index (BMI).
Methods: Our study was conducted as a retrospective, case-control type study. It included living kidney donors who underwent donor nephrectomy since 2004 (108 subjects). The parameters of interest were observed prior to donor nephrectomy, 6 months post-op and 1, 5, 10 and 15 years post-op as well. The control group consisted of donor nephrectomy patients themselves.
Results: In our donors with BMI between 19-24 kg/m², we observed a faster recovery of renal function. Namely, the aforementioned donors maintained the optimal limit values of eGFR CKD EPI even 5 years after donor nephrectomy, i.e. above 80 ml/min/1.73m². In obese kidney donors, with BMI >29 kg/m², 10 years post-op, the renal reserve calculated from eGFR CKD EPI was below 60 ml/min/1.73m². The onset of CKD in the group of donors with 24 <BMI<29 kg/m² was approximately 15 years (14.82 years to be exact) post nephrectomy, while in the thinnest donors, CKD was to be expected 17.61 years post-op. In our donors, we did not prove a clear correlation between uric acid values and renal reserve.
Conclusions: Obesity is the reason for slower kidney function recovery (BMI>29 kg/m²). The optimal donor is in the group of patients with 19<BMI<24 kg/m². Higher BMI correlated with a worse HDL/LDL ratio pre-op and with higher values of total cholesterol in the post-transplantation period as well. As far as the development of CKD depending on BMI is concerned, we found that there is a significant difference in the average time preceding the development of CKD in patients with different values of BMI. We proved that the expected occurrence of CKD in the group with 24 <BMI<29 kg/m² was around 15 years (14.82 to be exact), that is, in the thinnest donors, CKD was to be expected 17.61 years post-op.

BRIEF ORALS

Progress and challenges in Pancreas and Islet transplantation

BOS15_1 ISLET TRANSPLANTATION VERSUS INSULIN ALONE IN TYPE 1 DIABETIC KIDNEY TRANSPLANT RECIPIENTS: A FRENCH NATIONWIDE STUDY ON BEHALF OF THE TREPID GROUP

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Background: Islet transplantation is associated with a benefit on glycaemic control compared to optimized insulin therapy in recent clinical trials. However, there is a lack of evidence concerning the long-term impact of islet transplantation on type 1 diabetic kidney transplant recipients' prognosis.
Methods: Every type 1 diabetic recipient transplanted with a kidney in France between 2000 and 2017 was included. Patients transplanted with pancreatic islets were compared to controls treated with insulin alone according to a matching method based on time-dependent propensity scores (using the following variables : yera of transplantation, donor age, and recipient age, serum creatinine, HBA1c, BMI, cardiovascular background) which allow to ensure patients comparability at the time of islet transplantation. The primary outcome was graft failure, defined by death or return to dialysis.
Results: Among 2393 type 1 diabetic patients transplanted with a kidney during the study period, 381 were eligible to islet transplantation, including 47 that were actually transplanted with islets. Median time for islet transplantation was 34.8 months [21.8-48.4]. Probabilities of insulino-independence and islet graft survival at 1, 5 and 10 years were respectively 63.8% [51.5-79.2], 46.3% [33.9-63.2], 38.7% [25.9-57.8] and 89.4% [81.0-98.6], 87.2% [78.2-97.3], 78.2% [66.2-92.4]. After matching, we observed a significant benefit of islet transplantation compared to insulin alone on graft failure, with a HR of 0.48 [0.20-0.94], mainly explained by a protective effect on the risk of death (HR= 0.38 [0.11-0.95]). We finally estimated the life-expectancy for a 10-year follow-up and found 9.61 years [9.02-10.00] in the islet transplantation group versus 8.85 years [7.97-9.56], with a difference of 8.88 months [-2.16-20.44]
Conclusions: We observe a significant benefit of islet transplantation on the risk of graft failure and death in type 1 diabetic kidney transplant recipients. These results provide incentives to promote islet transplantation in this population.

BOS15_2 RELATION BETWEEN PRIMARY GRAFT FUNCTION AND 5-YEAR OUTCOMES OF ISLET TRANSPLANTATION: A RETROSPECTIVE STUDY IN 1210 PARTICIPANTS

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Background: Allogeneic pancreatic islet transplantation (IT) is a validated therapy for diabetes associated with severe hypoglycemia, and/or after kidney transplantation. This beta-cell replacement strategy currently consists of one or more intraportal infusions of allogeneic pancreatic islets, aiming to restore regulated endogenous insulin secretion and improve blood glucose control. The mechanisms underlying the decline of islet graft function with time are unclear. We evaluated the distinct relation between primary graft function (PGF) measured 28 days after last islet infusion and 5-year IT outcomes in the Collaborative Islet Transplant Registry (CITR), a comprehensive global registry that compiles all data from most islet transplant programs in North America, Eurasia and Australia.
Methods: This retrospective multicenter cohort study enrolled all participants from the CITR, who received IT alone (ITA), or after kidney transplantation (IAK), between 1999 and 2020 with a calculable PGF (exposure of interest), measured 28 days after last islet infusion with a validated composite index of islet graft function (Beta2-score). Primary outcome was 5-year cumulative incidence of unsuccessful IT explored with a competing risk analysis adjusted for all covariates suspected or known to impact outcomes. A predictive model based on PGF was built and internally validated by using bootstraps resampling method.
Results: In 39 centers, 1210 patients, 712 (59.5%) females, mean age 47±11 years received a median of 10.8 thousand islet-equivalents per kg of body-weight (IQR 7.4-13.5). Among them, 211 (17.6%) were islet after kidney recipient and 758 (62.6%) received multiple islet infusions. Mean PGF was 14.3± 8.8. The 5-year incidence of unsuccessful IT was 70.7% (95%CI 67.2-73.9), and was inversely and linearly related to PGF with adjusted subhazard ratio (sHR) of 0.77 (95% CI 0.72-0.82) per 5 units increase of Beta2-score (p<0.0001). Our model based on PGF predicted IT outcome with a good accuracy (median C-statistic 0.70 (range 0.69-0.71)).
Conclusion: We present the largest multicenter cohort study on islet transplantation and demonstrated a linear relation between PGF and 5-year clinical outcomes of IT, independently from known or suspected prespecified covariates.

BOS15_3 SIMULTANEOUS ISLET KIDNEY TRANSPLANT – OUTCOMES FROM 2 UK TRANSPLANT CENTRES

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Background: Simultaneous Islet Kidney (SIK) transplant is a treatment option for type 1 diabetic patients with an eGFR<20. It is primarily aimed at patients that are deemed unfit for a simultaneous kidney pancreas transplant. Here we report the results of SIK transplants performed in 2 UK centres (Edinburgh and Manchester) between 2018 and 2022.
Methods: Transplant outcomes from 31 consecutive SIK transplants were analysed retrospectively including patient and graft survival, stimulated c-peptide, HbA1c and insulin dose. Renal transplants were performed on Day 0 and islet transplants from the same donor were performed via a transhepatic portal infusion 24-48 hours later. Selected recipients received a 2nd islet transplant from a different donor. All values are expressed as means +/- SD and groups compared with a 2-tailed student t-test.
Results: 15 male and 16 female patients received SIK transplants. All recipients were c-peptide negative pre-transplant. The mean age of recipients was 50.6 years and mean follow-up was 2.7 years. 12 patients received a second 'priority' islet cell transplant (between 1 and 13 months after 1st transplant). Mean islet cell counts and viability for the first transplant were 314,000 +/- 120,00 and 85% +/- 5%, and for the second transplant 337,000 +/- 111,000 and 84% +/- 7% respectively. Total islet IEQ/kg was significantly higher in patients who received a 2nd islet transplant (9,717 IEQ/kg versus 4,089 IEQ/kg, p<0.00001). 1- and 3-year patient survival was 93% and 89% and 1- and 3-year kidney graft survival (censored for death) was 96% and 94% respectively. Primary islet graft function was 93.5% and 1- and 3-year islet graft survival was 88% and 63.5% respectively. HbA1c was significantly lower post-transplant (52 +/-16 vs. 65 +/-15 mmol/mol, p<0.01) and insulin requirements were reduced (25 +/-17 vs. 37 +/-24 units/24hrs, p<0.05). Only one patient was insulin independent post-transplant. Stimulated c-peptide was significantly higher in those that received 2 transplants (811 +/- 480 vs. 164 +/-136 pmol/L, p<0.001).
Conclusions: SIK transplant results in excellent renal transplant outcomes and improves glycaemic control. A second islet transplant significantly improves beta-cell outcomes. Further work is needed to assess the longterm benefits of a SIK transplant versus kidney alone.

BOS15_4 EXPLORING PRESERVATION MODALITIES IN A SPLIT HUMAN PANCREAS MODEL TO INVESTIGATE THE EFFECT ON THE ISLET ISOLATION OUTCOMES

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Background: In islet transplantation, the use of dynamic hypothermic preservation methods is a current challenge, aiming to include in the the donor pool extended criteria pancreas without altering islet isolation results.
We here report a paired comparison of three pancreas preservation methods-cold storage (CS), hypothermic machine perfusion (HMP), and oxygenated machine perfusion (HMP O2)- using a split human pancreas model to assess the impact of the preservation method on islet function and isolation performance.
Methods: We used a human pancreas split model from discarded donors in which the pancreas head was preserved through the conventional CS method ("control group") and the pancreas tail was preserved through three different preservation methods: CS, HMP, and HMP O2 ("study group"). After a same ischemia time in both head and tail of each organ, a separate islet isolation was performed in parallel. Donor characteristics, isolation data and functional tests results of isolated islets at one- and seven-day cultures of both segments were collected.

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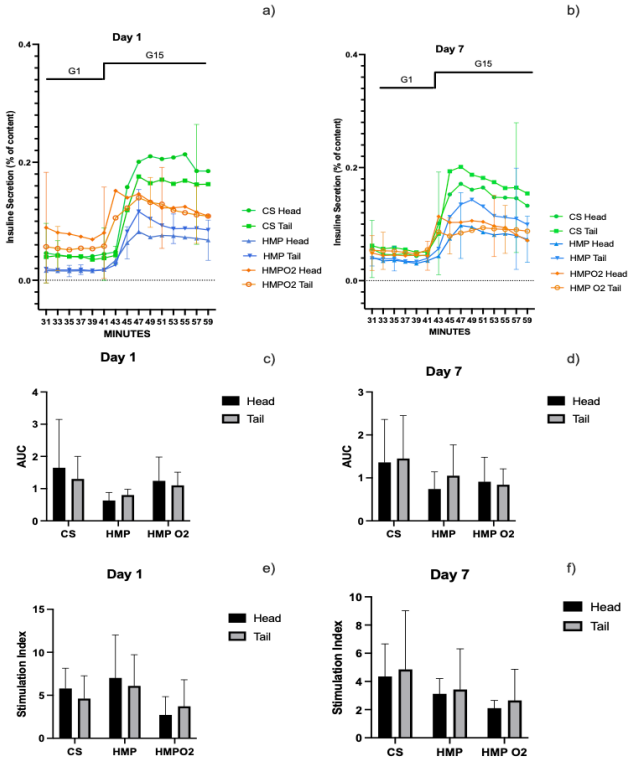
Results: Eight human pancreases were used in each group. Donor demographics, ischemia times and isolation data were similar in all groups (Table 1). Compared to controls, IEQ/gr obtained was higher in both CS and HMP study groups (1219.77±844.3 IEQ vs 230±193 IEQ, p=0.006 and 1476.25±992.2 IEQ vs 251.33±195.8 IEQ, p=0.004 respectively). In contrast, the difference was not significant in the HMP O2 study group vs control (p=0.19) (Table 1, Figure 1). No other significant paired isolation data differences were found. In each paired group (study vs control) and between the three study groups, functional testings of isolated islets were similar, including area under curve of insulin secretion and stimulation index (Table 1, Figure 1).

Conclusions: Our results suggest that all preservation methods show similar efficacy in terms of islet secretory function. Despite similar results in CS group and HMP group, the addition of a full oxygenation during the time of hypothermic machine preservation seems to negatively impact the performance on the islet isolation procedure.

Figure 1



Functional testing of isolated islets after pancreas preservation by three different methods: cold storadge (CS, green), hypothermic machine perfusion (HMP, blue) and oxygenated machine perfusion (HMP O2, orange).
Each study group (Tail, gray) had its own control group (Head, black),preserved by a conventional method (CS), following a split organ model in which the two pancreas segments had the same ischemia times and the same isolation method performed in parallel. At day 1 and day 7 cultured islets from every isolation were perifused with a low concenration glucose solution (1nm Glucose, G1), followed by a high concentration glucose solution (15 nm glucose,G15).(a,b).Both area under curve of insulin secretion (AUC) and stimulation index of each paired group were not statistically significant. (c,d,e,f).

Table 1
Donor characteristics and isolation data of CS group, HMP group and HMP O^2 group.

	CS n=8	HMP n=8	HMP O^2 n=8	p
Donor Demographics				
Age, (years)	56,12±14,6	61,8±14,49	53,05±15,6	0,5
Gender, n				
Male	4	5	7	
Female	4	3	1	
Weight (mean Kg±SD)	79±15,6	74±9,78	78,2±12,68	0,71
Height (mean cm±SD)	171±8,6	174,3±7,77	175,4±6,7	0,5
BMI (mean±SD)	26,8±4,3	24,3±3,5	25,2±3,7	0,44
Donor Organ Source, n				
DCD	5	5	5	
DBD	3	3	3	
Cause of Death, n				
CVA	4	7	6	
Trauma	4	1	2	
Cardiac Arrest, n	2	2	1	
Medical History				
HBP, n	3	1	2	
Diabetes mellitus, n	0	0	0	
Smoking, n	3	3	2	
Drug Abuse, n	0	1	1	
Alchol Abuse, n	1	2	2	
Infections, n	2	1	4	
Malignancy, n	0	0	0	
Vasopressor use, n	3	7	5	
Laboratory Results				
Lipase, (mean U/l)	40±36,4	21,27±46,99	57,33±67,31	0,38
Amylase, (mean U/l)	10,02±23,3	49,25±27,38	23,02±42,02	0,06
Hemoglobine, (mean g/dl)	10,45±2,23	10,27±2,57	12,08±2,9	0,28
Ischemia time				
Cold Ischemia time, h,min (±SD)	18,12±9,52	19,26±6,08	19,32±6,05	0,87
Warm Ischemia time, min (±SD)	0,26±0,007	0,26±0,05	0,22±0,2	0,74
Total Ischemia time, h,min (±SD)	18,14±5,49	19,37±7,28	19,52±6,24	0,89
Time of Machine Perfusion	/	14,23±7,37	15,26±5,8	0,76
Isolation data's				
		Head		
Islet yeald (mean IEQ,±SD)	11077±8332,38	23960±25536	25220±25600	0,15
Islet purity(mean %,±SD)	53,3±5,7	46,6±18,6	66,6±15,7	0,11
IEQ/gr (mean IEQ/gr,±SD)	230±193	251,33±195,81	488,96±537,3	0,27
Weight (mean g±SD)	49,5±12,5	61,25±18,74	65,3±15,7	0,14
100/150 size (mean %)	31±9,5	24,2±15,93	32±28,1	0,67
150/200 size (mean %)	27±6,9	20,4±11,62	15,2±5,71	0,43
200/250 size (mean %)	23±8,7	21,18±7,27	20,6±10,51	0,85
250/300 size (mean %)	10,17±5,4	10,9±10,02	12±12,4	0,93
300/350 size (mean %)	7±3	9,5±9,53	7,66±9,33	0,8
350/ size (mean %)	4,2±1,6	13,94±11,17	12,54±8,31	0,053
		Tail		
Islet yeald (mean IEQ,±SD)	45910±32742,9	50235±62443	63181,25±85259,3	0,85
Islet purity (mean %,±SD)	58,7±11,81	62,8±20,7	63,3±14,71	0,82
IEQ/gr (mean IEQ/gr,±SD)	1219,77±844,3	1476,25±992,25	1313,37±1610	0,91
Weight (mean g±SD)	40,3±11,35	50,3±14,58	49,2±14,61	0,25
100/150 size (mean %)	26,93±8,6	17,38±10,17	36,77±53,19	0,48
150/200 size (mean %)	27,45±6,3	21,65±7,52	23,5±11	0,39
200/250 size (mean %)	21,32±7,2	25±4,7	17,8±8,28	0,11
250/300 size (mean %)	12,39±4,9	14±6,83	13,6±9,5	0,9
300/350 size (mean %)	6,84±3,2	11,45±5,88	7,17±2,13	0,06
350/ size (mean %)	5,05±3,2	10,58±7,84	7,36±4,75	0,16

	Head	Tail	p	Head	Tail	p	Head	Tail	p
Islet yeald (mean IEQ,±SD)	11077±8332	45910±32742,9	0,01	23960±25536	50235±62443	0,29	25220±25600	63181,25±85259,3	0,25
Islet purity(mean %,±SD)	53,3±5,7	58,7±11,81	0,26	46,6±18,6	62,8±20,7	0,12	66,6±15,7	63,3±14,71	0,67
IEQ/gr (mean IEQ/gr,±SD)	230±193	1219,77±844,3	0,006	251,33±195,81	1476,25±992,2	0,004	488,96±537,3	1313,37±1610	0,19
Weight (mean g±SD)	49,5±12	40,3±11,35	0,14	61,25±18,74	50,375±14,58	0,21	65,3±15,7	49,25±14,61	0,052
100/150 size (mean %)	31±9,5	26,93±8,6	0,39	24,2±15,93	17,38±10,17	0,31	32±28,1	36,77±53,19	0,83
150/200 size (mean %)	27±6,9	27,45±6,3	0,89	20,4±11,62	21,65±7,52	0,81	15,2±5,71	23,5±11	0,08
200/250 size (mean %)	23±8,7	21,32±7,2	0,67	21,18±7,27	25±4,7	0,22	20,6±10,51	17,8±8,28	0,56
250/300 size (mean %)	10,17±5,4	12,39±4,9	0,38	10,9±10,02	14±6,83	0,48	12±12,4	13,6±9,5	0,77
300/350 size (mean %)	7±3	6,84±3,2	0,89	9,5±9,53	11,45±5,88	0,63	7,66±9,33	7,17±2,13	0,88
350/ size (mean %)	4,2±1,6	5,05±3,2	0,51	13,94±11,17	10,58±7,84	0,48	12,54±8,31	7,36±4,75	0,14

Following a split model each organ was divided in head, as control group preserved through a conventional method (CS), and tail as study group preserved through the 3 preservation methods (CS, HMP, HMP O^2).
No significant difference was found in terms of donor démographics, ischemia times and isolation data between the three groups for both head and tail.
In both CS and HMP groups, a significant difference in IEQ/gr tail/head differential was identified p=0.006 and p=0.004 respectively, but not in HMP O^2 group (p=0.19).No other statistically significant differences were found in both paired isolation data.

BMI, body mass index; CS, cold storadge; CVA, Cerebrovascular Accident; DBD, donation after brain death; DCD, donation after circulatory death; HBP, high blood pressure; HMP,hypthermic machine perfusion; HMP O^2, Oxygenated machine perfusion; IEQ, islet equivalent; SD, standard deviation

BRIEF ORALS

Progress and challenges in Pancreas and Islet transplantation

BOS15_5 RE-ANIMATING PANCREATIC GRAFTS SUBJECTED TO PROLONGED COLD ISCHEMIA IN A PORCINE MODEL USING NORMOTHERMIC EX VIVO PERFUSION: A FEASIBILITY STUDY

Samrat Ray*[1], Catherine Parmentier[1], Masataka Kawamura[1], Emmanuel Nogueira[1], Christian Hobeika[1], Tunpang Chu[1], Sujani Ganesh[1], Sangeetha Kalimuthu[2], Markus Selzner[1], Trevor Reichman[1]

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Background: Despite promising results in Diabetes mellitus, pancreas transplantation is limited by lower graft acceptability and sparse applicability of "extended criteria grafts". Transportation of grafts might require prolonged periods of cold storage, having detrimental effects on islet function, limiting usage of such grafts. Accordingly, we aimed to establish feasibility of transplantation in porcine models using pancreato-duodenal grafts subjected to prolonged cold ischemia *(>21 hrs*) and optimise same using normothermic ex vivo perfusion (NEVP).
Methods: Study population consisted of an allo-transplantation porcine model with 3-day survival plan for recipient. Control group consisted of grafts subjected to cold storage (CS) for 24 hrs (n=2) and 21 hrs (n=4) and test group comprised of grafts subjected to further 3 hrs of NEVP (n=5). Outcome variables of interest and comparison were survival, tissue injury markers, endocrine graft function and histology.
Results: Table 1 shows comparison of graft characteristics between 2 groups. Figure 1 (a&b) shows comparison of survival and IV glucose tolerance test between the groups. Mean C-peptide (±2 SD; pmol/l) (Post-op day 1) was 82.7±84.4 for test vs 60.5±25.2 for control (p=0.78)
Conclusions: Bowel necrosis was identified as the cause of graft failure in all cases of prolonged cold storage precluding its feasibility. However, optimising the grafts with NEVP after a period of prolonged cold ischemia seemed promising in re-animating these grafts for transplantation by reviving vascularity and improving endocrine function.

Table 1: Graft characteristics

	Test (n=5)	Control (n=4)
Survival	60% (n=3)	0%
Gross		
Graft reperfusion	Patchy subcapsular hemorrhages	Minimal subcapsular hemorrhages
Bowel reperfusion	Uniform	Patchy
Necropsy (Corpus)	Preserved on cut section; oedema present (50-60% viability)	Patchy areas of devitalised tissue (<30% viability)
Necropsy (Bowel)	Well preserved	Transmural necrosis
Microscopy		
Necropsy-Day 3 (Corpus)	Moderate necrosis; islets preserved; acini preserved >50%	Moderate-severe necrosis; acini preserved <50%; islets preserved
Necropsy-Day 3 (Duodenum)	Mild ischemic damage; crypts preserved	Gross transmural ischemic necrosis; crypts distorted

Figure 1 (a&b): Survival (1a) and Endocrine graft outcome (1b)

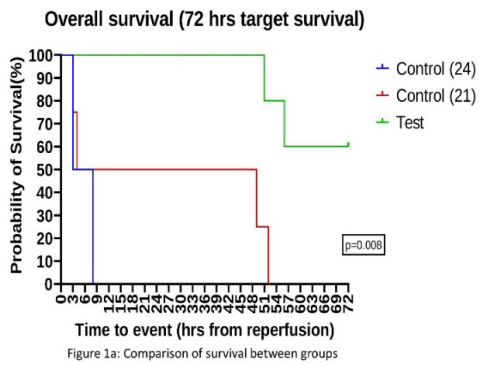

Figure 1a: Comparison of survival between groups

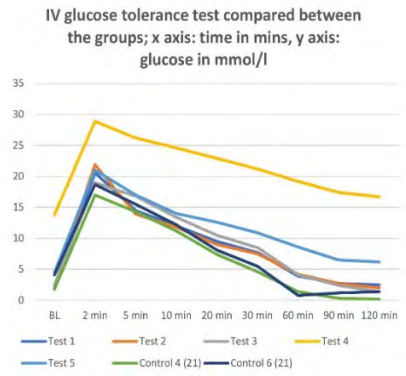

Figure 1b: IV Glucose tolerance test (Day 3)

BOS15_6 SINGLE-CENTER INITIAL EXPERIENCE OF DUODENO-DUODENOSTOMY FOR EXOCRINE DRAINAGE IN PANCREAS TRANSPLANTATION

Alba Torroella[1], Carlos Perez Serrano[2], Rocío García[1], Miguel Ángel López-Boado[1], Emma Folch Puy[3], Frederic Cofan[4], Ramón Rull[1], Pedro Ventura-Aguiar[4], Antonio J Amor[5], Enric Esmatjes[5], Fritz Diekmann[4], Mª Angeles Garcia-Criado[2], Juan Carlos García Valdecasas[1;6;7], Josep Fuster[1;6;7], Joana Ferrer-Fàbrega*[1;6;7]

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Background: Retroperitoneal disposition of the pancreatic graft offers a more physiologic drainage, similar to the native pancreas. We present our experience with duodenoduodenostomy (DD) for exocrine drainage, analyzing intestinal complications and their impact on patient and graft survival.
Methods: All pancreatic transplants performed between May 2016 and April 2022 were included. Results were compared with previously published data from our series of duodenojejunostomy (DY).
Results: A total of 105 transplants were performed using DD. Mean age was 43 years [36 - 38.5]. A 6% of donors were controlled asystole, and 94% brain death donors. Morbidity was 43.8% in the DD group. Regarding intestinal complications no statistical significance were found between groups (DD: 10 (9.5%) vs DJ: 23 (6.8%) (p=0.395)). The following were identified: intestinal occlusion (n=3); paralytic ileus (n=2); post-transplantectomy duodenal dehiscence (n=1); DD dehiscence (n=2). Seven cases required surgical treatment: adhesiolysis (n=3); transplantectomy (n=1); primary closure of the dehiscence (n=2); reconfection of the enteric anastomosis (n=1). According to the Clavien-Dindo classification, complications were: 3.8% Grade I, 16.2% Grade II, 3.8% Grade IIIa, and 20% Grade IIIB. The average stay was 13 days. After a median follow-up of 30.7 months [IQR 18.1-44], pancreatic graft survival was 85.8% at 1 and 5 years, and patient survival 100% at 1 year, and 97.7% at 1 year. fifth year.
Conclusions: Duodenoduodenostomy for enteric drainage in pancreas transplantation is an effective surgical alternative, offering more physiologic exocrine drainage, with similar complication rate and similar patient and graft survival, compared to duodenojejunostomy.

BRIEF ORALS

Progress and challenges in Pancreas and Islet transplantation

BOS15_7 HEALTH RELATED QUALITY OF LIFE AFTER SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION: HOW GOOD DOES IT GET?

Irene Mosca*[1], Shruti Sweeney[1], Richard Dumbill[1], Faysal El-Gilani[1], Rumyana Smilevska[2], Flavia Neri[2], Venkatesha Udupa[1], Isabel Quiroga-Giraldez[2], Shrikant Reddy[2], Sanjay Sinha[2], Rutger Ploeg[1], Edward Sharples[2], Coral Milburn-Curtis[3], Simon Knight[1], Alastair Gray[4], Peter Friend[1]

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Background: Better quality of life is considered a major benefit of pancreas transplantation (PT). The existing literature seems to support this notion, however the evidence available is at times contradictory and population sizes are often too small to accrue statistically significant data. The aims of this research were to assess the trajectory of Health-Related Quality of Life (HRQOL) before and up to one year after PT and identify potential predictors.
Methods: This was a single centre prospective longitudinal cohort study on adult patients undergoing PT for type 1 diabetes, recruited from October 2018 to March 2020. Participants completed validated Patient Reported Outcome Measures (PROMs): before transplant, at six weeks, six months and one year after surgery. The study portfolio included generic health status and disease specific instruments, to investigate diabetes and renal related HRQOL. Clinical data was collected prospectively at the same timepoints.
Results: 80 potential participants were recruited, of which 62 received the intervention and 57 reached the end of the study. Nearly 90% were Simultaneous Pancreas/Kidney (SPK) recipients with a median of 3 (1 to 7) chronic complications of diabetes. While interim timepoints were greatly affected by the pandemic, return rates at one year were adequate (77%).
Physical, diabetes and renal-related HRQOL at one year were statistically better than baseline, with a large effect size. This resulted in a statistically significant increment of health indexes. Mental health scores did not improve significantly; despite which these alone reached population norms. Biological male gender, older age, preserved ability to work, sexual function, urinary output at transplantation and a lower number of chronic complications were predictors of higher post-operative HRQOL. Gastrointestinal symptoms, history of psychiatric disorders, severe ophthalmic complications, low Body Mass Index, hypoglycaemia unawareness, HLA sensitisation and longer waiting list time were associated with poorer scores.
Conclusions: PT results in a remarkable improvement of HRQOL, but it does not restore patients to population normative levels. The presence of established chronic complications of diabetes seems to be a key determinant of post-transplant HRQOL.

BOS15_8 HYPERTENSION IN THE DONOR IS ASSOCIATED WITH AN INCREASED RISK OF EARLY PANCREAS ALLOGRAFT FAILURE

Christophe Masset*[1], Julien Branchereau[1], Georges Karam[1], Florent Leborgne[2], Karine Autain-Renaudin[1], Lionel Badet[3], Fanny Buron[3], Xavier Matillon[3], Christophe Legendre[4], Denis Glotz[5], Corinne Antoine[5], Magali Giral[1], Jacques Dantal[1], Diego Cantarovich[1]

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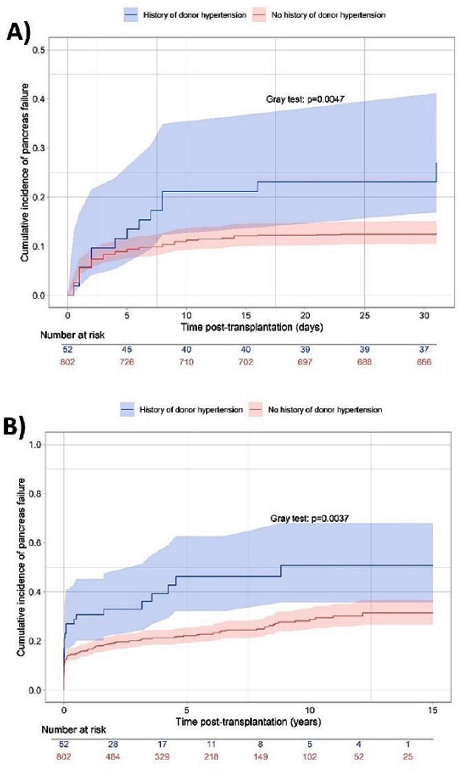
Background: About 10-20% of pancreas allografts are still lost in the very early postoperative period despite the identification of numerous risk factors that correlate with graft thrombosis.
Methods: We conducted a multicenter study including 899 pancreas transplant recipients between 2000 and 2018. Early pancreas failure occurring before the 30th postoperative day, long-term pancreas survival, kidney survival and patient survival were analyzed and adjusted to several donor, recipient and perioperative transplantation variables using a multivariate cause-specific Cox model also stratified to transplant centers.
Results: Pancreas from donors with hypertension, as well as with high body mass index, were independently associated with an increased risk of early pancreas failure (respectively, HR= 2.57, 95% CI from 1.35 to 4.89 and HR= 1.11, 95% CI from 1.04 to 1.19). Donor hypertension also impacted long-term pancreas survival (HR= 1.88, 95% CI from 1.13 to 3.12). However, when pancreas survival was calculated after the postoperative day 30, donor hypertension was no longer a significant risk factor (HR= 1.22, 95% CI from 0.47 to 3.15). As hypertension may correlate to BMI, we assessed the interaction between hypertension and BMI in the donor, which was negative. This confirms that donor hypertension was an independent risk factor for early allograft failure in our cohort analysis.
Conclusion: Donor hypertension was a significant independent risk factor of early pancreas failure. Unknown mechanisms linked to hypertension are possibly involved and will need further studies to allow effective preventive interventions.

Figure. A. Cumulative incidence of pancreas failure within the first 30 days after transplantation according to history of donor hypertension (Aalen-Johansen estimator). B. Cumulative incidence of pancreas failure in the long-term according to history of donor hypertension (Aalen-Johansen estimator).



BOS15_9 NORMOTHERMIC EX VIVO MACHINE PERFUSION OF THE PANCREAS IS SAFE AND FEASIBLE IN A PORCINE MODEL OF PANCREAS TRANSPLANTATION

Catherine Parmentier*[1], Samrat Ray[1], Laura Mazilescu[2], Masataka Kawamura[1], Emmanuel Nogueira[1], Christian Hobeika[1], Tunpang Chu[1], Sujani Ganesh[1], Markus Selzner[1], Trevor Reichman[1]

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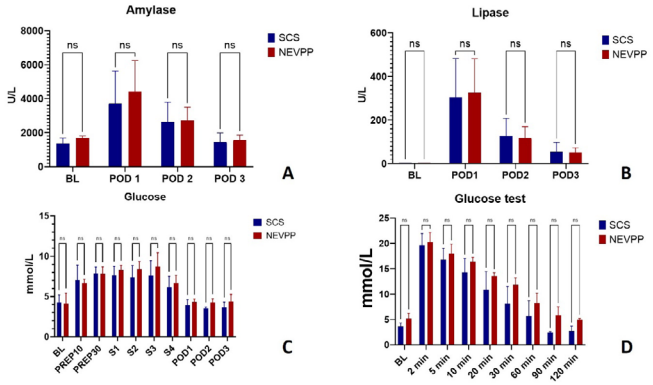
Background: Normothermic machine perfusion (NEVP) has already proved to be superior than static cold storage (SCS) for the preservation of organs like lungs, liver, kidney, and heart but studies with the pancreas are limited. Our group has already established the safety and feasibility of normothermic machine perfusion for porcine and human pancreases and successfully established a perfusion and transplantation model in swines. The purpose of this study was to prove the safety and feasibility of NEVP vs SCS.
Methods: Male Yorkshire pigs (30 to 40 kg) were used both as donors and recipients in a model of heart beating donation with limited warm ischemia.
The control group (SCS) consisted of 4 donors and 4 recipients, pancreas was procured using our previously established technique, kept in SCS for 5 hours and then transplanted. The study group (NEVP) consisted of 3 donors and 3 recipients, pancreas was procured and kept for 2 hours in SCS. Then subsequently placed on the normothermic machine for a 3-hour perfusion and transplanted into the recipient pig. Recipients in both groups were followed until POD3. Prior to sacrifice a glucose challenge test was performed.
Results:

Table 1. Baseline characteristics of donors and recipients.

	SCS	NEVP	P
Donor Weight (Kg)	41.6 ± 2.4	39.7 ± 1.9	0.31
Recipient Weight (Kg)	42.5 ± 1.8	39.7 ± 2.1	0.12
Donor BL amylase (U/L)	1262 ± 201	1734 ± 613	0.19
Recipient BL amylase (U/L)	1285 ± 278	1697 ± 115	0.06
Donor BL lipase (U/L)	4.5 ± 1	4	0.43
Recipient BL lipase (U/L)	4	4	1
Donor BL LDH (U/L)	733 ± 195	603 ± 12	0.31
Recipient BL LDH (U/L)	728 ± 186	771 ± 218	0.77

Figure 1. A. Amylase. B. Lipase. C. Glucose. D. Glucose test. (BL- baseline; POD – postoperative day; PREP10, 30 – Postreperfusion 10, 30 minutes; S1,2,3,4 – postreperfusion 1, 2, 3 and 4 hours).



Discussion: Our study demonstrates that NEVP of the pancreas is feasible and can be performed safely. No injury was observed by NEVP and the results of the perfused group were comparable to SCS. Both groups presented homogenous baseline characteristics and the parameters measured during and after surgery showed no significant differences between the groups. Further studies will focus on the outcome of NEVP in the setting of reduced cold storage time in marginal grafts.

BOS15_11 DIFFERENCES IN GLUCOSE HOMEOSTASIS BETWEEN TYPE 1 VS. TYPE 2 DIABETES AFTER PANCREAS TRANSPLANTATION

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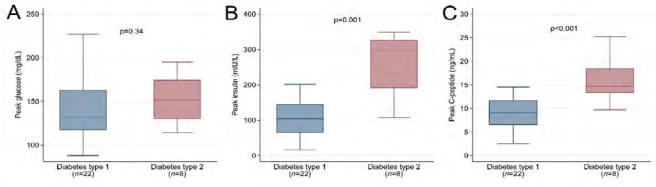
Background: Pancreas transplantation outcomes are equivalent between type 1 and selected type 2 recipients with IDDM. We sought to determine differences in glucose homeostasis between groups by comparing results of glucose tolerance tests in the early post-transplant period.
Methods: A retrospective single center review of IDDM recipients of kidney/pancreas transplants between 2016 and 2022. Type 2 recipients were non-obese with a small insulin requirement. A subset of recipients underwent a modified glucose tolerance test (OGTT) early post-transplantation. Diabetes type was determined using a composite scoring system as previously published [1]. Variables included age at diagnosis of DM, immediate use of insulin or not, c-peptide level, presence of islet autoantibodies or not, and daily amount of insulin. OGTT results were compared between groups by calculating the mean area under the curve (AUC) and peak glucose, insulin, and c-peptide levels.
Results: Demographics of the study group (n=72) included a mean age of 44.5±10years, 65 percent male, and BMI of 25.2±0.3mg/m2. Baseline characteristics of age, gender, race, years of diabetes, dialysis history, and BMI were equivalent between groups. There were 59 recipients with type 1 and 13 recipients with type 2 diabetes. At one-year post-transplant, for type 1 versus type 2 recipients; mean fasting glucose (91±13 versus 88±13 mg/dl) and mean HgbA1c (5.4±0.6vs 5.5±0.6%,) levels were equivalent. As shown in Table 1 and Figure 1; 22 type 1 and 8 type 2 recipients underwent an OGTT between 6- and 12-months post-transplant. Whereas mean glucose AUC and peak glucose levels were equivalent between groups, both the mean insulin and c-peptide AUC and peak insulin and c-peptide levels of the type 2 recipients were significantly greater than that of the type 1 recipients.
Conclusions: The fasting glucose and HgbA1c levels were equivalent between type 1 and 2 pancreas recipients at one year, yet the OGTT results showed that type 2 recipients demonstrated insulin resistance early post-transplant, necessitating a much greater insulin response to a glucose challenge compared to type 1recipients. Thus, despite equivalent graft outcomes, glucose homeostasis is fundamentally different between these groups.

Table 1.

	Total (n=30)	Diabetes type1 (n=22)	Diabetes type 2 (n=8)	p
Total AUC glucose median (IQR)	13162.5 (12390, 16380)	13140 (12210, 16380)	14137.5 (12600, 16920)	0.54
Total AUC insulin, median (IQR)	9292.5 (6019.5, 15940.5)	6877.5 (5500.5, 9604.5)	18981.8 (14721, 20997)	<0.001
Total AUC c-peptide, median (IQR)	864 (712.5, 1206)	795.8 (639.8, 965.3)	1251 (880.5, 1695)	0.01

IQR: interquartile range

Figure 1.



BRIEF ORALS

Progress and challenges in Pancreas and Islet transplantation

BOS15_12 RISK FACTORS FOR GREATER THAN 10 YEARS PANCREAS GRAFT SURVIVAL IN THE UK; SHORT TERM RISK FACTORS ARE NOT ALWAYS THE BEST GUIDE FOR LONG TERM SURVIVAL

Argiris Asderakis[*1;2], Laszlo Szabo[1], Tarique Sabah[1], Elijah Ablorsu[1], Mohamed Ilham[1], Doruk Elker[1]

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Background: The nationally funded Pancreas transplant program in the UK started in 2003-04. Long-term survival of the pancreas is required for improvement of the secondary complications of diabetes. We hypothesise that risk factors affecting long term survival are not necessarily identical to those predicting early failure.
Methods: We included all patients, recorded in the UK transplant registry (NHS BT), who had a pancreas transplant between 2004 and 2012, so every patient had the chance to reach 10 year follow up. Factors that correlate with > 10 years survival in UK were studied and contrasted with those affecting the early 60-day failures. Binary and Cox regression was used.
Results: There were 1512 pancreas transplants, 81% being SPK, 13% from DCD donors, and 4% retransplants. 10 year graft survival was 65%. Among those grafts that failed in the first 60 days, it was more likely that the recipient had a prior MI, CVA or amputation (p=0.02), an older donor (p=0.01), a donor following a CVA (vs. trauma, p=0.01), a heavier donor (p=0.0010), a longer CIT (p=0.001), or received a pancreas alone (PAK and PTA vs. SPK, p=0.01). Among grafts with >10 year survival compared to those with less, having SPK (87% vs 78%, p=0.001), Roux en Y duodenum drainage (16% vs 11% p=0.03), younger donor age (p=0.04) and low waiting time (p=0.001) was more common, whilst fewer recipients had a prior MI, CVA or amputation (p=0.048). The donor type (DCD vs DBD, p=0.08), and the duration of diabetes, p=0.08) marginally affected the >10 year outcome whereas donor BMI (p=0.8), CIT (p=0.6), donor cause of death (CoD) (p=0.4) did not
Conclusions: In the UK, whereas most factors that affect early pancreas failure mirror those predicting long term survival, donor BMI, CIT, and donor CoD are important in early failures but do not affect the long-term outcome if the graft survives at least 60 days. The type of duodenum drainage, donor type, and the duration of diabetes mainly affect the long-term survival but not the early 60 days failures.

BOS15_13 OUTCOMES OF PANCREAS TRANSPLANTATION ALONE FROM DONATION AFTER CIRCULATORY DEATH

Rumyana Smilevska[1], Shruti Mittal[1], Irene Mosca*[1], Edward Sharples[1], Srikanth Reddy[1], Isabel Quiroga-Giraldez[1], Venkatesha Upuda[1], Sanjay Sinha[1], Rutger Ploeg[1], Peter Friend[1;2], Simon Knight[1;2]

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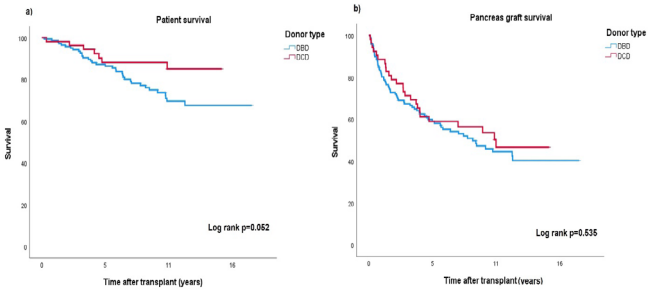
Background: Donation after circulatory death (DCD) is not frequently used for pancreas transplantation worldwide, because of a presumed higher risk of complications and lower graft survival. The aim of this study is to compare the outcomes of DCD vs donation after brain death (DBD) in pancreas transplantation alone (PTA) in a large single centre series.
Methods: A database of pancreas transplant recipients for the period from July 2004 to August 2022 was analysed. The DBD and DCD cohorts were compared for demographic and transplant variables; Kaplan-Meier for patient and graft survival was undertaken.
Results: During the study period 216 PTA were performed, 19 cases were excluded due to early graft loss in the first 30 postoperative days. 197 PTA were included in the analysis: 54 (27.4%) from DCD and 143 (72.6%) from DBD. 70.4% PTA, 24.1% PAK and 5.6% were pancreas after SPK (PASPK) in the DCD cohort, and 63.6% were PTA, 26.6% were pancreas after kidney (PAK) and 9.8% were PASPK in the DBD group. Demographic data for recipients, postoperative complications and length of hospital stay showed no statistical difference. The donor BMI was statistically lower in the DCD group (21.9 vs 23.2 kg/m^2, p=0.009). The cold ischemic time was numerically, but not significantly higher in the DCD group (706 vs 672 min, p=0.197). There was no significant difference in 5-year and 10-year patient and pancreas graft survival.
Conclusions: Outcomes for DCD PTA are comparable to DBD. Donation after circulatory death should be considered for pancreas transplantation and donor selection is paramount. DCD is a safe option to expand the donor pool in many countries.

Figure 1: Patient (a) and pancreas graft survival (b) for PTA from DBD and DCD donors.



BOS15_14 IMPACT OF NORMOTHERMIC REGIONAL PERFUSION ON OUTCOMES AFTER SPK TRANSPLANTATION – A UK ANALYSIS FROM THE NHSBT PANCREAS ADVISORY GROUP

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Background: A quarter of UK SPK transplants are from Deceased Cardiac Donors (DCD), with an increasing number recovered following in-situ normothermic regional perfusion (NRP). The aim of this study was to review the UK experience of SPK transplantation following NRP in DCD.
Methods: Data were collected on all first DCD SPKTs (n=360) performed during 2013-2021 from the UK Transplant Registry. Non-NRP DCD SPK were compared to NRP DCD SPKs. Kaplan Meier plots and cox regression analyses were performed. Multiple imputation was used to deal with missing data.
Results: 198 pancreas were offered from NRP donors with 83 being retrieved. The majority of SPK grafts were from nonNRP donors n=324 (90.0%) with n=36 (10.0%) from NRP donors. The median cold ischaemic time (CIT) from NRP donors (9.7 hours) was significantly less than nonNRP donors (10.2 hours) (p=0.013). For all other parameters, including pancreas donor risk index (PDRI), donors were well matched. Recipients who received a graft from an NRP donor were also well matched with the recipients who received a graft from a nonNRP donor. Univariable analysis showed no statistically significant difference in one-year pancreas graft (NRP 97.2%, non-NRP 89.2%, p=0.145), kidney graft (NRP 100%, nonNRP 95.9%, p=0.221) or patient survival (NRP 100%, nonNRP 98.3%, p=0.442) despite an increasing trend in favour of NRP SPK. A multivariable model which adjusted for a range of donor and recipient factors showed better pancreas graft survival in those who underwent NRP but this did not reach statistical significance (HR 0.253, 95%CI (0.059-1.088, p=0.065). A further sensitivity analysis was performed using PDRI in the multivariable model which showed similar results.
Conclusions: This is the largest reported analysis of NRP for SPK transplants to date. NRP has previously been shown to be beneficial for liver transplants. Despite some concerns that NRP may preferentially benefit the liver at the expense of other organs our study has shown no adverse effects. Larger studies are needed to evaluate whether NRP improves graft utilisation rates for SPK.

Table 1. Multivariate Graft Survival. *NRP- Normothermic Regional Perfusion BMI – Body Mass Index.*

Variable	Hazards Ratio	95% CI	p value
NRP	0.253	(0.059-1.088)	0.065
Recipient Age	**0.930**	**(0.898-0.964)**	**<0.001**
Recipient BMI	1.001	(0.925-1.082)	0.986
Recipient Sex	1.272	(0.724-2.233)	0.402
Donor Age	0.998	(0.976-1.021)	0.868
Donor BMI	**1.115**	**(1.040-1.196)**	**0.002**
Donor Sex	1.396	(0.810-2.404)	0.230
Cold Ischaemic Time (hours)	0.937	(0.810-1.083)	0.374
Functional warm ischaemia (minutes)	1.000	(0.966-1.035)	0.992

BOS16_2 REFINING AUXILIARY PARTIAL ORTHOTOPIC LIVER TRANSPLANTATION (APOLT) FOR ACUTE LIVER FAILURE IN 48 ADULT PATIENTS

Riccardo Pravisani*[1], Lorenzo Cocchi[1], Manuela Cesaretti[1], Federica Dondero[1], Ailton Sepulveda[1], Emmanuel Weiss[2], Claire Francoz[3], Olivier Roux[3], Jacques Belghiti[1], Francois Durand[3], Mickael Lesurtel[1], Safi Dokmak[1]

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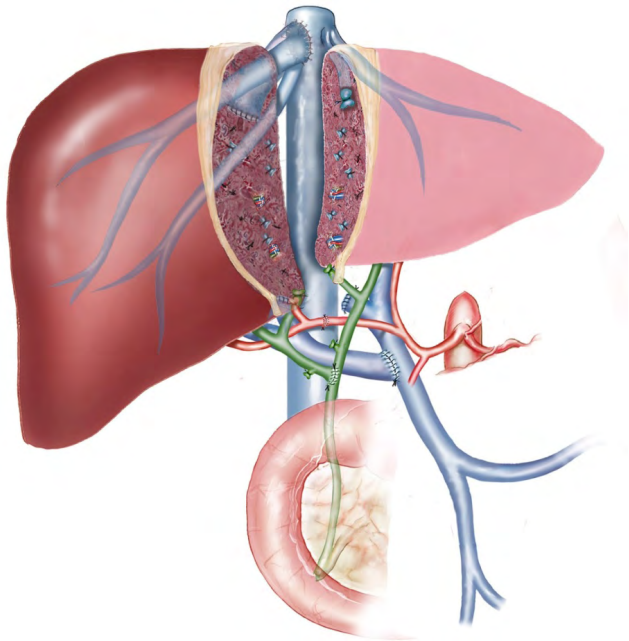
Background: Auxiliary partial orthotopic liver transplantation(APOLT) for acute liver failure(ALF) provides the unique chance of complete immunosuppression withdrawal after adequate native liver remnant regeneration. However, the surgical technique is generally seen as complex and associated with significant morbidity. The aim of this study was to present our current surgical strategy in APOLT focusing on its evolution over time, experience accumulation and assessing the impact of such refinements on clinical outcomes.
Methods: This is a retrospective study on a single center cohort of 48 patients with ALF who underwent APOLT between January 1993 and December 2019. Our surgical technique was standardized in 2012 and implies (i) a restrictive use of a high quality whole liver graft or G145678 associated with a recipient H145678 (according to the ''NewWorld'' terminology); (ii) direct anastomosis of graft hepatic artery with recipient right hepatic artery; (iii) end-to-side hepatico-choledocostomy.
Results: Overall patient survival at 1, 3 and 5 years was 81,1%, 74,6%, 71,3%, respectively. Only two patients required re-LT due to graft primary non-function. Complete immunosuppression withdrawal was achieved in 82,1% of patients and none of them required graft explant. The most recent experience after surgical standardization (2012-2019,n=22), compared with earlier experience (1993-2012,n=26), was associated with shorter operative time (median, 322min vs 540min, p<0.001), lower blood loss (median transfused blood units, 3 vs 7, p=0.001) as well as lower biliary (18.2% vs 53.8%,p=0.017) and arterial complications (0% vs 15.4%,p=0.115), and improved overall survival(p=0.045).
Conclusions: The promising results of our experience may promote APOLT implementation among LT centers.

Schematic representation of APOLT with end-to-side duct-to-duct biliary anastomosis.



BOS16_3 ROBOTIC KIDNEY TRANSPLANTATION : A SINGLE INSTITUTIONAL EXPERIENCE

Hyun-jeong Kim*[1], Seok Jeong Yang[2], Wooju Jeong[3], Joon Chae Na[1], Woong Kyu Han[1], Kyu Ha Huh[2]

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Background: Minimally invasive surgery reduces perioperative pain and morbidity, facilitating rapid recovery. However, the field of kidney transplantation has lagged in this regard, its customary open surgical techniques going nearly unchanged until recently. Robotic kidney transplantation (RKT) is a novel and welcomed innovation yielding good surgical outcomes. As the first institution to perform a RKT in Korea, our aim is to evaluate and share our surgical and functional results of RKTs performed in our center.
Methods: This is a retrospective study of all RKTs perforemd between November 2019 and December 2022 at the Severance Hospital. We analyzed the surgical, functional outcomes and complication rates.
Results: During the aforementioned peridod, 40 patients successfully underwent RKT from living donor. The mean age was 44.3±11.2 years old and male to female ratio was 26:10. Mean body mass index was 21.9±2.9 kg/m^2 and KT was performed preemptively in 55.6% of cases. Surgical console time was 212.9±41.6 min(154-327) with vascular anastomoses time 39.9 ±5.9 min(28-58), rewarming time 67.3±12.1 min(43-112), and mean estimated blood loss 122.8±82.4cc(50-400). No patient was converted to open transplantation. Subsapsular hematoma and penetrating injury of proxial ureter during ureteral stent insertion occurred in one patient , but this improved after conversvative management. No anastomosis revision and wound infections occurred. Delayed graft function was not shown in all RKT cases.The mean serum creatinine level at discharge day was 1.3±0.3mg/dL (0.7-2.1) .
Conclusions: RKT with regional hypothermia may be a safe and effective, minimally invasive alternative to open KT, yielding comparable clinical outcomes.

BOS16_4 IPSILATERAL SIMULTANEOUS NEPHRECTOMY WITH URETERO-URETERAL ANASTOMOSIS IN KIDNEY TRANSPLANTATION FOR POLYCYSTIC KIDNEY DISEASE

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Background: In kidney transplantation (KT) ureterocystoneostomy (UCN) remains the standard. Uretero-ureteral anastomosis (UUA) has been described as an alternative for patients that undergo simultaneous nephrectomy at the time of KT. In patients with polycystic kidney disease (PKD), recipient nephrectomy frequently is performed before KT. Here we propose our “reinvented” strategy of simultaneous recipient nephrectomy and ipsilateral KT with UUA.
Methods: Single center analysis of KT in adult PKD pts (n=61), divided into 2 groups: standard UCN (n=50) vs. UUA (n=11). Standard UCN was performed as end-to-side modified Gregoir anastomosis with anti-reflux sutures. UUA was performed as End-to-End-Anastomosis. Both groups had anastomotic stenting with Double-J-catheters (DJ) to avoid leaks and stenosis.
Results: From 2011 to 2022, 61 patients underwent KT for PKD. The median age was 56 years. 45.9% of patients were female and 32.8% had a living-donor KT. 11 had a KT with ipsilateral nephrectomy and UUA, 4 of these had contralateral nephrectomy pre-KT. The UCN group of 50 patients had direct ureteral anastomosis to the bladder. Of these, nephrectomy was performed pre-KT in n=7, during KT in n=5 and post-KT in n=4. Both groups were similar with regards to age (56 vs. 56 years, p = 0.280), BMI (26.9 vs. 25.3kg/m², p = 0.320) and waiting time (82 vs. 72 months, p = 0.988). In the UUA group were more males (91% vs 46%, p = 0.008) and LD-KT was more frequent (55% vs 28%, p = 0.090). Procedure time (237min vs 154min, p < 0.001) and time to removal of the DJ were longer in the UUA group (35 days vs. 19 days, p < 0.001). One patient in the UUA group developed a leak on POD 1, two patients in the UCN group had early anastomotic stenosis (9% vs. 4%, p = 0.480). Long term ureteral complications appeared to be more common after UCN (9% vs. 18%, p = 0.470) as were readmissions for urinary tract infections (18% vs. 30% p = 0.429). Graft loss was 4% in the UCN and 0% in the UUA group. None was due to vesicoureteral reflux (VUR).
Conclusions: Patients affected by PKD may benefit from simultaneous nephrectomy with UUA for many reasons. Fluid homeostasis can be preserved until KT. Preserving the native ureteral ostium may prevent VUR and prevent ascending UTI. The procedure time and morbidity of two separate procedures (Nephrectomy and KT) may be increased in the UCN group.

BOS16_5 LAPDOCTOR: TELL ME HOW DIFFICULT WILL BE MY DONOR. MULTICENTRIC VADITATION OF A NEW SCORING SYSTEM THAT ANTICIPATES DIFFICULTY OF LDN

Gionata Spagnoletti*[1], Francesco Emilio Rossini[2], Roberto Iezzi[3], Alessandro Posa[3], Maria Paola Salerno[2], Patrizia Silvestri[2], Aldo Eugenio Rossini[2], Lucrezia Furian[4], Barbara Franchin[4], Alessandro Giacomoni[5], Leonardo Centonze[5;6], Marco Spada[1], Zoe Larghi Laureiro[1], Maurizio Iaria[7], Carmelo Puliatti[7], Jacopo Romagnoli[2]

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Background: Living donor nephrectomy (LDN) is a surgical procedure performed on healthy individuals, therefore every effort should be made to increase preoperative surgeon's awareness of potential technical risks and, as a result, safety. We previously developed and validated a new scoring system for preoperative prediction of difficulty of LDN (LAP DOCTOR: **LAP**aroscopic **DO**nor nephre**CT**omy sc**OR**e). In order to increase the power of the study we further investigated this aspect in the setting of a prospective, multicentre national study.
Methods: Difficulty of LDN was graded by the operating surgeon at the end of the operation on the basis of a scale from 1 to 3 (*standard*, *moderately difficult*, *very difficult*) based on the following 8 parameters: availability of laparoscopic space, difficulties encountered in mobilizing the colon, kidney, gonadal vein, adrenal vein, renal vein, renal artery, ureter. One surgeon per center performed all operations and blindly scored them, one radiologist blindly reviewed all preoperative CT scans. The LAPDOCTOR scores were compared with the degrees of difficulty assigned by the operating surgeon to investigate the match rate.
Results: Between Jan-2020 and Dec-2022, 120 living donors from five transplant centres were enrolled in the study. Thirty-two percent (39/120) male, mean age 52 ± 11 yrs, BMI 25 ± 3.7 kg/m^2. The operations were blindly rated standard (51%), moderately difficult (47%) and very difficult (2%) by the surgeons. LAPDOCTOR showed a 95.8% match with surgeon grade (*standard* 53 vs 51 %, *moderately difficult* 44 vs 47 %, *very difficult* 2 vs 2%).
Conclusions: LAPDOCTOR allows for an accurate preoperative definition of the level of difficulty of LDN. It could be a very useful tool in the pre-operative risk assessment of living kidney donors, now with a multi-center validation.

BOS16_6 HAND ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY (HARP-DN); LESSONS LEARNED FROM 1001 CASES

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Background: Hand assisted retroperitoneoscopic donor nephrectomy (HARDN) combines the advantages of manual control with the benefits of retroperitoneal access, and offers direct and quicker approach to the vessels in the renal hilum.
Methods: We are presenting our series with 1001 cases performed in between February 2009 and December 2022. Paramedian and Pfannensteil incisions were used for hand port and two 12 mm trocars were introduced from subxiphoid (camera, stapler) and anterior axillary line (assisting hand).
Results: There was no mortality. One donor died 2 months after surgery for unknown reasons. None required switched to open procedure. None of the donors required blood transfusion. There was no major intraoperative complication except one renal artery injury during a left-sided HARP-DN. The most frequent intraoperative complication was major peritoneal opening (232 right, 769 left). There was 13 donors (1.3%) with incisional hernia (13 left, 12 Paramedian, 1 Pfannenstiel). There was no incisional hernia in patients with the right-sided HARP-DN group. 14 patients (2.47 %) had surgical site infection (9 left, 5 right) requiring wound care moreover to antibiotic treatment. There was one Clavien-Dindo Grade 3 complication, a donor required surgery for infection. There were thrombosis of transplanted kidney at 3 cases (2 right). There was no significant difference between the right and left-sided kidney recipients regarding graft and patient survival. Death censored 1st and 5th year graft survival was 98.2% and 92.4% respectively. 6 out of 10 patients with ureter stenosis required surgical treatment.
Conclusions: HARDN avoided intraabdominal complications for all cases. Right and left sided donor nephrectomy has similar outcome with HARPDN technique.

Demographics and operative data of the donors.

HARP-DN	Right-sided N=232 (23%)	Left-sided N=769 (77%)
Age	45	44
Body mass index (kg/m^2)	27.1	27.6
Dissection time (min)	92	95
Multiple arteries	46	121
Major peritoneal opening	21	36

BOS16_7 MINIMALLY INVASIVE APPROACH FOR RAPID LIVER TRANSPLANTATION: ARE WE READY FOR PRIME TIME? EXPERIENCE WITH LAPAROSCOPIC SECOND STEP APPROACH

Alessandra Bertacco*[1], Domenico Bassi[1], Riccardo Boetto[1], Jacopo Lanari[1], Francesco Enrico D'amico[1], Enrico Gringeri[1], Umberto Cillo[1;1]

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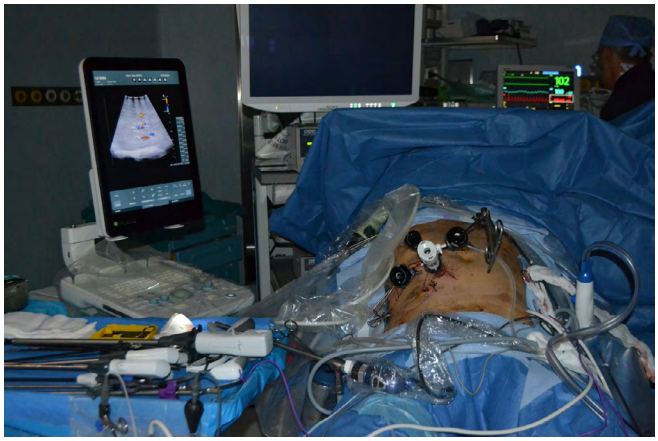
Background: RAPID is a surgical technique recently adopted for unresectable ColoRectal Liver Metastases (uCRLM). It enables little grafts for transplantation, overcoming the small-for size syndrome and expanding the donor pool. RAPID technique includes a Step-1 surgery with temporary auxiliary transplant of left lateral segment (either from split liver or from LDLT) and a Step-2 (right hepatectomy) in which the remnant native liver is removed.
Methods: We report a single-center experience of liver transplantation (LT) for uCRLM using RAPID tecnhique. On the basis of our surgical experience, we decided to apply technical refinements to the original technique to overcome some critical issues. Aim of this study is to describe and report safety and feasibility of this cutting-edge surgery with the application of a minimally invasive approach for Step-2.
Results: From december 2018 to december 2022 we completed 4 cases of RAPID-LT. Mean patients age was 47 yrs, mean BMI 24.6: all patients had previous laparoscopic/robotic colon surgery and open surgery for LT. In 3 cases biliary drainage was established by a bilioenteric anastomosis. In 3 cases for Step-2 a laparoscopic approach was preferred over the open. Mean time for step-2 from LT was 17 days (range 14-19). Mean operative time was 5h 15 min including left lobe biopsy and US doppler of liver remnant. Two 5-mm trocars and 2 10/12-mm trocars were used (**Fig.1**) Hem-o-lok and EndoGIA were used for vascular/biliary ligation and transection. Liver was extracted by a 10 cm incision at the previous right subcostal scar. One silicon drain was inserted in the subhepatic space. Mean right lobe weight was 765 gr. Not EC trasfusion was required during the surgery with minimal EBL. For patient 1, ICU stay was 3 days with long hospitalization (37 days) due to bile leak and liver hematoma; other patients had short ICU stay (<1 days) and rapid post-operative functional recovery (LOS 4 days) without complications
Conclusions: Despite the small cohort included in this report, our favorable outcomes have demonstrated that laparoscopic surgery is a promising platform for the partial conversion of an aggressive procedure as RAPID into a minimally invasive setting.

Fig.1: Patient and trocar position



BOS16_8 FULL-LEFT/FULL-RIGHT LIVER SPLITTING WITH MIDDLE HEPATIC VEIN AND CAVAL PARTITION DURING DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION

Alessandro Furlanetto*[1], Enrico Gringeri[1], Nicola Canitano[1], Domenico Bassi[1], Francesco Enrico D'amico[1], Riccardo Boetto[1], Andrea Lauterio[2], Luciano De Carlis[2], Umberto Cillo[1]

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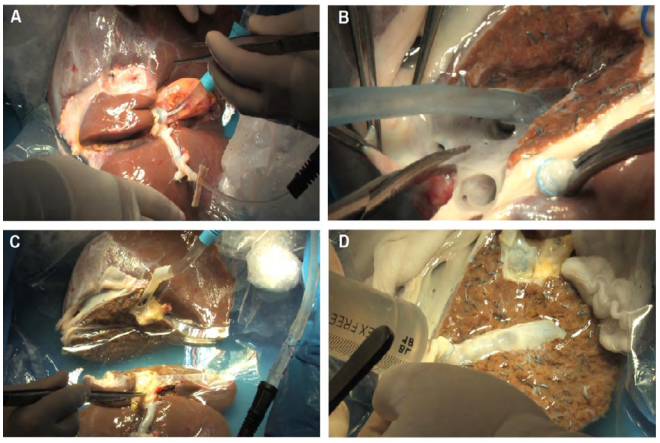
Background: Split liver transplantation is a useful mean to reduce organ shortage and waitlist mortality, but requires logistical efforts and relevant surgical expertise. We hereby describe a novel technique of full-left/full-right (FLG/FRG) liver splitting, with concomitant splitting and reconstruction of the vena cava and middle hepatic vein (MHV), with the aid of dual arterial and portal hypothermic oxygenated machine perfusion (D-HOPE, Fig A), in order to reduce cold ischemia (CIT) and ischemia-reperfusion injury.
Methods: The donor was a 22-year-old with no comorbidities. The recipient for the FLG was a 7-year-old boy affected by methylmalonic acidemia and chronic kidney disease, requiring liver – kidney transplantation. The FRG went to a 64-year-old woman with HCC on HBV-related cirrhosis. Ex-situ splitting allowed to perform a complete partition of the graft and of his outflow (Fig C), as previously described by Broering, thus allowing for optimal venous drainage of both grafts. Portal vein and hepatic artery were dissected to the bifurcation. Parenchymal transection was performed with scissors and cavitron ultrasound surgical aspirator using the MHV as a landmark. The vena cava and MHV were split in two (Fig B) and then reconstructed with donor's iliac vein patch (Fig D).
Results: The splitting procedure, during which the graft was constantly perfused both through the portal vein and celiac trunk (D-HOPE time), lasted 94 minutes, while the single-vessel perfusion time during reconstruction phases lasted 58 minutes for the FLG (artery only) and 173 minutes for the FRG (portal vein only). Flow parameters and perfusate temperature remained stable throughout all the splitting procedure, although significant changes occured when grafts were separated. Both grafts were implanted with piggy-back technique and termino-terminal portal, arterial and biliary anastomosis. The pediatric patient also received single kidney transplantation
Conclusions: This approach offers several advantages: a) the prolonging of CIT is counterbalanced by the positive effect of HOPE on graft's viability; b) reconstructions may be performed during cold storage, thus reducing warm ischemia c) it avoids extremely skilled surgeons to reach the donor's hospital, with consequent positive logistical drawbacks



BOS16_9 CLAMSHELL VERSUS BILATERAL ANTEROLATERAL THORACOTOMY FOR DOUBLE LUNG TRANSPLANTATION: IMPACT ONFUNCTIONAL AND CLINICAL OUTCOMES

Alessandro Palleschi*[1], Antonella Lo Mauro[2], Emilia Privitera[1], Giovanni Caffarena[3], Valeria Musso[3], Letizia Corinna Morlacchi[1], Valeria Rossetti[1], Rosaria Carrinola[1], Valentina Vaira[3], Davide Tosi[1], Mario Nosotti[1]

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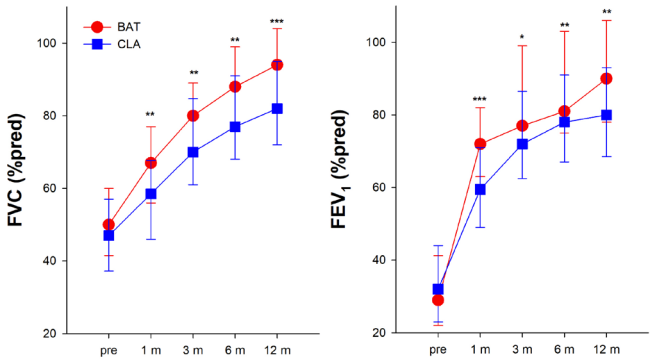
Background: The bilateral anterolateral thoracotomy with sternum sparing is considered the approach of choice for bilateral lung transplantation, mainly for the reported lower rate of sternal complications and better respiratory function in the early postoperative period compared to the clamshell incision. We report the influence of the incision on functional outcomes within one-year follow up and late clinical outcomes.
Methods: We collected data from 144 double lung transplantations between 2015 and October 2021 (85 cystic fibrosis, 46 interstitial lung diseases, 12 COPD, 1 pulmonary vascular disease). We retrospectively analysed relevant clinical variables as well as the spirometry performed before (pre), one month (1 m), 6 months (6 m) and one year (12 m) after the transplantation. Forced vital capacity (FVC) and forced expiratory volume in the 1 second (FEV1) were considered as percentage predicted.
Results: The majority of patients received clamshell incision (CLA 71.5%, n=103; BAT 28.5% n=41). Age was similar between the clamshell (median 36 years) and the bilateral anterolateral thoracotomy (median 39 years, p=0.626) groups, while the former was characterized by higher LAS (median 41.1 vs median 37.9, p=0.019). Both FVC and FEV1 were similar between the two groups before surgery, but they became systematically lower in the clamshell group in the four considered follow-ups (Figure 1). On the contrary, we found no correlation with the onset of chronic rejection.
Conclusions: The clamshell incision results in more postoperative lung restriction as compared with bilateral anterolateral thoracotomy and this effect persists throughout the first year. However, of note, this condition does not appear to have an impact on rejection incidence and survival rates.

Figure 1.



BOS16_10 A SINGLE CELL AND SPATIAL TRANSCRIPTOMICS APPROACH TO ELUCIDATING CD8 T CELLS IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION REJECTION

Michael Cassidy[1], **Ren-Wen Huang**[1], **Joy Barrett**[1], **Juliana Remark**[1], **Piul Rabbani**[1], **Bruce Gelb***[1], **Daniel Ceradini**[1], **Eduardo Rodriguez**[1], **Catherine Lu**[1]

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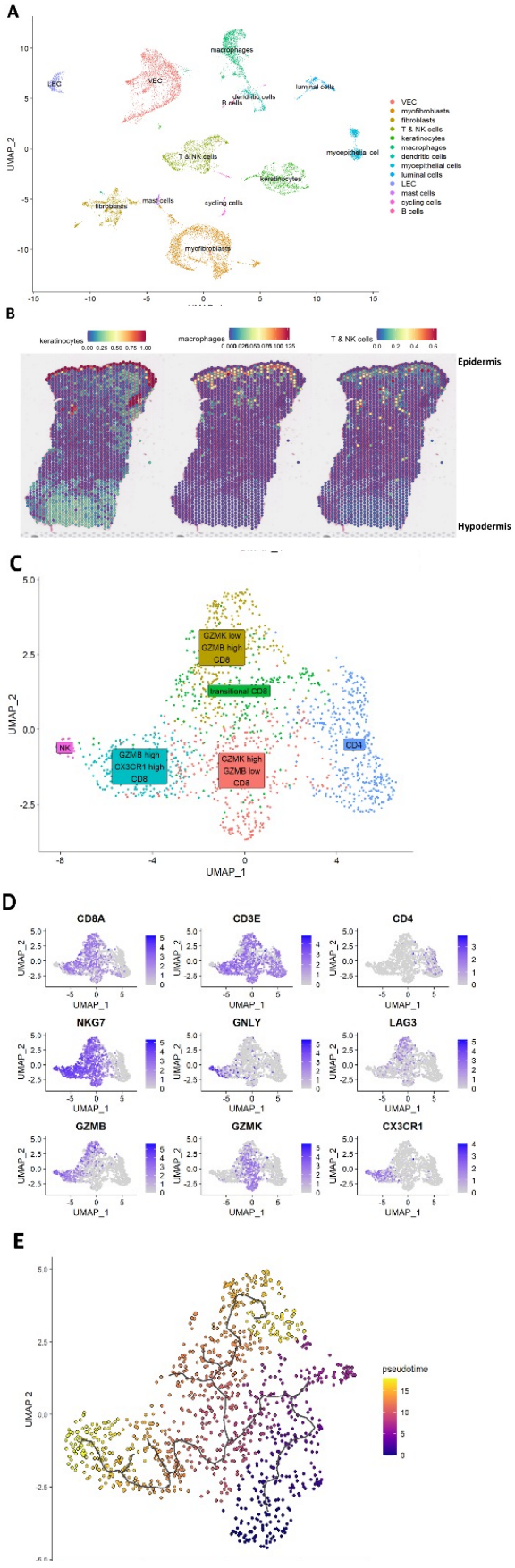
Background: Much of our understanding of acute rejection in vascularized composite allotransplantation (VCA) is drawn from principles in solid organ transplantation. However, there remains much speculation given the unique immunogenicity of skin and involvement of multiple tissue types. Current studies suggest the implication of T cells in VCA rejection, though the exact molecular mechanisms have not yet been elucidated.
Methods: Single cell RNA sequencing (scRNAseq) was performed on 10 fresh skin biopsies (5 face, 5 hand) from one VCA recipient; 2 were categorized as nonrejection (NR) and 8 as acute rejection (AR) by clinical status. Spatial transcriptomics was performed on 8 FFPE skin biopsies (7 face, 1 hand) from 3 VCA patients; 3 were NR and 5 were AR. Data collection is summarized in Table 1. Analysis and visualization was performed using the Seurat and Monocle3 packages in R.
Results: We identified 13 clusters on scRNAseq corresponding to 14 distinct cell types (Figure 1A). Spatial transcriptomics demonstrated colocalization of macrophages, T cells, and NK cells near the basement membrane during a rejection episode (Figure 1B). We then focused on the T and NK cell cluster, further subsetting these cells by relative expression of key genes in the literature (Figures 1C-D). Specifically, we identified 4 subsets of CD8 T cells: GZMK^{low}GZMB^{high}, GZMK^{high}GZMB^{low}, GZMB^{high}CX3CR1^{high}, and "transitional" CD8 T cells, named for their lack of strongly expressed markers and indistinct clustering. To better understand the dynamic states of CD8 T cells in VCA rejection, we performed trajectory analysis starting at GZMK^{high}GZMB^{low} T cells, which did not express the exhaustion marker LAG3 or cytotoxic markers. Trajectory analysis revealed a shared path through transitional CD8 T cells which then diverged into 2 distinct endpoints: GZMK^{low}GZMB^{high} and GZMB^{high}CX3CR1^{high} cells (Figure 1E).
Conclusions: Our analyses demonstrate colocalization of T cells and macrophages near the basement membrane and the involvement of dynamic CD8 T cell states in VCA rejection. Cytotoxic markers such as GZMB and CX3CR1 are seen, however the role of GZMK^{high}GZMB^{low}-expressing cells is largely unknown. Future studies aim at clarifying CD8 T cell differentiation and their interaction with other cell types during AR.

Table 1: scRNAseq and Spatial Transcriptomics Sample Collection

	Site	Patient Number	Clinical Status
scRNAseq	Face	1	NR
	Face	1	AR
	Face	1	AR
	Face	1	AR
	Face	1	AR
	Hand	1	NR
	Hand	1	AR
	Hand	1	AR
	Hand	1	AR
	Hand	1	AR
Spatial Transcriptomics	Face	1	NR
	Face	1	NR
	Face	1	NR
	Face	1	AR
	Face	1	AR
	Face	2	AR
	Face	3	AR
	Hand	1	AR



BOS16_11 HAND TRANSPLANTATION AT A TERTIARY CARE CENTRE IN INDIA

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Background: To assess the outcomes of 13 hand transplant patients who underwent transplant at Amrita institute of medical sciences, Kochi, India
Methods: This is a retrospective, cross sectional observational analysis of 13 hand transplant patients who underwent hand transplant at Amrita institute of medical sciences, Kochi, India.
Results: 13 patients underwent hand transplant from Jan 2015 to Dec 2022. 12 patients received bilateral hand transplant and one unilateral. Average age at transplant was 31years (24yrs to 52yrs). The mean follow-up of these patients were 2yrs. The cause of graft loss was due to electrical burns (n=6); crush injury (n=5) and blast(n=2). All patients were induced with ATG and maintenance immunosuppression was tacrolimus, mycophenolate mofetil and prednisolone. The average cold ischaemia time was 320 minutes for each limb and the average warm ischaemia time was 15 minutes. 8 out of the 13 patients had at least one episode of rejection (all were acute cellular rejection). The average number of rejections was 2.5 episodes. Rejection occurred within the first two months. Most rejections were successfully treated with steroids. One patient alone received IVIG and rituximab for rejection and rejection did not recur. The infectious complications noted were CMV colitis (n=1), herpes labialis (n=1), Giardiasis (n=1). One patient developed monomorphic B cell lymphoma of the gastrointestinal tract which was successfully treated with Rituximab and cure was attained. One of them had graft loss and underwent amputation of limb and one patient expired due to complications of sepsis. Rest of the limbs are functioning well.
Conclusions: Hand transplant's long term functional status remains good. With advances in immunosuppression and treatment for the complications this can be offered to a wider population

BOS16_12 DISCORDANT HISTOLOGICAL FINDINGS DURING ACUTE REJECTION IN A COMBINED FACE AND HAND TRANSPLANT RECIPIENT

Ogechukwu Onuh[1], Jorge Trilles[1], William Rifkin[1], Hilliard Brydges[1], Ricardo Rodriguez Colon[1], Daniel Baczar[1], Daniel Ceradini[1], Bruce Gelb*[1], Eduardo Rodriguez[1]

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Background: The gold standard for rejection diagnosis following vascularized composite allotransplantation (VCA) is skin biopsies and grading via Banff Classification. As rejection is considered a systemic process, it is classically proposed that clinical and pathologic findings will manifest relatively uniformly across allografts—a principle that underlies the use of sentinel flaps for rejection monitoring. We report discordant histologic findings in a face and bilateral hand transplant recipient monitored with multi-site allograft biopsies during an episode of steroid-refractory acute rejection (AR).
Methods: Skin biopsies were taken from both the patient's facial and hand allografts, at multiple time points over a 5-month period, during which there was ongoing clinical rejection. Dermatohistopathologic assessment and Banff grading were conducted at each time point, with findings evaluated in the context of the patient's clinical presentation
Results: A total of 20 biopsies were collected at eight separate time points. At four of the eight (50.0%) time points, histological assessments revealed a discordance in Banff grade between the facial and hand allografts. At three of four discordant time points, the overall Banff grade was greater in the hand relative to the face. This discordance was driven by higher inflammatory infiltrate sub-scores in the hands.
Conclusion: We found discordant histological findings during an episode of AR in a face and bilateral hand transplant recipient. These findings warrant ree-valuation of the utility of the Banff Classification system for rejection diagnosis and clinical decision-making in VCA patients and challenge the value of sentinel flaps as a means for rejection monitoring. Further, these findings revealed differing cross-sectional patterns of inflammatory infiltrates in the face and hand allografts at multiple time points, suggesting that despite the systemic nature of AR, different allograft sites do not appear to be affected uniformly by this process.

BOS16_13 DEVELOPMENT OF A SHARED DECISION MAKING CONVERSATION AID FOR VCA

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Background: The decision to proceed, or not, with VCA for face or hand transplant is highly complex. Patients and their caregivers require support in thinking, feeling, and talking their way through this decision. A focus on clinical evaluation does not support this need.Shared decision making (SDM) is a process by which patients, clinicians, and caregivers together work to reach a decision that makes sense intellectually, practically, and emotionally. Conversation SDM aids can enable SDM. Our team is developing an online conversation aid for use by hand transplant patients at home and in conversations with their clinicians.
Methods: A user-centered design process was used to develop prototype versions of the conversation aid. These prototypes were informed by IRB-approved: Interviews with: 1. 5 VCA transplant recipients regarding their decision making experience. 10 potentially eligible VCA transplant recipients regarding perceptions and expectations of VCA. 21 VCA clinicians regarding VCA practice and patient evaluation. 2. Review of the medical records of (10) patients evaluated for VCA candidacy at an American Academic Medical Center
Results: Medical (e.g., risks of immunosuppression) and nonmedical (e.g., caregiver willingness, practical barriers to undergoing transplant) issues contribute to VCA decisions. Legacy models of SDM are ill-equipped to account for these range of issue types. Purposeful SDM, a novel theoretical model for SDM, that addresses distinct decisional issue types (pros/cons, intra/interpersonal conflicts, problematic situations, and existential matters), guided prototype development.
Conclusions: A prototype online conversation aid has been developed for field testing with patients considering hand transplant (figure).

BOS16_14 MULTI-LEVEL ANALYSIS OF THE NEOVASCULARIZATION AND INTEGRATION PROCESS OF A NON-VASCULARIZED RECTUS FASCIA FOLLOWING INTESTINAL TRANSPLANTATION

Laurens J. Ceulemans*[1], Ewout Muylle[2], Antoine Dubois[2], Gert De Hertogh[2], Arne Maes[3], Greet Kerckhofs[3], Steven Pans[2], Vincent Vandecaveye[2], Marie-Paule Emonds[2], Diethard Monbaliu[2], Emilio Canovai[2], Tim Vanuytsel[2], Jacques Pirenne[2]

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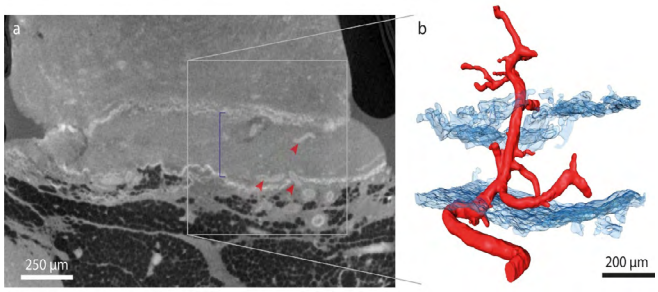
Background: Failure to close the abdominal wall after intestinal (ITx) and multivisceral transplantation (MvTx) remains a challenge, associated with increased morbidity. An attractive method is the use of non-vascularized rectus fascia (NVRF) in which both layers of the abdominal rectus fascia are used as an inlay patch without vascular anastomosis. The aim of our study is to provide a multilevel analysis (clinical, radiological, histological, contrast-enhanced microCT (CECT) and immunological) of the neovascularization and integration process based on three cases.
Methods: Three patients underwent a NVRF transplantation in combination with an ITx between 09/19-09/22. A retrospective analysis was performed. Ethical approval was obtained (S67453).

Results: The first patient was a 49-year-old female who received a NVRF during combined liver-ITx. At 1 month, doppler confirmed neovascularisation of the graft. At 6mo, at time of continuity surgery, the fascia was macroscopically integrated. H&E on biopsy confirmed integration of the graft with intense fibrotic reaction without rejection. CD31 showed neovascularisation on the interface with the native fascia. CECT analysis revealed presence of microvasculature enveloping the donor fascia as well as penetrating the graft; **Fig**. The second patient was a 51-year old male who received a NVRF after MvTx. Two weeks later, during a re-operation the fascia showed macroscopic neovascularization. Since the skin could not be closed, a VAC-system was placed on top of the fascia and secondary closure was obtained. The patient died six months post-transplant from a metastasized mesothelioma.The third patient was a 31-year old male who underwent MvTx. Eleven days post-transplant and after re-operation for intra-abdominal collections, primary closure could not be attained and a non-ABO-matched third party fascia was used. Six days later, anti-A natural and immune antibodies were increased suggesting the presence of de-novo specific antibodies against the third party. Twelve days later, the patient died of a mycotic aneurysm.
Conclusions: We showed evidence of the neovascularization and integration, by fibrotic reaction, of donor NVRF.

Figure 1a: sagittal view of CECT, red arrow indicating blood vessels in the NVRF (blue).
1b: 3-dimensial render of neovascularisation.



Paediatric Transplantation - Stronger Together

BOS17_1 LANDSCAPE OF SUBCLINICAL REJECTION IN A LARGE INTERNATIONAL COHORT OF PEDIATRIC KIDNEY TRANSPLANT (KTX) RECIPIENTS

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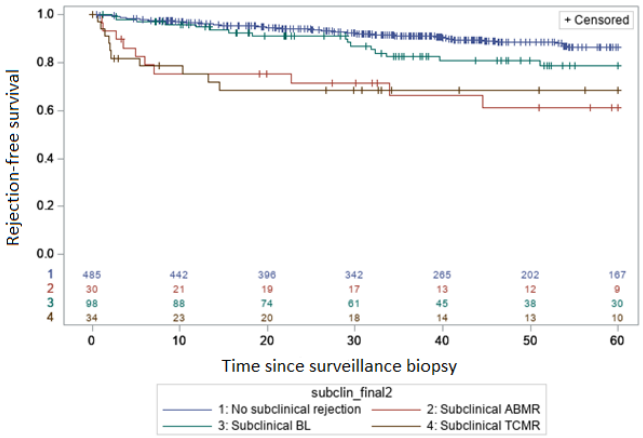
Background: Kidney allograft rejection can occur in clinically stable patients, but long-term significance in pediatric kTx recipients is unknown. Previous single-center studies demonstrated that subclinical borderline (SC-Borderline) or T-cell mediated rejection (SC-TCMR) are associated with an increased risk of acute rejection. However, the prevalence and significance of subclinical antibody-mediated rejection (SC-AMR) and the impact of subclinical rejection phenotypes on graft survival remained to be assessed.
Methods: We used data from pediatric (<21) patients transplanted between 2005 and 2017 from 8 institutions in France and the United States performing surveillance biopsies. Biopsies were identified as surveillance if they were recorded as such in the medical record with no significant increase in serum creatinine or proteinuria. Biopsies were graded according to the Banff 2019 criteria. DSA screening was performed according to each center protocol. Kaplan Meier method and log-rank test were used to compare the risk of acute rejection, transplant glomerulopathy and graft loss stratified on the surveillance biopsies' findings.

Results: 1400 surveillance biopsies were performed in 772 kTx recipients including 133 (9,7%) SC-borderline, 46 (3,3%) SC-TCMR, 54 (3,9%) SC-ABMR, 8 (0,6%) subclinical mixte rejections. Subclinical rejection was associated with acute rejection with 5-year rejection-free survival of 86%, 79%, 68% and 61% in the no rejection, SC-borderline, SC-TCMR and SC-AMR groups, respectively (p<0,0001). Treatment of SC-Borderline was associated with a lower incidence of clinical rejection. SC-TCMR and SC-AMR were associated with the development of transplant glomerulopathy, p<0,0001. Subclinical AMR only was associated with a lower 5-year graft survival (79% vs. 93% (SC-TCMR), 95% (SC-Borderline), 94% (no rejection)), p=0,002.
Conclusions: Subclinical rejection is prevalent in pediatric kidney recipients without clinical dysfunction and is associated with acute rejection. Subclinical AMR is associated with the development of transplant glomerulopathy and with an increased risk of allograft failure.

Figure 1: Rejection-free survival following surveillance biopsies stratified by surveillance biopsies' results.



BOS17_2 DETERMINATION OF SHORT AND LONG TERM RESULTS OF LIVER TRANSPLANTED PATIENTS WITH THE DIAGNOSIS OF INBORN ERRORS OF METABOLISM

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Background: Inborn errors of metabolism (IEM) are a group of inherited diseases that cause morbidity and mortality in childhood. Liver transplantation (LT) is curative treatment in some of them.
Methods: Between 2001-2021, 301 children underwent LT. 40 (13.2%) of them were diagnosed with IEM. Crigler-Najjar syndrome (n:0), PFIC (n:36), and Wilson's disease (n:37) patients were not included. The data were respectively recorded from the hospital charts.
Results: Forty-two LT were performed in 40 patients (2 re-transplantations). The consanguinity rate was 72.5%. Five deceased and 37 living-related donors were used. Tyrosinemia type-1 (TT1) (n=10, HCC=6), glycogen storage diseases (GSD1a) (n=7, adenoma=4), urea cycle disorders (n=6), primary hyperoxaluria (n=5, 2 renal-liver sequential), homozygous familial hypercholesterolemia (FH)(n=4) propionic acidemia (PA)(n=2), deoxyguanosine kinase deficiency (n=2), methylmalonic acidemia (MMA)(n=1), Niemann-Pick Disease type-B (n=1), alkaptonuria with unknown neonatal cholestasis (n=1), bile acid synthesis disorder (n=1) were the diagnosis. The mean age at LT was 78,7±9,7 months (range=5-218), the post-transplant follow-up time was 83,5±10,6 months (range=0-211), and mean current age for surviving patients was 178,5±19,1 months (range=20-375). Eleven (27.5%) patients [GSD (n=4), TT1 (n=4), FH (n=2), PH(n=1)] reached to adulthood. Eleven (27.5%) patients died. Survival rates at 1, 5, 10 and 15 years were 79,8%, 76,9%, 76,9%, and 64% respectively. Height and metabolic status parameters were improved after LT. HCC recurrence was seen in 2 patients with TT1. Protein restriction, frequent feeding, and specific medical therapy have not been required after LT. Four patients are attending to or graduated from university, 6 patients are attending to or graduated from high school, 11 patients are attending to or graduated from primary school, 3 patients are having special education, and 2 patients are physically disabled.
Conclusions: In IEM, early diagnosis and liver transplantation increase the survival rate, improve the growth, mental-motor development, and quality of life with normal diet.

BOS17_3 THE UK KIDNEY DONOR RISK INDEX POORLY PREDICTS LONG-TERM TRANSPLANT SURVIVAL IN PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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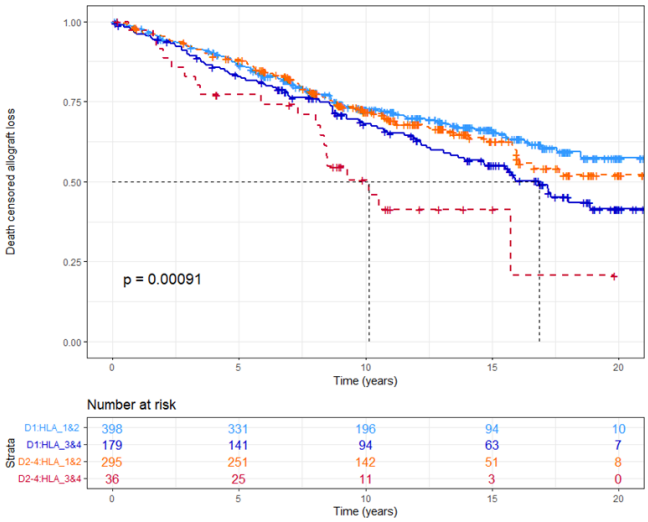
Background: The UK Kidney Offering Scheme introduced a Kidney Donor Risk Index (UK-KDRI) to improve the utility of deceased donor kidney allocations. The UK-KDRI was derived using adult donor and recipient data. We assessed the UK-KDRI in the respective paediatric cohort from the UK Transplant Registry.
Methods: We performed Cox survival analysis on first kidney-only donation after brain death (DBD) transplants in paediatric (<18 years) recipients from 2000 to 2014. Primary outcome was death-censored renal allograft failure >30 days post-transplant. The main study variable was UK-KDRI derived from seven donor risk-factors, categorised into four groups (D1-low risk, D2, D3 and D4-highest risk). Follow-up ended on 31 December 2021.
Results: 35% (319/908) patients experienced renal allograft loss with rejection as the main cause (55%). The majority of paediatric patients received donors from D1 donors (64%). There was an increase in D2-4 donors during the study period while the level of HLA mismatching improved. The KDRI was not associated with allograft failure. In multi-variate analysis, increasing recipient age [adjusted HR and 95%CI: 1.05(1.03-1.08) per-year, $p < 0.001$], recipient minority ethnic group [1.28(1.01-1.63), $p < 0.05$), dialysis before transplant [1.38(1.04-1.81), $p < 0.005$], increasing donor age [1.01 (1.00-1.01) per year, $p = 0.05$], donor height [0.99 (0.98-1.00) per centimetre, $p < 0.05$] and level of HLA mismatch [Level 3: 1.92(1.19-3.11); Level 4: 2.40(1.26-4.58) versus Level 1, $p < 0.01$] were associated with worse outcome. The level of HLA mismatch modulated the risk within UK-KDRI groups [Figure1]. Donor hypertension, smoking, CMV, terminal GFR and cause of death were not statistically significant.
Conclusions: Adult donor risk scores were not associated with long-term renal allograft survival in paediatric patients. The level of HLA mismatch had the most profound effect on survival. As prediction models become more complex and are used in organ allocation, we advocate that children and young people should also be included in the model development.

Figure1: Kaplan-Meier curve of death-censored allograft survival dependent on UK-KDRI (D1 v D2,3,4) and HLA mismatch level (L1&2 v L3&4).



BOS17_4 IMPACT OF ANTI-ENDOTHELIN-1 RECEPTOR TYPE A ANTIBODIES IN PEDIATRIC RENAL TRANSPLANTATION

Marta Vadori*[1], Elisa Cuciz[1], Susanna Negrisolo[2], Andrea Carraro[2], Benedetta Antoniello[2], Emanuele Vianello[3], Josè Igeno[3], Elvira Poggi[4], Annarita Manfreda[4], Raffaella Labbadia[5], Viviana Sioli[6], Elena Longhi[6], Tullia De Feo[6], Marco Spada[7], Marco Andreani[8], Elisa Benetti[3], Emanuele Cozzi[1]

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Background: Non-HLA antibodies (Ab) against specific allogeneic molecules have been identified as a possible cause of graft damage. The detrimental role of anti-AT1R Ab has been demonstrated both in paediatric and adult renal transplantation. However, the potentially harmful role of *anti-endothelin-1 receptor Type A (*anti-ETAR) Ab remains speculative. This project aims to evaluate the incidence and impact of anti-ETAR Ab in paediatric kidney transplantation.
Methods: In a cohort of pediatric renal transplant recipients, anti-AT1R and anti-ETAR Ab were measured pre- and post-transplant for at least 2 years. The influence of anti-AT1R and ETAR Ab on chemotaxis of immune cells was also evaluated. Histological and immunohistochemical analyses were performed on protocol biopsies at 6, 12, and 24 months post-transplantation. The relationship between non-HLA antibodies, antibody-mediated rejection and clinical outcomes has been evaluated.
Results: Currently, 169 paediatric kidney recipients have been enrolled. More than 500 sera were evaluated. In this cohort 48,4% and 49% of patients had pre-formed anti-ETAR and anti-AT1R ab, respectively. At all timepoints, 42,2 % and 39,1 % of patients were negative for anti-ETAR and anti-AT1R Ab, respectively. Anti-ETAR Ab were significantly associated with anti-AT1R Ab. *De novo* appearance of anti-ETAR or AT1R Ab was detected in 9,4% and 11,7% of patients, respectively. Preliminary in vitro data suggest a positive correlation between T cell migration and anti non-HLA antibody levels.
Conclusions: Our study demonstrates that anti-ETAR Ab are detectable in half of the paediatric renal transplant recipients. Anti-ETAR Ab are highly associated with anti-AT1R Ab. Preliminary data suggest a role of these antibodies on T cell recruitment. The studies underway are expected to determine the possible role of anti-ETAR Ab on the survival of pediatric renal allografts.

BOS17_5 SIMULTANEOUS TOTAL INTERNAL BILIARY DIVERSION IN LIVER TRANSPLANTATION FOR PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS TYPE 1: A STANDARD OF CARE?

Jagadeesh Menon*[1;1], Naresh Shanmugam[1], Fadl Veerankutty[2], Mukul Vij[3], Ashwin Rammohan[2], Rajesh Rajalingam[2], Mohamed Rela[2]

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Background: Post Liver transplant (LT) outcomes in patients with PFIC-1 is relatively poor due to progressive graft steatohepatitis and fibrosis, intractable diarrhea & growth failure. A total internal biliary diversion (TIBD) if offered simultaneously with a LT may prevent these adverse events and improve their quality of life.
Methods: Children with PFIC-1 who were offered a biliary diversion during LT or in the post-LT period were included in this retrospective analysis. Various pre-LT and intraoperative parameters were looked into (Table 1). In the post-LT period, graft function and complications especially pertaining to PFIC -1 were analysed. The catch-up growth of these children was also plotted against time.
Results: Of 593 pediatric LT performed in our unit from 2011 - 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT. Three of them died in the post-LT follow-up. We hence started offering a simultaneous or a post-LT biliary diversion for the other 7 patients (Table 1). This also included 3 patients who had a failed partial internal biliary diversion previously (No.1,5&6). All had severe pruritus and 2 each had compensated (No. 1&4) & decompensated cirrhosis (No.5&7) for which they underwent a LT. Five (No. 2,3,5,6 & 7) underwent simultaneous TIBD, whereas 2 (No. 1&4) were offered TIBD, 60 & 24 months post-LT due to progressive & severe graft steatosis. The

diversion was revised in those patients who had the proceedure done in pre LT period. Median age of LT was 60 months and all were living donor LT. None had rejection, infection, vascular or biliary complications in the post-LT period. After a median follow-up period of 48 months, all had normal graft function and resolution of diarrhea. They strikingly attained a median height velocity of 7.8cm/year. Two with post-LT TIBD showed complete resolution of graft steatosis within 1 year of performing TIBD.

Conclusions: In the largest series to date with medium-term outcomes, we demonstrate that simultaneous TIBD in patients undergoing LT should be standard practice as it helps dramatically improve outcomes in PFIC-1 patients who otherwise have a sub-optimal post-LT course with allograft steatohepatitis, intractable diarrhea and growth failure. Large multi-centre society-led studies will help substantiate our recommendations.

Table 1: Clinical profile and outcomes of patients with PFIC-1 following LT along with biliary diversion

No	Onset (Months)	PELD	Indication for LT	Other symptoms	Age at LT (Months)	Type	TIBD Simultaneous/ post LT	Follow up (Months)	Complicati on post LT	Diarrhea in follow up	Growth Catch up cm/year	Graft steatosis	Status (Alive/Di ed)
1	6	13.5	Compensated cirrhosis, intractable pruritus: Failed diversion	Diarrhea	24	LDLT-LLS	60 months post LT: Graft had 90 % steatosis in biopsy	108	Clavien 0	Nil	8.8	Nil	Alive
2	3	0	Intractable pruritus	Nil	48	LDLT-LLS	Simultaneous	66	Clavien 1	Nil	7.2	Nil	Alive
3	5	0	Intractable pruritus	Diarrhea	108	LDLT-RL	Simultaneous	60	Clavien 0	Nil	7.6	Nil	Alive
4	12	3.7	Compensated cirrhosis, portal hypertension, intractable pruritus	Diarrhea	72	LDLT-LLS	24 months post LT (Graft had 90 % steatosis in biopsy)	40	Clavien 0	Nil	3	Nil	Alive
5	6	13.5	Decompensated cirrhosis, intractable pruritus: Failed diversion	Diarrhea	60	LDLT-LLS	Simultaneous	37	Clavien 0	Nil	9	Nil	Alive
6	6	9	Intractable pruritus: Failed diversion	Diarrhea	24	LDLT-LLS	Simultaneous	8	Clavien 0	Better, on cholestya mine	8 (Over 6 months)	Nil	Alive
7	8	22	Decompensated cirrhosis, pruritus	Diarrhea	60	LDLT-LL	Simultaneous	6	Clavien 1	Nil	-	Nil	Died* (acute graft failure of viral etiology at 6th month)

Abbreviations: LL : Left lobe, LLS : Left lateral segment, LT : Liver transplant, LDLT : Living donor liver transplantation, PELD: Pediatric end stage liver disease (score), RL: Right lobe, TIBD : Total internal biliary diversion
Clavien Dindo classification : I : Deviation from normal post-operative course without need of any interventions, II : Complication s requiring administration of medicines other than analgesics, antipyretics, antiemetics, diuretics, electrolytes, physiotherapy, IIi: Complications requiring endoscopic, surgical or radiological intervention IIIA without general anesthesia, IIIB under general anaesthesia, IV: Life threatening complication requiring ICU admission (IV A: uniorgan dysfunction including dialysis, IV B : Multiorgan dysfunction); V : Death

BOS17_6 HYPOTHERMIC OXYGENATED MACHINE PERFUSION IN PEDIATRIC KIDNEY TRANSPLANTATION: A PRELIMINARY SINGLE CENTER EXPERIENCE

Gionata Spagnoletti[*1], **Alberto Maria Fratti**[1], **Zoe Larghi Laureiro**[2], **Riccardo Cirelli**[1], **Isabella Guzzo**[2], **Marco Spada**[1]

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Background: Hypothermic machine perfusion has become the new gold standard in clinical donor kidney preservation, decreasing risk of delayed graft function (DGF), improving graft survival, thanks to the influence of many different pathways involved in ischemia-reperfusion injury (IRI).
To date, low data are available about HMP for kidney transplantation (KTx) in pediatric population.
Methods: We report a retrospective analysis of our clinical experience using Hypothermic Oxygenated Machine Perfusion (HOMP) in pediatric KTx recipients. Between November 2019 and September 2022, we performed 83 KTx at our institution. We excluded 26 living donor transplantation and we included 57 KTx comparing 16 HOMP versus 41 static cold storage (SCS).
Results: Recipients were predominantly of male gender (57.8%) with a median age of 12.2 (1.9-21.4) years. We found similar demographics characteristics between the two groups. Despite a higher Cold Ischemia Time (HOMP 24.7±2.1 vs SCS 13.4±1.8 hours, *p<0.001*), we did not find differences in terms of DGF, graft survival, acute rejection rate, post-operative hospital stay (TABLE_1).
Conclusions: With the limitation of a retrospective analysis, our data confirm the safety and the efficacy of the use of HOMP in the pediatric setting: the longer CIT did not reflect on graft survival. Based on our preliminary experience, we can speculate and consider HOMP a useful and safe tool in the management of kidney transplantation also in the pediatric field.

TABLE_1	HOMP (16)	SCS (41)	p
	Mean (SD) or N (%)		
Age at Transplant (Yrs)	12.1 (6.03)	12.3 (5.84)	ns
Male sex	11 (68)	22 (53)	ns
Hemodialysis pre-KTx	9 (56)	19 (46)	ns
Cold Ischemia Time (hours)	24.7±2.1	13.4±1.8	<.001
Delayd graft function	1 (6)	2 (4.8)	ns
Post-operative hospital stay (days)	18.6 (7.21)	19.9 (8.6)	ns
Graft survival	15 (94)	39 (95)	ns
Patient survival	16 (100)	41 (100)	ns

BOS17_7 LIVER RETRANSPLANTATION IN CHILDREN

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Background: Liver retransplantation (re-LT) is the only therapeutic treatment for initial graft failure. The purpose of this project was to investigate indications and evaluate outcomes of paediatric re-LT.
Methods: Data of paediatric liver transplant (LT) patients who required re-LT between January 1991 and December 2021 were retrospectively analysed. Demographics, clinical and laboratory findings were collected. For survival evaluations, the Kaplan – Meier estimations and the log rank test were used. Significance was set at p<0,05.
Results: A total of 887 liver transplantations were performed. Re-LT constituted 73 procedures (8%), of which 10 were second retransplantations. Sixty-three subjects (39 (62%) female, median age at re-LT 13,9 years; range 0,53 – 25,17) were enrolled. Primary indications for LT were mainly biliary atresia (n=23, 37%) and acute liver failure (n=12, 19%). Liver malignancy was seen in 3 patients (5%). The main causes of initial graft loss were biliary complications (n=13, 20%) and primary non-function (n=10, 16%). Nineteen patients (30%) received an early re-LT (<30 days post primary LT) and in forty-four subjects (70%) a late re-LT was performed. Fifty-six re-LT patients (89%) received the second liver graft from a deceased donor and in 7 cases (11%) the graft came from a living related donor. Early biliary and vascular complications occurred in 8 (13 %) and 6 (9%) patients, respectively. There were 23 deaths (37%) during the median follow-up of 9,3 years (range: 0-30,2). Seventeen patients died with functioning graft. The highest mortality rates were seen among early re-LT patients (n=8, 42%) and recipients of the 3rd liver graft (n=6, 60%). Patients' survival rates at 1, 5 and 10 years post re-LT were 72%, 69% and 66%, respectively, and were inferior when compared with long-term survival post primary LT (92%, 90% and 89%, respectively; p<0.001)
Conclusions: Retransplantation accounted for 8% of all LTs. Preliminary data showed inferior survival rates after re-LT. Retransplantation with partial graft from a living related donor offers acceptable outcome. Results of detailed comparable analyses identifying factors of poor prognosis after LT and re-LT are essential for improvement of long-term outcomes.

BOS17_8 KIDNEY TRANSPLANTATION IN PEDIATRIC PATIENTS WITH SEVERE LOWER URINARY TRACT DYSFUNCTION. IS ILEAL CONDUIT M.BRICKER AS GOOD AS NORMAL BLADDER?

Dorota Broniszczak-Czyszek[*1], **Hor Ismail**[1], **Katarzyna Pankowska-Wozniak**[1], **Marek Szymczak**[1], **Jacek Rubik**[1], **Ryszard Grenda**[1], **Piotr Gastol**[1], **Lidia Skobejko**[1], **Malgorzata Syczewska**[1], **Piotr Kaliciński**[1]

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Background: The strategy of kidney transplantation (KTx) in children with lower urinary tract dysfunction demands a choice between using dysfunctional bladder or alternatively urinary diversion to ileal conduit m.Bricker.
The aim of the study was to present the outcome of pediatric KTx into an ileal conduit m.Bricker in comparison with patients transplanted into normal or native dysfunctional bladder.
Methods: Between 2000 and 2020 there were 789 KTx performed in our institution in patients < 18 years old. We divided them in to 3 groups: 89 KTx into ileal conduit m.Bricker (group I); 165 KTx performed into a native dysfunctional bladder (group II) and 535 KTx into a normal bladder (group III). We analysed graft and patient survivals, frequency of urological complications (leaks, ureteral stenosis, vesicourinary reflux etc) and clinically significant urinary tract infections (UTI). Clinically significant UTI were defined as those with clinical symptoms (altogether: fever, positive cultures, leucocyturia, graft function deterioration) and reccurent. All statistical calculations were performed in MedCalc v 18 software. The cut-off level of statistical significance was assumed on the level 0.05.
Results: Comparison of 1 -, 5 - and 10 - years graft and patient survival curves in group I, II and III showed no statistical diffrence (p>0.05). The highest frequency of clinically significant UTI was in the group of patients with native dysfunctional bladder, lower in group of patient with ileal conduit and the lowest in group of patients with normal bladder (p<0.05). The frequency of urological complications was higher in the groups of patients with native dysfunctional bladder and with ileal conduits in comparison with the group of patients with normal bladder (p<0.05). There was no impact of UTI and urological complications on patient and graft survival. The analysis of causes of graft loss in the group I was done and in no case was related to the ileal conduit.
Conclusions: Ileal conduit urinary diversion is good and safe alternative in comparison with native dysfunctional bladder.Urological complications and UTI, however are more often in the group of patients transplanted into ileal conduit, do not put at risk the functionality of the graft and have no impact on patient's survival in comparison with a conventional KTx.

BOS17_9 GOOD OUTCOMES AFTER PEDIATRIC LIVER-RE-TRANSPLANTATIONS: THE ETHICAL DISCUSSION SHOULD BE ENDED

Markus Götz*[1], Henrik Junger[1], Leonhard Schurr[1], Daniel Wöhl[1], Birgit Knoppke[2], Michael Melter[2], Frank Brennfleck[1;3], Hans Schlitt[1], Stefan Brunner[1]

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Background: Pediatric liver transplantations generally represent advanced surgery for selected patients. In case of acute or chronic graft failure, biliary or vessel complications a retransplantation (reLT) can be necessary. In these situations, massive adhesions, critical patient condition or lack of good vessels for anastomosis can be problematic.
Methods: Between 2008 and 2021, 208 pediatric patients received a liver transplantation in our center. Retrospectively, all cases with at least one retransplantation were identified and stored in a excel database. Indication, intra- and postoperative course and overall survival (OS) were analyzed. Early retransplantation was defined < 1 month, late retransplantation > 1 month after primary transplantation.
Results: Altogether 31 patients (14.9%) were retransplanted. In 22 cases only one retransplantation was done, 8 patients received 2 retransplantations and 1 patient needed a fourth graft. Median age for primary transplantation, first, second and third retransplantation was 14 (range: 1-192 months), 60.5 (range: 1-246 months), 58.5 (range: 14-131 months) and 67 months, respectively. While bile duct atresia (42%) and acute liver failure (23%) represented the main indications for the primary liver transplantation, acute and chronic graft failure (1. reLT: 36%, 2. reLT: 38%), thrombosis of the hepatic artery (1. reLT: 29%, 2. reLT: 25%, 3. reLT: 100%) and biliary complications (1. reLT: 26%, 2. reLT: 37%) were the most frequent indications for retransplantation. Warm ischemia time (WIT) was similar between primary transplantation and retransplantations (*Fig.1*). Complications of grade 3 or higher according to the Clavien-Dindo classification occured in 78.1% over all cases. After a median follow-up of 79 months (range: 0-180 months) OS was 81.8% for patients with 1 reLT, 87.5% with 2 reLTs and 100% with 3 reLTs.
Conclusions: Pediatric liver retransplantations can be done safe and with good patient outcome. Nevertheless, a carefully patient and graft selection as well as good preoperative conditioning are essential for success. But with regard to the excellent survival rates even after multiple retransplantations a further discussion over prioritization of patients needing a first liver transplantation is in our opinion ethically questionable.

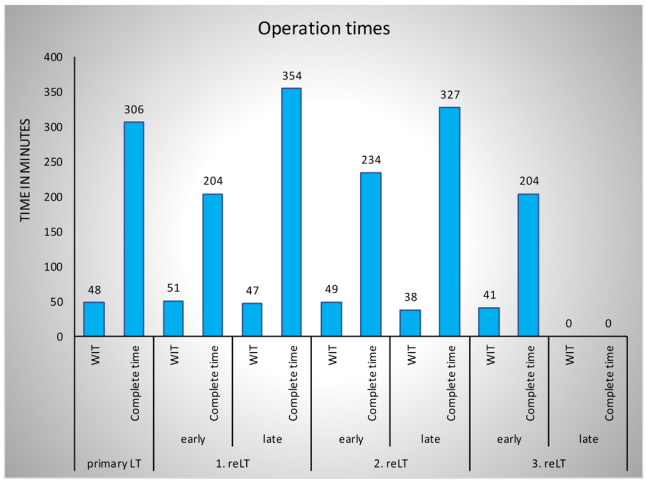

Fig. 1: *Shown are warm ischemia time and complete operation time for primary transplantation, 1. reLT, 2. reLT and 3. reLT. Early and late reLT are listed seperately. WIT was very similiar between primary transplantation and all reLT. While primary LTx and late reLTs showed no relevant difference in complete operation time, early reLTs lasted significant shorter.*

BOS17_10 KIDNEY GRAFT OUTCOMES FOLLOWING KIDNEY VERSUS SIMULTANEOUS LIVER-KIDNEY TRANSPLANTATION IN CHILDREN – ANALYSIS OF THE UNOS DATABASE

Ioannis D. Kostakis*[1;2], Pankaj Chandak[2;3], Mikaela Maria Charalambides[2], Petrut Gogalniceanu[2], Georgios Papadakis[2;4], Jelena Stojanovic[4], Francis Calder[2;4], Ioannis Loukopoulos[2;4], Nicos Kessaris[2;4]

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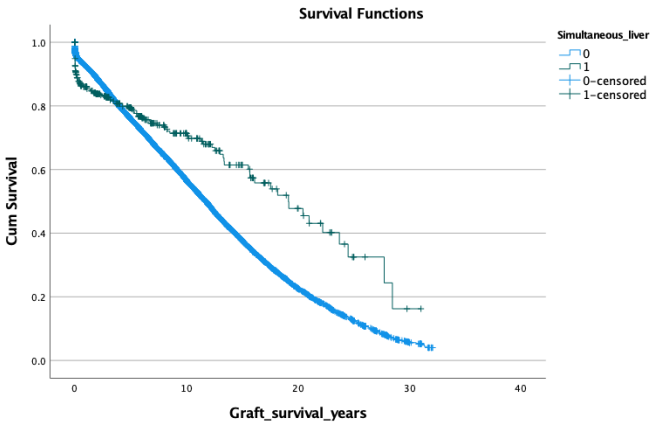
Background: Simultaneous liver-kidney transplantation may confer an immunological advantage to the kidney graft. The aim of this study is to explore kidney graft outcomes after kidney versus simultaneous liver-kidney transplantation in children following an analysis of the United Network for Organ Sharing (https://unos.org/) database.
Methods: Data were retrieved and analysed on kidney and combined liver-kidney transplants performed in paediatric recipients (<18 years old) from October 1987 until September 2020, from the UNOS database. Statistical analysis was performed using SPSS v28.
Results: There were 23597 kidney transplants (Group 1, 9628 female, median age 12, IQR 8) and 373 simultaneous liver-kidney transplants (Group 2, 183 female, median age 9, IQR 9) performed during the times period. All simultaneous liver-kidney transplants were from brain dead donors. In Group 1 there were 10649 (45.1%) kidney transplants from living donors, 12592 (53.4%) from DBD donors and 356 (1.5%) from DCD donors. The most common renal disease in Group 1 was glomerulonephritis (4396 cases, 18.6%) followed by pyelonephritis/obstruction/reflux (3234 cases, 13.7%). In Group 2, the most common disease was hereditary/metabolic (134, 35.9%) followed by cystic disease (88, 23.6%). Some 10785 (45.7%) kidney grafts failed compared to 109 (29.2%) kidneys from the simultaneous liver-kidney transplant group (P<0.001). Delayed graft function was present in 2068 cases (8.8%) in Group 1 and 70 cases (19%) in Group 2 (P<0.001). Primary non-function was present in 248 patients (1.1%) in Group 1 versus 7 (1.9%) in Group 2 (P=0.198). Kaplan-Meier Survival analysis showed a statistically significant difference between the two Groups with a Log Rank of <0.001.
Conclusions: In this large comparative database analysis, delayed graft function was worse following simultaneous liver-kidney transplantation in children when compared to kidney transplantation alone. Nevertheless, simultaneous liver-kidney transplants in children have a better kidney graft survival than those who have a kidney transplant alone. This may be due to a protective immunological effect following liver transplantation.



BOS17_11 KIDNEY GRAFT OUTCOMES FOLLOWING PAEDIATRIC BLOOD GROUP INCOMPATIBLE TRANSPLANTATION – ANALYSIS OF THE UNOS DATABASE

Ioannis D. Kostakis[*1;2], Pankaj Chandak[2;3], Mikaela Maria Charalambides[2], Petrut Gogalniceanu[2], Georgios Papadakis[2;4], Jelena Stojanovic[4], Francis Calder[2;4], Ioannis Loukopoulos[2;4], Nicos Kessaris[2;4]

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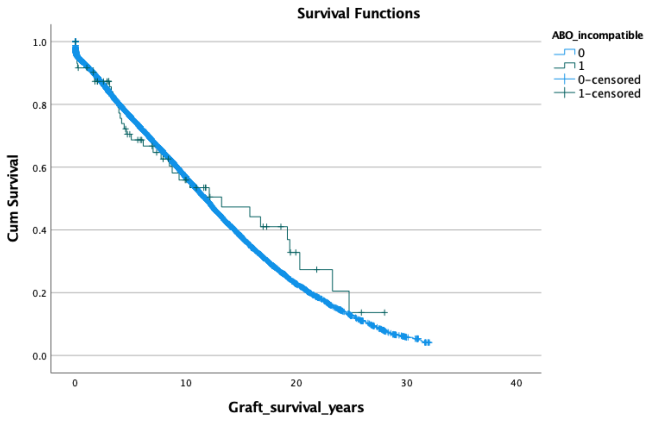
Background: Kidney transplantation is the gold standard treatment for children with kidney failure. Blood group incompatible (ABOi) kidney transplantation is sometimes used in the paediatric population when a compatible transplant is impossible. The aim of this study is to explore kidney graft outcomes following ABOi kidney transplantation and compare that to blood group compatible (ABOc) transplants following the analysis of the United Network for Organ Sharing (https://unos.org/) database.
Methods: Data were retrieved and analysed on blood group incompatible kidney transplants performed in paediatric recipients (<18 years old) from October 1987 until September 2020, from the UNOS database. Statistical analysis was performed using SPSS v28.
Results: There were 23886 ABOc kidney transplants (F=9777, median age 12, IQR 7-15) and 73 ABOi kidney transplants (F=29, median age 14, IQR 9-16) during the study period. The blood groups of those who had an ABOi transplant were, blood group A=10, B=19 and O=44. There were 5 cases of delayed graft function in the ABOi group and 2132 in the ABOc group (p=0.682). There was no graft thrombosis in the ABOi group. In comparison, there were 457 cases of graft thrombosis in the ABOc group (p=0.652). There was one case of primary non-function in the ABOi group and 254 in the ABOc group (p=0.543). The median creatinine at discharge following ABOi transplantation was 0.90 mg/dL (IQR 0.6-1.42), whereas the median creatinine following ABOc transplantation was 0.89 mg/dL (IQR 0.5-1.30) [p=0.551]. Kaplan-Meier Survival analysis showed no significant difference between the ABOc and ABOi transplants (Log Rank of <0.487).
Conclusions: In this large comparative study, kidney graft outcomes after ABOi transplantation in children were similar to those after ABOc transplantation. Despite the limitations of large database analysis, this outcome is reassuring when balancing whether to proceed to a blood group incompatible transplantation or not, when other options are limited.



BOS17_12 VALIDATION OF A PREDICTION SYSTEM FOR RISK OF ALLOGRAFT LOSS (IBOX) IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

Julien Hogan[*1;2;3], Gillian Divard[1], Olivier Aubert[1], Rouba Garro[4], Olivia Boyer[5], Lee Cooper[6], Alton Farris[7], Marc Fila[8], Mickael Seifert[9], Jodi Smith[10], Burkhard Toenshoff[11], Alexander Fichtner[11], Katherine Twombley[12], Brad Warady[13], Meghan Pearl[14], Rima Zahr[15], Carmen Lefaucheur[1], Rachel Patzer[3], Alexandre Loupy[1]

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Background: Predicting long-term kidney allograft failure is an unmet need for clinical care and clinical trial optimization in children. We aimed to validate a kidney allograft failure risk prediction system in a large international cohort of pediatric kidney transplant (kTx) recipients.
Methods: Patients from 20 centers from Europe and the United States, transplanted between 2004 and 2017 were included. Allograft assessment included eGFR, urine protein/creatinine ratio, circulating anti-HLA donor specific antibody and kidney allograft histology according to the Banff international classification. Individual predictions of allograft failure were calculated using the iBox system. Prediction performances were assessed using discrimination and calibration.
Results: Among the 706 kTx recipients included, 80 allografts failed. The allograft evaluations were performed at a median time of 9.1 [3.3-19.2] months post-transplantation, mean eGFR was 68.7+/-28.1 mL/min/1.73m2 while median UPCR was 0.1[0.0-0.4]g/g and 134 (19.0%) patients had circulating anti-HLA DSA. The iBox exhibited accurate calibration (Fig 1) and discrimination (Fig 2) for predicting the outcomes up to ten-year after evaluation with a C-index of 0.81 (95% CI 0.75 to 0.87).
Conclusions: This study confirms for the first time the generalizability of the iBox scoring system to predict long-term kidney allograft failure in children with performances similar to those reported in adults. The iBox risk prediction score can be extended to the pediatric population to further improve patient monitoring and be used as an endpoint for clinical trials.

Figure 1: Discrimination (Concordance Harrel's C-index) of the iBox risk score to predict kidney allograft failure in the pediatric population from 1 to 10 years after kidney allograft evaluation.

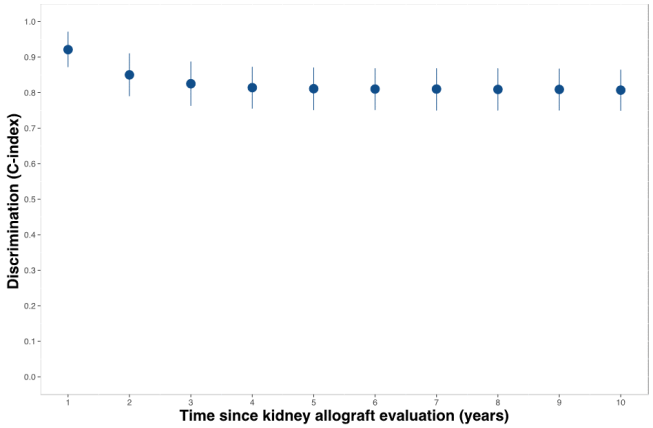
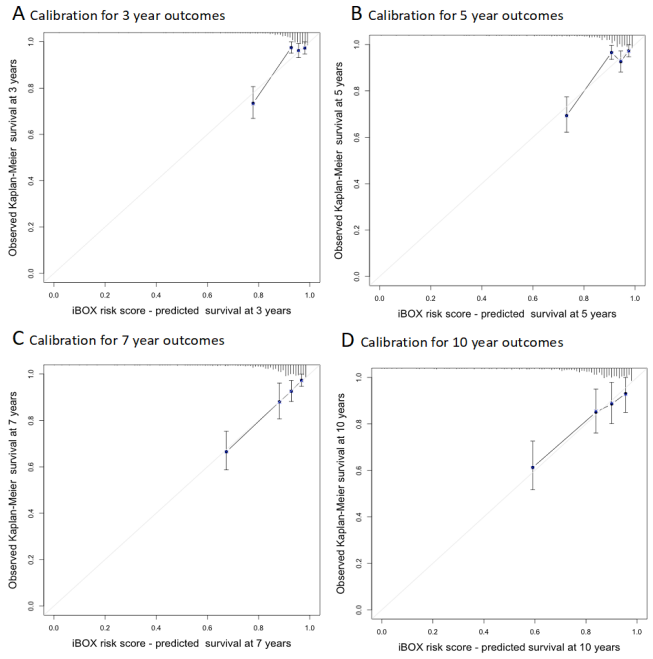


Figure 2: Calibration plots at three, five, seven and ten years of the iBox system in the pediatric validation cohort.



BOS17_13 BRIDGING THE RENAL TRANSPLANT GAP IN PEDIATRIC PATIENTS IN GREECE: A 3-YEAR EXPERIENCE OF A PEDIATRIC TRANSPLANT PROGRAM IN AN ADULT TRANSPLANT CENTER

Eleni Kapsia*[1], Andromachi Mitsioni[2], Varvara Askiti[2], Ioanna Soukouli[3], Ioannis Michelakis[4], Evangelia Kalliardou[5], Ekaterini Lampadariou[6], Ioannis Bokos[7], Maria Darema[3], Ioannis Boletis[3], Smaragdi Marinaki[3]

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Background: During the last decade, in Greece, a significant decline in pediatric renal transplantations has occurred, resulting in a prolonged time on dialysis or forcing children to travel abroad to be transplanted. In an effort to bridge this transplant gap, on November 2019, an experienced adult transplant center formed the basis of a pediatric renal transplant program.
Methods: We studied the pediatric renal transplant activity of our joint transplant program between November 2019 and December 2022 and reported patients' characteristics and transplantations' outcomes.
Results: Between November 2019 and December 2022, 24 patients <18 years underwent kidney transplantation in our joint transplant center. Median age of patients was 15 years (IQR 3), while 75% (18/24) were male. Body weight ranged from 29 to 38 kg for patients 10-12 years old (5/24, 21%), 28-58 kg for those 12-16 years old (10/24, 42%) and 34-79kg for patients 16-18 years old (9/24, 37%). Living donor transplantations accounted for 19/24 cases (79%), five of which were preemptive. Median time on renal replacement therapy was 78 months (IQR 90). Five of 24 (21%) transplantations were ABO and/or HLA incompatible. There were no major surgical complications, except one hemorrhage, which resolved without sequelae. Acute rejection episodes occurred in 4patients and were all treated successfully with no impact on renal function. Median hospitalization time was 12 days (IQR 6). At a median follow up of 22.5 months (IQR 11), median eGFR was 56.5ml/min (IQR 26.8). Between November 2019 and December 2022, 30 pediatric renal transplantations were performed in our country, with our joint transplant center undertaking 80% of them (24/30), thereby increasing the number of pediatric kidney transplantations by 76% compared to the preceding period (January 2016 - October 2019), when only 17 transplantations were performed.
Conclusions: The implementation of a pediatric kidney transplantation program in the setting of an experienced adult transplant center, with the collaboration of pediatric transplant physicians, is safe and may result in a significant increase in pediatric kidney transplants.

BOS17_14 FIRST REPORT ON THE USE OF A TRANSPLANTED RECTUS SHEATH FASCIA FOR A COMBINED LIVER AND KIDNEY TRANSPLANT IN A PAEDIATRIC PATIENT WITH MMA

Alicia Paessler*[1], Miriam Cortes Cerisuelo[2], Wayel Jassem[2], Hector Vilca-Melendez[2], Akash Deep[2], Vandana Jain[2], Andrew Pool[2], Stephanie Grunewald[1], Judith Van der Voort[3], Nicos Kessaris[4], Jelena Stojanovic[5]

[1]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [2]King's College Hospital NHS Foundation Trust, London, United Kingdom, [3]University Hospital of Wales, Cardiff, United Kingdom, [4]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, [1]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom

Background: As medicine is advancing, more complex children are becoming multi-organ transplant candidates, bringing new challenges in all aspects of their care. We describe the first case of a small child receiving a combined liver and kidney transplant (CLKT) and an abdominal rectus sheath fascia transplant on a background of Williams Syndrome and Methylmalonic Acidaemia (MMA).
Methods: A 3 year old with MMA, and a weight of 12.5kg, was listed for CLKT. There were many anaesthetic, medical, metabolic and surgical challenges to consider. Pre-operative planning included close collaboration between 9 specialties in 4 hospitals. A long general anaesthetic increased the risk of cardiac complications and metabolic decompensation given the patient's metabolic background. Gaining an in depth understanding of the metabolic state of the patient pre- and peri-operatively was crucial in avoiding metabolic decompensation. Hour by hour management protocol was drafted to facilitate transplant and included five domains: 1. Management at the time of organ offer, 2. Before the admission, 3. At admission and before theatre time, 4. Intra-operative management and 5. Post-operative management in the first 24 hours.
Results: The patient's post-transplant recovery was complicated by sepsis, transient CNI toxicity, de-novo DSAs and difficulty in achieving abdominal closure due to thepatient's small size and organ size mis-match. To achieve abdominal closure, the patient received an abdominal rectus sheath fascia transplant, which to our knowledge, was the first case for this indication. Through a MDT approach and detailed pre-operative planning, a good outcome was achieved and 18 months post-transplant the child has good kidney and stable liver function, no transplant-related complications, improved growth and neurodevelopment, and an excellent quality of life as reported by the parents. This peri-transplant protocol was used for all other patients with MMA we transplanted with excellent outcomes.
Conclusions: Rectus sheath fascia transplant for abdominal closure following CLKT can lead to good results. Using our experience of this complex case and other transplanted MMA patients, and thorough literature review, we recommend MDT approach and propose an hour by hour peri-operative management pathway for MMA patients.

MODERATED POSTER

Moderated poster session on cardiac transplantation

MPS1_1 TRANSPLANT RECIPIENT OUTCOMES WITH EXTENDED CRITERIA DONORS: AN ANALYSIS OF THE GUARDIAN HEART REGISTRY

Roxana Moayedifar[1], Andreas Zuckermann*[1], Yasuhiro Shudo[2], Masashi Kawabori[3], Scott Silvestry[4], Jacob Schroder[5], Dan Meyer[6], David D'alessandro[7]

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Background: The prevalence of end stage heart failure and patients that could benefit from heart transplantation requires expansion of the donor pool, relying on the transplant community to continually re-evaluate and expand the use of marginal donor organs. Introduction of new technologies such as the Paragonix SherpaPak Cardiac Transport System (CTS) aids in this shift. We seek to analyse the impact of the CTS system on recipient outcomes who receive extended criteria organs in the GUARDIAN Heart Registry.
Methods: Between October 2015-August 2022, 761 adults from 9 US centers receiving donor hearts utilizing either CTS (N=419) or conventional ice storage (ICE, N=342) were analysed from the GUARDIAN Heart registry using summary statistics. A modified EXPAND OCS Trial criteria was used to delineate cohorts of extended criteria donors, which included 176 CTS and 132 ICE (see Table).
Results: Forty percent of the total US donors in the registry population met the extended criteria definition. There were few baseline differences among recipients in the 2 cohorts, most notably both distances travelled, and total ischemic time was significantly greater in CTS, and significantly more donor hearts in the CTS cohort had >4 hours total ischemia time, although baseline VAD was higher in the ICE cohort. Post-transplant MCS utilization and New ECMO/VAD was significantly reduced, and the rate of severe PGD was significantly reduced by over 50% in hearts preserved using CTS. Survival between cohorts was similar.
Conclusions: This subgroup analysis demonstrates that SherpaPak CTS can be safely used to utilize extended criteria donors, with low severe PGD rates. This is encouraging toward use of extended criteria donors in European transplant programs, though further clinical evaluation in Europe is warranted.

Table:

	ICE n = 132	CTS n = 176	*p-value*
Donor Inclusion Criteria			
>4h Total Ischemic Time	**66 / 132 (50.0%)**	**120 / 176 (68.2%)**	**0.001**
>2h Total Ischemic Time AND			
Age > 55 years	4 / 132 (3.0%)	9 / 176 (5.1%)	0.37
Downtime > 20 mins	23 / 132 (17.4%)	35 / 176 (19.9%)	0.58
LVEF 40-50%	34 / 132 (25.8%)	35 / 176 (19.9%)	0.22
LVPW 12-16 mm	18 / 132 (13.6%)	14 / 176 (8.0%)	0.11
Luminal Irregularities	5 / 132 (3.8%)	7 / 176 (4.0%)	0.93
Donor Characteristics			
Donor Age (years)	33.2 ± 10.7	34.6 ± 11.0	0.26
Donor BMI (kg/m²)	28.8 ± 7.2	28.8 ± 7.5	0.97
Recipient Characteristics			
Recipient Age (years)	54.8 ± 11.0	55.5 ± 13.2	0.42
Recipient BMI (kg/m²)	28.1 ± 4.5	27.8 ± 4.7	0.65
LVEF at Baseline (%)	23.0 ± 13.7	21.5 ± 11.3	0.31
Implantable VAD	**61 / 132 (46.2%)**	**45 / 176 (25.6%)**	**<0.001**
Temporary IABP	27 / 132 (20.5%)	43 / 176 (24.4%)	0.41
Temporary ECMO/VAD	**10 / 132 (7.6%)**	**24 / 176 (13.6%)**	**0.09**
Match Characteristics			
F/M Mismatch	16 / 132 (12.1%)	27 / 176 (15.3%)	0.42
PHM Mismatch	0.0 ± 0.2	0.0 ± 0.2	0.43
Distance to Organ (nautical miles)	**356.0 ± 295.1**	**605.8 ± 365.8**	**<0.001**
Total Ischemic Time (minutes)	**223.8 ± 55.7**	**251.8 ± 48.8**	**<0.001**
Outcomes			
All Post Tx MCS	**48 / 132 (36.4%)**	**36 / 176 (20.5%)**	**0.002**
New IABP Post Tx	18 / 132 (13.6%)	17 / 176 (9.7%)	0.28
New ECMO/VAD Post Tx	**21 / 132 (15.9%)**	**14 / 176 (8.0%)**	**0.03**
Cardioversion	16 / 132 (12.1%)	15 / 176 (8.5%)	0.3
PGD	30 / 132 (22.7%)	23 / 176 (13.1%)	0.026
PGD Severe	**18 / 132 (13.6%)**	**11 / 176 (6.3%)**	**0.03**
LVEF at 24hrs (%)	**53.1 ± 14.2**	**56.8 ± 13.0**	**0.03**
30-Day Survival	127 / 132 (96.2%)	172 / 176 (97.7%)	0.43
In-hospital Survival	125 / 132 (94.7%)	171 / 176 (97.2%)	0.27
1-year Survival	109 / 123 (88.6%)	124 / 136 (91.2%)	0.49

Abbreviations: BMI = body mass index; CTS = (Paragonix) cardiac transport system; ECMO = extracorporeal membrane oxygenation; F/M mismatch = female to male mismatch; IABP = intra-aortic balloon pump; LVEF = left ventricular ejection fraction; LVPW = left ventricular posterior wall; MCS = mechanical circulatory support; PGD = primary graft dysfunction; PHM = predicted heart mass; Tx = transplant; VAD = ventricular assist device.

MPS1_2 VALIDATION OF THE 2014 CONSENSUS PRIMARY GRAFT DYSFUNCTION DEFINITION USING THE GUARDIAN-HEART REGISTRY

Andrea Eixeres Esteve*[1], David D'alessandro[2], Jeffrey Jacobs[3], Yasuhiro Shudo[4], Dan Meyer[5], Scott Silvestry[6], Marzia Leacche[7], Koji Takeda[8], Christopher Sciortino[9], Maria Rodrigo[10], Si Pham[11], Umar Boston[12], Andrija Vidic[13], Hannah Copeland[14], Masashi Kawabori[15], Juan Bustamante-Munguira[16], Rajamiyer Venkateswaran[17], Jacob Schroder[18], Andreas Zuckermann[19]

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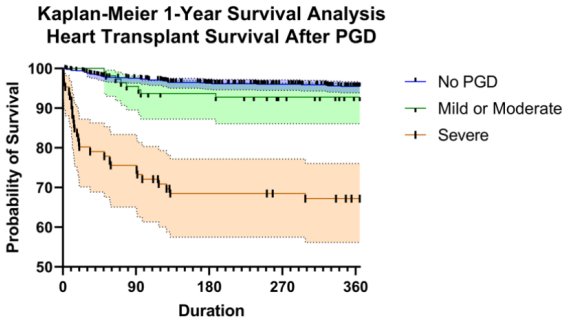
Background: In 2014, an international collaboration developed the first modern, universal definition of Primary Graft Dysfunction (PGD), which allowed for increased standardization in evaluation and treatment of post-transplant graft dysfunction. This definition was developed based on expert opinion and surgical experience of clinical risk factors. Validation of this definition has proved challenging as historic registries such as the UNOS registry do not capture the necessary information to report PGD, and single center studies are too limited in power to generate meaningful analyses. The GUARDIAN-Heart Registry is the largest multicenter registry focused on analysis of peri-operative and early post operative outcomes following donor heart preservation. This registry provides a unique opportunity to validate the 2014 PGD consensus definition, demonstrating that increasing degrees of severity of graft dysfunction leads to decreased patient survival.
Methods: The GUARDIAN-Heart Registry is a global, multicenter registry studying transplant outcomes using various donor heart transport or preservation methods between October 2015 and August 2022. A comparison of clinical outcomes was performed using probabilistic methods of patients without PGD, and with mild, moderate and severe PGD.
Results: Of the 1,056 patients enrolled in the GUARDIAN database, 86 were identified with severe PGD, 111 with mild or moderate PGD and 859 were identified with no PGD. Using Kaplan-Meier analysis, severe PGD had significantly lower survival than either mild and moderate PGD or the no PGD cohorts (<0.001). Mild and Moderate PGD was not significantly different from no PGD (0.20). The ICU length of stay (median and interquartile) were 6 days (4-10) for No PGD, 8 days (5-14) for Mild and Moderate, 12.5 days (8-27.25) for Severe PGD (p<0.001).
Conclusions: This analysis substantiates the 2014 definition of severe PGD as a clear risk factor for reduced 1 year survival. The separation of the curves continues to widen beyond the first 30 days post-transplant, continuing through 6 months and even 1 year, suggesting that severe PGD is an initial insult that initiates a sequalae of complications. This mechanism warrants further investigation.

Figure:



No PGD	859	834	804	759	710
Mild or Moderate	111	107	103	97	89
Severe	86	66	57	55	49

MODERATED POSTER

Moderated poster session on cardiac transplantation

MPS1_3 LOWER BASOPHIL COUNT AFTER ANTI-THYMOCYTE GLOBULIN INDUCTION IS ASSOCIATED WITH A LOWER INCIDENCE OF CARDIAC ALLOGRAFT REJECTION

Bosko Skoric[*1;2], Dora Fabijanovic[2], Petra Mjehovic[2], Mia Dubravcic Dosen[2], Dubravka Sipus[2], Andrija Nekic[1], Ivo Planinc[2], Nina Jakus[2], Marijan Pasalic[2], Hrvoje Jurin[2], Jure Samardzic[1;2], Maja Cikes[1;2], Zeljko Colak[1;3], Hrvoje Gasparovic[1;4], Davor Milicic[1;2]

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Background: The role of basophils in cardiac allograft rejection is poorly understood. An animal model described the infiltration of basophils in allografts from day 10 to day 20 after heart transplantation (HTx). Anti-thymocyte globulin (rATG) used as induction therapy contains antibodies to antigens expressed by many immune cell subsets, including basophils. While lymphodepletion is considered a therapeutic effect, a decrease in basophil count after administration of rATG has unknown clinical significance. The aim of this study was to investigate an association between basophil count following rATG induction and the development of acute cellular-mediated rejection (ACR) during 1-year follow-up.
Methods: We performed a retrospective single-centre study in HTx patients transplanted between 2010 and 2020. All patients received rATG induction therapy for 5 days. Absolute lymphocyte count (ALC) and basophil counts were assessed on days 0, 7, 14, and 21 following HTx. The primary outcome was the first occurrence of ACR defined as grade ≥1B within 1 year after HTx.
Results: A total of 182 patients were transplanted. During the 12-month follow-up period, 17% of patients had ACR. Both ALC and basophil counts decreased after rATG. Patients with ACR ≥1B had significantly higher median basophil count on day 14 (17 x 10^3/µL (IQR 9-43) vs 10 x 10^3/µL (IQR 4-19), p=0.050), and higher median ALC on days 14 (308 x 10^3/µL (IQR 171-530) vs 180 x 10^3/µL (IQR 93-317, p=0.016) and 21 (529 x 10^3/µL (IQR 240-610) vs 225 x 10^3/µL (IQR 121-328), p<0.01) than those without rejection. Univariate analysis showed that ACR was associated with basophil count on day 14 (HR 1.014, 95% CI 1.004-1.023, p=0.004), ALC on days 14 and 21, recipient age, and donor/recipient CMV mismatch (D+/R-). In multivariable Cox regression analysis, the adjusted risk of ACR was significantly lower for patients with lower basophil count on day 14 (HR 1.015, 95% CI 1.005-1.025, p=0.003).
Conclusions: Lower basophil count 2 weeks after induction with rATG is associated with a lower risk of acute cellular rejection during the first year after HTx. This coincides with the timing of basophil infiltration of heart allograft reported in an animal model and indicates the potential contribution of basophils in shaping alloimmune response during the early post-transplant period.

MPS1_4 HEART TRANSPLANTATION IN ADULTS WITH PERIPARTUM CARDIOMYOPATHY

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Background: Peripartum cardiomyopathy is a disease characterized by the occurrence of acute heart failure in late pregnancy or in the post-partum period, in the absence of any other pathology of the heart. According to the literature, about 5% of women diagnosed with peripartum cardiomyopathy require heart transplantation.
Methods: The study included 143 female patients aged 18 to 50 years, who underwent heart transplantation from January, 2013, to December, 2018. The first group (group 1) included 26 recipients with a pre-transplant diagnosis of peripartum cardiomyopathy, the second group (group 2) included 117 recipients. The mean age of patients in the first and second groups was 31.7±6.05 and 33.3±12.6 years, respectively. In the first group, in 1A and 1B UNOS statuses heart transplantation waiting 21 patients. In the second group, there were 83 patients in status 1A and 1B. The primary endpoint was death from any cause; secondary endpoints were transplant-related complications (rejection and cardiac allograft vasculopathy). A value of p<0.05 was considered of statistical significance. Survival curves were generated with the Kaplan Meier method.
Results: There were no significant differences of acute cellular rejection between the groups prior heart transplantation (23.07% (group 1) vs 18,8 (group 2), respectively (p=0.41). Acute antibody-mediated rejection was diagnosed in 30.7% of recipients of the first group and 13.6% of recipients of the second group (p<0.05). Cardiac allograft vasculopathy was diagnosed in 7.7% and 10.2%, respectively. On Kaplan-Meier survival analysis the median survival in two groups, taking into account hospital mortality, was 9.2 years.
Conclusions: Heart transplantation in patients with peripartum cardiomyopathy is the method of choice to save the life with good long-term results, despite the increased risk of developing antibody-mediated rejection in this category of recipients.

MPS1_5 INFLAMMATION IN BRAIN DEATH DONORS PROTECTS TO PRIMARY GRAFT DYSFUNCTION IN HEART TRANSPLANTATION

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Background: Brain death induces an inflammatory state that can affect the organ function for transplantation. We address the effect of this inflammatory mediators of donors after brain death (DBD) in the heart transplant (HT) recipients.
Methods: Retrospective multicentre longitudinal study of 39 heart transplant recipients from September 2013 to June 2019. The hearts were procured from 39 DBD from Bellvitge University Hospital. The demographic, clinical and analytical data of the donors and recipients were recorded. The serum of the donors was processed and maintained at -20ºC until analysis. We performed a multiplex analysis of IL-1A, IL-1RA, IL-2, IL-6, IL-10, TNFa, TWEAK, Ferritin, GDF, MCP1 and C5a inflammatory mediators of the serum of DBD. The characteristics and inflammatory markers of DBD were analyzed comparing the heart recipients that required or not a ventricular assist device (VAD) after HT. The quantitative data were expressed as a mean and median and the qualitative data as percentage. IBM SPSS 24 Statistics package was used.
Results: There were not differences in the characteristics of the DBD in the VAD group compared to the group that not required VAD post HT except that levothyroxine was used in the management of organ donors exclusively in the second group in 17,2% (Table 1). The median of inflammatory markers in the serum of heart donors that not required or that required VAD post transplantation (Table 2) were: IL-1A 78 pg/mL (32 - 358) vs 64 pg/mL (27 – 598); IL-1RA 3354 pg/mL (123 – 44256) vs 1661 pg/mL (333 – 11742); IL-2 10 pg/mL (0 – 71) vs 0 pg/mL (0 – 10); IL-6 172 pg/mL (10 – 1707) vs 60 pg/mL (14 – 1067); IL-10 8 pg/mL (0 – 301) vs 4 pg/mL (0 – 10); TNFalpha 3 pg/mL (0 – 70) vs 1 pg/mL (0 – 7); TWEAK 429 pg/mL (95 – 1618) vs 250 pg/mL (146 – 475); Ferritin 604 pg/mL (83 – 9911) vs 359 pg/mL (39 – 1019); GDF 4409 pg/mL (225 – 18976) vs 2746 pg/mL (407 – 20550); MCP1 218 pg/mL (26 – 1594) vs 180 pg/mL (75 – 1269) and C5a 448 pg/mL (5 – 1995) vs 286 pg/mL (197 – 740).
Conclusions: The inflammatory markers IL1A, ILRA, IL2, IL6, IL10, TNFalpha, TWEAK, Ferritin, GFD, MCP-1 and C5a in serum of DBD donors are higher in heart recipients that not required VAD post transplantation.

Table 1

	Heart recipients			
	NO Ventricular assist device post HT		Ventricular assist device post HT	
	Mean	Median	Mean	Median
DBD				
Age	44,9 ± 13	49 (19 – 63)	51,2 ± 9,7	54 (31 – 61)
Weight	74,7 ± 13,0	75 (52 – 100)	78,4 ± 14,4	83 (50 – 98)
Heigh	171,3 ± 9,2	174 (150 – 190)	171,8 ± 9,4	173 (159 – 185)
DM	0		0	
Hypertension	17,2% (5)		11,1% (1)	
Dyslipidemia	10,3% (3)		33,3% (3)	
Smoking	58,6% (17)		66,7% (6)	
Higher Heart rate (HR)	114,8 ± 21,2	120 (73 – 160)	120,6 ± 22,8	126 (88 – 152)
HR in last 6h	93,3 ± 24	98 (60 – 160)	90,5 ± 21,9	82 (70 – 140)
Mean arterial Press last 6h	83,5 ± 16,9	81,5 (55 – 120)	78,5 ± 11,6	74 (68 – 101)
Central Venous Press 6h	8,4 ± 4,1	9 (1 – 18)	11,7 ± 8,0	9,5 (5 – 23)
Noradrenaline (NA)	96,6% (28)		88,9% (8)	
Dose of NA in last 6h	9,0 ± 9,2	7 (0 – 38)	5,2 ± 3	5 (1 – 9)
Dobutamine	0%		0%	
Dose dobutamine	NA		NA	
Dopamine	3,4% (1)		0%	
Adrenaline	3,4% (1)		0%	
Troponin	170,7 ± 356,2	61 (3 – 1537)	102 ± 143	28,5 (6 – 369)
Lactate	1,7 ± 1,1	1,5 (0,6 – 5,6)	1,4 ± 0,5	1,2 (0,7 – 2,2)
LVEF	67,1 ± 6,7	67 (56 – 80)	61 ± 7,0	59 (55 – 75)
TAPSE	20 ± 1,5	20 (18 – 23)	23 ± 3,6	24 (19 – 26)
pH	7,42 ± 0,06	7,43 (7,31 – 7,58)	7,45 ± 0,05	7,45 (7,36 – 7,54)
pCO2	38,4 ± 6,3	38 (23 – 50)	40 ± 4,8	41 (32 – 48)
pO2	295 ± 133	273 (48 – 594)	304 ± 90	335 (87 – 402)
HCO3	25,3 ± 3,4	26 (20 – 35)	27 ± 4,7	27 (21 – 37)
Days of MV	3,2 ± 3,3	2 (1 – 13)	3,1 ± 2,3	2 (1 – 7)
PEEP max6h	5,7 ± 1,4	5 (4 – 9)	7 ± 1,8	7,5 (5 – 10)
Creatinin (Cr) initial	77,9 ± 42,1	70 (35 – 212)	78,5 ± 29,4	65 (40 – 117)
Worst Cr	88,7 ± 53,2	70 (35 – 276)	84,3 ± 29,5	90 (42 – 117)
Urine output 6h	891,5 ± 747	732 (250 – 3100)	816,6 ± 246	700 (650 – 1100)
Sodium	150 ± 7,5	150 (138 – 167)	150 ± 8,5	150 (137 – 170)
Balance 24h	20,8 ± 1524	47,5 (-2670 – 3107)	1191 ± 3253	91,5 (-2000 – 8656)
Albumin	35,2 ± 7,6	37 (19 – 48)	36 ± 6,7	35,5 (28 – 45)
ALT	0,8 ± 0,9	0,5 (0,2 – 4,1)	0,8 ± 1,1	0,33 (0,2 – 3,6)
AST	1,02 ± 1,1	0,55 (0,14 – 4,1)	0,5 ± 0,4	0,33 (0,19 – 1,65)
Bilirubin	12,7 ± 10,8	9 (4 – 47)	10,6 ± 9,2	7 (4 – 34)
Hemoglobin	11,6 ± 2,7	11,4 (7,8 – 17,7)	11,9 ± 1,9	12,5 (9,2 – 15)
Leucocytes	16,7 ± 5,6	17 (6,6 – 28,5)	17,5 ± 4,9	16,7 (9,8 – 24,2)
Antibiotics	75,9% (22)		66,7% (6)	
levothyroxine	17,2% (5)		0%	
Desmopressin	79,3% (23)		88,9% (8)	
Mineralocorticoids	27,6% (8)		44,4% (4)	

Table 2

	Heart Recipients			
	NO Ventricular assit device post HT		Ventricular assist device post HT	
	Mean	Median	Mean	Median
Inflammatory mediators DBD				
IL1A	108,4 ± 66,7	78 (32 – 358)	137,7 ± 178	64 (27 – 598)
IL1RA	8254,1 ± 11231	3354 (123 – 44256)	3443,8 ± 3825	1661 (333 – 11742)
IL2	13,1 ± 17,5	10 (0 – 71)	2,6 ± 3,8	0 (0 – 10)
IL6	383,4 ± 495,1	172 (10 – 1707)	270,7 ± 419,3	60 (14 – 1067)
IL10	24,3 ± 61,7	8 (0 – 301)	3,8 ± 3,6	4 (0 – 10)
TNFa	11,4 ± 20,6	3 (0 – 70)	1,7 ± 2,2	1 (0 – 7)
Tweak	459 ± 323	429 (95 – 1618)	271 ± 110	250 (146 – 475)
Ferritin	1056 ± 1848	604 (83 – 9911)	436 ± 306	359 (39 – 1019)
GDF	6206 ± 5467	4409 (225 – 18976)	4774 ± 6470	2746 (407 – 20550)
MCP1	354 ± 374	218 (26 – 1594)	337 ± 374	180 (75 – 1269)
C5a	485 ± 426	448 (5 – 1995)	369 ± 191	286 (197 – 740)

MPS1_6 LOCAL LABORATORY-RUN DONOR-DERIVED CELL-FREE DNA TESTING IN STABLE HEART TRANSPLANTATION: TWO-CENTRE EUROPEAN FEASIBILITY STUDY

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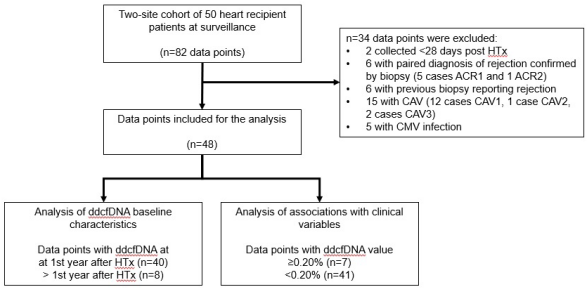
Background: Monitoring allograft rejection and adverse events are crucial after heart transplantation (HTx). The ISHLT guidelines for the care of HTx recipients have included non-invasive surveillance such as testing for donor-derived cell-free DNA (dd-cfDNA). While major studies have been conducted with patient cohorts and centralised testing in the USA, hereby we explored a European two-site cohort where dd-cfDNA was quantified at local centres by next generation sequencing-based CE-marked assay. We aimed to assess feasibility of assay and evaluate dd-cfDNA values in clinically stable HTx recipients.
Methods: This cross-sectional study in 2 European HTx centres included 50 patients at their scheduled visits. By drawing whole blood into blood collection tubes (Streck), dd-cfDNA fraction in plasma was analysed using AlloSeq cfDNA assay (CareDx). For analysis, clinical stability was defined as asymptomatic patients >28 days post-HTx with normal graft function, without CMV infection, history of rejection, or graft vasculopathy.
Results: Demographic and clinical data are shown in the table. Out of 82 clinical visits, 34 were excluded as they did not meet stability criteria. Median dd-cfDNA value of stable patients was 0.11% (95% CI 0.08%–0.13%), and there was no difference between samples taken in the first post-HTx year (n=40) and at later time (n=8) [0.11% vs. 0.11%; p=0.41]. Based on dd-cfDNA cut-offs from previous clinical validation trials, 7 out of 48 samples had values at risk: 4 at the injury cut-off of ≥0.20% and 3 at the severe injury threshold of ≥0.35%. Comparing clinical variables of samples with dd-cfDNA ≥0.20% (n=7) and <0.20% (n=41), median tacrolimus trough level was significantly lower (8.7 ng/ml vs. 10.5 ng/ml; p=0.03). Of note, we observed a 3-fold, non-significant increase in rate of de novo DSA formation (33.3% vs. 10.8%; p=0.19).
Conclusions: Our data show feasibility to analyse dd-cfDNA at the local level. Median dd-cfDNA value of 0.11% in our two-site European reference cohort is within former reported ranges for clinically stable HTx recipients and does not vary beyond the first post-HTx year. Although not statistically significant, the fact that higher levels are found in patients with de novo DSA suggests that dd-cfDNA may be a marker of subclinical rejection and require further study.

	Study Cohort	Site 1	Site 2	*p* value
Patients (n)	50	12	38	
Sex (% female)	26.0%	25.0%	26.3%	n.s.
Age (years) *median* *95% CI*	55.5 50.5 – 56.9	55.5 53.3 – 62.0	55.5 48.5 – 56.5	n.s.
Time from Transplant (days) *median* *95% CI*	274 112 - 395	274 112 - 395	263 77 - 951	n.s.
Tacrolimus trough level (ng/ml) *median* *95% CI*	9.62 8.36 – 10.73	9.20 5.9 – 12.2	9.84 7.68 – 11.66	n.s.



MPS1_8 LIVER AFTER HEART AND COMBINED HEART LIVER TRANSPLANTATION IN HEREDITARY TRANSTHYRETIN AMYLOIDOSIS: A CROATIAN EXPERIENCE

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Background: Hereditary transthyretin amyloidosis (hATTR) is a rare disease caused by mutations in transthyretin protein produced by the liver, characterized by multisystem extracellular deposition of amyloid that leads to multiple organ dysfunction. An endemic region of hATTR in southern Croatia has been recognized, with a specific mutation present in all patients detected so far. Current treatment options are expanding yet still limited, while liver transplantation (LT) remains to be the only curative treatment. We present the overall Croatian experience with hATTR in the context of the heart (HT) and LT.
Methods: Until 2023, two patients with hATTR received heart-liver transplantation at the University Hospital Centre Zagreb. Case 1. A male patient received an urgent HT with a standard bicaval technique followed by liver after heart transplantation (LAHT) using the piggy-back technique several months later. Case 2. A male patient on prior tafamidis meglumine therapy underwent combined heart liver transplantation (CHLT) from a single donor, with HT first using a standard bicaval technique followed by LT utilizing the piggy-back technique. Laboratory and clinical data were retrieved from medical records.
Results: Table 1. shows the demographic, clinical, pre- and perioperative characteristics of the hATTR patients.Follow-up: Case 1: Two years after HT and eight months after LT, the patient has good cardiac and hepatic function with no signs of neurologic progression. Case 2. A month after the transplant, the patient has been discharged home, with normal function of both transplanted organs.
Conclusions: Highly selected patients with hATTR and predominant heart involvement resulting in refractory heart failure can be considered as candidates for HT; however, SHLT or CHLT may be considered as they remove the source that produces the mutant protein. The LAHT approach poses a risk for further disease progression and immunological complications. The CHLT approach presents challenges, such as prolonged surgical times, yet provides immunological benefit due to single donor exposure and simultaneous resolution of ATTR formation. In our experience, both approaches have comparable early postoperative outcomes; long-term outcomes remain to be determined, with expected benefits from the CHLT approach.

Pre-operative variables	Case 1 LAHT	Case 2 CHLT	Perioperative variables	Case 1 LAHT		Case 2 CHLT	
				Heart	Liver	Heart	Liver
Age (yrs)	57	47	Donor sex	F	M	M	M
Sex	M	M	Donor age (yrs)	50	56	21	21
Mutation	Asp38Glu	Asp38Glu	EC	YES	NO	YES	NO
Polyneuropathy	moderate	mild	TIT (min)	232	270	209	605
CMP	restrictive	restrictive	CIT (min)	-	220	-	540
LVEF%	30	45	WIT (min)	-	50	-	65
Ascites	NO	YES	Domino	-	NO	-	NO
MELD score	11	13	AST 1/7/discharge	-	2148/39/28	-	1289/21/23
Child-Pugh score	A	B	ALT 1/7/discharge	-	1046/116/55	-	677/47/31
			PT (%)	-	76/87/96	-	97/85/114
			ICU stay (days)	6	4	6	6
			AR	NO	NO	NO	YES
			Hospital stay (days)	30	18	31	31

AR – acute rejection; CIT – cold ischemia time; CMP – cardiomyopathy; EC- extracorporeal circulation; ICU – intensive care unit; LAHT – liver after heart transplantation; MELD – Model of End-Stage Liver Disease; PT – prothrombin time; TIT – total ischemia time; WIT – warm ischemia time

MPS1_9 LEFT VENTRICULAR ASSIST DEVICES AS BRIDGE-TO-TRANSPLANTATION IN A LOW ORGAN DONOR ENVIRONMENT

Michael Bonios[1], **Dimitris Miliopoulos*[1], Iakovos Armenis[1], Angeliki Gkouziouta[1], Evangelos Leontiadis[1], Eirini Kitsou[1], Dimitris Zarkalis[1], Konstantinos Ieromonachos[1], Panagiota Georgiadou[1], Dimitrios Degiannis[1], Nektarios Kogerakis[1], Sokratis Fragkoulis[1], Antigoni Koliopoulou[1], Themistoklis Chamogeorgakis[1], Stamatis Adamopoulos[1]**

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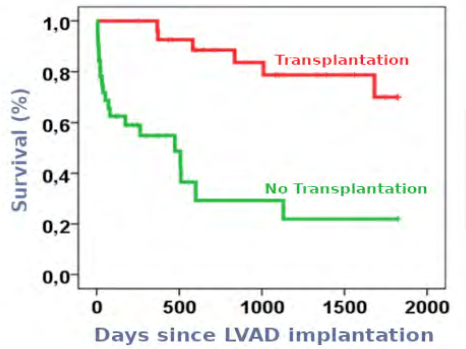
Background: In advanced heart failure patients, left ventricular assist devices (LVAD) are the optimal treatment option as bridge-to-transplantation. What is the outcome of LVAD use in a low organ donor environment?
Methods: 60 heart failure patients who underwent LVAD implantation as bridge-to-transplantation were included in the study. The patient characteristics and outcomes of those who managed to reach heart transplantation (HTx group) were compared with those (noHTx group) who did not in a 5-year period after LVAD implantation.
Results: 26 out of 60 patients underwent heart transplantation. The transplantation was performed 691 ± 538 days after LVAD implantation. 5-year survival rates were 70% for the HTx group and 21% for the noHTx group. Patients of the noHTx group were supported with intra-aortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) at a higher percentage compared to the HTx group (65% vs. 35%, p=0.02) and had a lower cardiac index (1.6 ± 0.3 L/min/m² vs. 1.9 ± 0.6 L/min/m², p=0.02) at the time of LVAD implantation. Cox proportional hazard regression analysis with time to transplantation as a varying coovariate showed that heart transplantation did not have any survival benefit for the follow-up period (CI=0.6 ± 6.2, p=0.263). 5-year survival rate of the transplanted patients was 70%.
Conclusions: LVAD supported patients who did not undergo heart transplantation had a more severe clinical condition at the time of device implantation along with increased mortality during the early post-operative period compared to those who did achieve heart transplantation. Future improvements of the technical characteristics of LVADs is expected to provide additional benefits in low organ donor environment.



MPS1_10 INITIAL EXPERIENCE WITH LOCAL LABORATORY RUN ASSAY TO DETECT DONOR-DERIVED CELL FREE DNA FOR NONINVASIVE DIAGNOSIS OF ACUTE MYOCARDIAL REJECTION

Stefania Manno[*1], **Laura Borgese[1], Annamaria Minervini[1], Marco Masetti[1], Laura Giovannini[1], Arianna Orsini[1], Bianca DE Nicolo[1], Maria Francesca Scuppa[1], Chiara Baldovini[1], Barbara Corti[1], Elena Bonora[1], Luciano Potena[1]**

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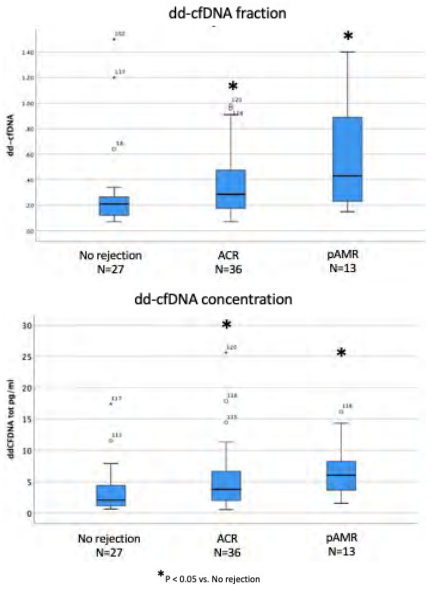
Background: Diagnosis of rejection in heart transplantation (HT) still relies on histopathology analysis of endomyocardial biopsies (EMB), despite limited by invasiveness and low reproducibility across pathologists. Donor-derived cell-free DNA (ddcfDNA) is a sensitive biomarker of graft injury and is proposed to rule out rejection in heart transplant (HT) recipients. However, the vast majority of available data refer to assays performed by centralized laboratories in USA, reporting ddcfDNA as a fraction of total cfDNA. The clinical validation and repeatability of a local laboratory assay in Europe (Alloseq) is lacking, and the role of absolute concentration of ddcfDNA in detecting rejection is limited.
Methods: Among patients receiving a protocol or for-cause EMB in 2017-2021, we selected those with available biobanked plasma. ddcfDNA was measured in our laboratory using MiSeq Illumina platform, according to the AlloSeq cfDNA protocol (CAREDx, San Francisco, CA, USA). Significant rejection was defined as ACR grade ≥ 1B and pAMR grade ≥ 1. ddcfDNA was expressed as % of total cfDNA and as absolute concentration in pg/ul.
Results: We assayed samples coupled with 78 EMBs (9[3-25] months after HT), of which 51(65%) from cases of EMB-proven rejection. Both ddcfDNA fraction (p<0.01) and ddcfDNA concentration (p<0.01) were higher in samples with rejection. Both ddcfDNA fraction and concentration were highest in AMR samples and intermediate in ACR (figure). ROC curve analyses identified a ddcfDNA cut off of 0.25% with the best predictive accuracy for rejection with 59% sensitivity and 70% specificity, and a ddcfDNA concentration of 2.4 pg/ul accounting for a 71% sensitivity and 63% specificity
Conclusions: In this preliminary experience with AlloSeq cfDNA in a selected cohort of samples with high rate of rejection, we found that both fraction and absolute concentration of ddcfDNA increase in presence of AMR and ACR. In this cohort the threshold for fraction of ddcfDNA was different than previous studies, and concentration seems to provide better diagnostic accuracy. While confirming that ddcfDNA is a powerful biomarker indicating the likelihood of AMR and ACR, further prospective studies are needed to validate optimal thresholds in context of local laboratories, and the role of concentration over fraction of ddcfDNA.



MODERATED POSTER

Moderated poster session on infections complications in kidney transplantation

MPS2_1 BKEVER STUDY: BKV CLEARANCE IN KIDNEY TRANSPLANT RECIPIENTS AFTER REPLACEMENT OF MMF BY EVEROLIMUS AND REDUCTION OF IMMUNOSUPPRESSION

Sophie Caillard*[1], Dominique Bertrand[2], Maite Jaureguy[3], Dany Anglicheau[4], Laure Ecotiere[5], Matthias Buchler[6], Nicolas Bouvier[7], Betoul Schvartz[8], Jean-Philippe Rerolle[9], Anne Elisabeth Heng[10], Lionel Couzi[11], Agnes Duveau[12], Emmanuel Morelon[13], Yannick Le Meur[14], Leonard Golbin[15], Eric Thervet[16], Ilies Benotmane[1], Samira Fafi Kremer[1]

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Background: BK virus nephropathy, a consequence of intense immunosuppression, remains a major problem after kidney transplantation. In this context, developing strategies to avoid BKV nephropathy is currently a major challenge. mTor inhibitors are immunosuppressive drugs which have shown anti-viral effects. Previous non randomized studies suggested an inhibitory role of mTor inhibitors on the proliferation of BK Virus. The aim of our study was to evaluate the effect of everolimus on BKV clearance compared to a simple reduction of immunosuppression in kidney transplant patients who develop a BKV viremia.
Methods: we conducted a French randomized multicenter study including 130 patients at the time of apparition of BK viremia. In 65 patients (experimental group), MMF was replaced by everolimus concurrently with a calcineurin inhibitors decrease, whereas in 65 patients, MMF was decreased by 50% (control group) with a lowering in calcineurin inhibitors in the same ranges (T0 tacrolimus 4-6 or ciclosporin 50-75 ng/ml). The primary endpoint was the percentage of patients achieving a viral clearance at 6 months and secondary endpoints included BKV replication kinetics, incidence of BKV nephropathy, graft function, incidence of rejection, and tolerance within 2 years after randomization.
Results: patients were comparable at baseline within both groups. At 6 months, BKV viral clearance was 56% in the experimental group vs 81% in the control group (p=0.002). The decrease of BK viral load was more rapid in the control group (p<0.001). Trough levels of calcineurin inhibitors were not different between both groups from randomization to month 6 and were in the expected targets. Two grafts were lost throughout the study (one in both group, one from pyelonephritis and one due to rejection). Nine patients developed a proven biopsy BKV nephropathy in the experimental group and 6 in the control group. There was no difference in rejection episodes or de novo donor specific antibodies occurrence between both groups.
Conclusions: in this randomized study, replacing MMF by everolimus together with reduction of CNI targets in the same levels was not associated with a more frequent clearance of BK virus at 6 months. Another (preventive ?) strategies should be identified to avoid BK nephropathy in kidney transplant recipients.

MPS2_2 OUTCOME OF KIDNEY TRANSPLANTS FROM VIREMIC AND NON-VIREMIC HEPATITIS C VIRUS POSITIVE DONORS INTO NEGATIVE RECIPIENTS: RESULTS OF THE SPANISH REGISTRY

Antonio Franco*[1], Francesc Moreso[2], Patricio Más Serrano[3], Marta Crespo[4], Nuria Esforzado[5], Asunción Sancho[6], Javier Paul[7]

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Background: Hepatitis C virus(HCV) positive kidney donors offer acceptable results. However, in Spain, only 24 out of 43 adult renal transplant units accept kidneys obtained from HCV non-viremic donors and 9 from HCV viremic donors. The aim of this study is to compare patient and graft outcome in recipients from HCV non-viremic and viremic donors.
Methods: This is an observational, multicenter, prospective study including all kidney transplants from HCV positive donors into negative recipients reported to the Spanish registry from May 2013 to December 2021. Viral RNA in donor was performed with the Xpert HVC viral load quantitative assay (Cepheid). Recipients from viremic donors received peri-transplant treatment with glecaprevir and pribentasvir for 8-12 weeks. Donor and recipient age and gender, panel reactive antibodies ,HLA mismatch, recipient weight , cold ischemia and the percentage of induction treatment, retransplant recipients, asistolic donors were similar in both groups.
Results: We included 116 renal recipients,75 from 44 non-viremic HCV positive donors and 41 from 25 viremic donors. Primary non function, delayed graft function, acute rejection rate and renal function at the end of follow up were not different between groups. None of the recipients from non-viremic donors(75) or from viremic donors receiving treatment before transplant(26) developed viremia but recipients from viremic donors starting treatment after transplantation (n=15) showed viremia in all cases. All recipients from viremic donors had a negative HCV viral load at 14 days and at 12 weeks after transplant. All patients from viremic donors completed treatment with glecaprevir and pribentasvir without reported adverse events or treatment interruptions. HCV seroconversion was more frequent in recipients from viremic donors (80.0% vs. 16.4%, p<0.001). Patient and graft survival were not different between recipients from viremic(1) and non-viremic donors(2).
Conclusions: Donor HCV viremia is not a risk factor for kidney transplant recipients receiving direct-acting antiviral agents in the peri-transplant period but virémia can only be avoided if treatment starts before transplantation

Patient survival at 12 and 24 months Graft survival at 12 and 24 months	93.3% 93.3%(1) 84.7% 80.0%	94.4% 92.0%(2) 90.7% 83.7%	0.65

MODERATED POSTER

Moderated poster session on infections complications in kidney transplantation

MPS2_3 LATE OPPORTUNISTIC INFECTIONS AFTER KIDNEY TRANSPLANTATION IN THE ERA OF CONTEMPORARY IMMUNOSUPPRESSION: ROOM FOR IMPROVEMENT

Violaine Esnault[1;2], Léa Hoisnard[3;4], Bastien Peiffer[5], Vincent Fihman[6], Slim Fourati[6], Cécile Angebault[6], Cécile Champy[7], Sébastien Gallien[1], Philippe Attias[8], Antoine Morel[8], Philippe Grimbert[8], Giovanna Melica[1], Marie Matignon*[8;9]

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Background: Opportunistic infections (OI) remain a major concern after kidney transplantation (KT). While antimicrobial prophylaxis during the first-year post-KT is well codified, focus on late OI is scarce but would prove helpful for preventive strategies. We performed a single center retrospective cohort study over a ten-year period to describe time-dependent OI after KT.
Methods: We defined three groups of patients: (i) late OI occurring beyond the first-year after KT, (ii) early OI within the first-year after KT and (iii) control group without OI surviving at least one year after KT. Primary endpoints were patient and allograft survival. Secondary endpoints were late and early OI description and comparison.
Results: One-hundred-eighty-five KT recipients developed at least one OI episode within 21 (8-45) months after KT. Among those, 120 were late (64.9%) and 65 early (35.1%) OI. Three-year patient survival was similar between the late and early OI groups (78.7% and 74.5%, p=0.6, respectively), as was three-year allograft survival (84.3% and 85.2%, p=0.99, respectively). Patient and allograft survival rates were also similar between late OI and control groups (Figure 1). Viruses were the leading cause of OI (65.4 %) including mostly zoster in late OI (43.4%) and BK virus nephropathy in early OI (31.6%) (Table 1). Fungal infections were the second cause of OI (23.2%). Pneumocystis was significantly more frequent among late OI (n=12 versus 0, p=0.012), while aspergillosis was significantly predominant among early OI (n=10 versus 3, p=0.01) (Table 1). Older age was significantly associated with early OI (OR 0.97 [95% CI 0.94-0.99], p=0.009) and the sole independent factor associated with mortality.
Conclusions: Our results suggest that the period at risk for OI spans beyond the first-year post-transplantation. We did not find significant deleterious effect of late and early OI on patient and allograft survival. Late OI mostly included zoster and pneumocystis while BK virus nephropathy and aspergillosis were predominant among early OI. Pretransplant screening of aspergillosis, systematic zoster vaccination and life-long pneumocystis prophylaxis should be considered to prevent OI after KT.

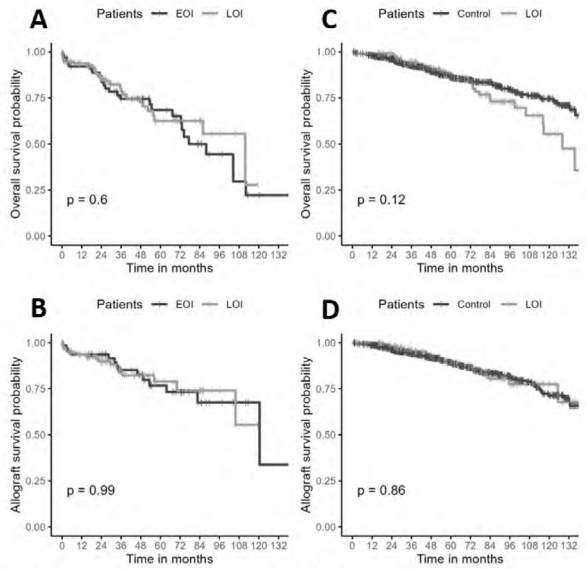

Figure 1: Impact of late OI versus early OI on overall survival (A) and allograft survival (B). Impact of late OI versus control group on overall survival (C) and allograft survival (D).

A and B curves begin at the occurrence of an OI. C and D curves begin at one-year post-transplantation.

Table 1: Description of late and early opportunistic infections

	Total N=185	Late opportunistic infection N=120	Early opportunistic infection N=65	p-value
Type of infection				0.33
Viral, N (%)	121 (65.4)	83 (69.2)	38 (58.5)	
Fungal, N (%)	43 (23.2)	25 (20.8)	18 (27.7)	
Bacterial, N (%)	11 (5.9)	5 (4.2)	6 (9.2)	
Parasitic, N (%)	10 (5.4)	7 (5.8)	3 (4.6)	
Viral infections	N=121	N=83	N=38	
Herpesviridae (CMV/HSV/VZV)	64 (52.9)	49 (59.0)	15 (39.5)	0.07
VZV	46 (38.0)	36 (43.4)	10 (26.3)	-
CMV disease	15 (12.4)	11 (13.3)	4 (10.5)	-
BK virus nephropathy	27 (22.3)	15 (18.1)	12 (31.6)	0.16
Norovirus/rotavirus/adenovirus	12 (9.9)	7 (8.4)	5 (13.2)	0.51
VHB/VHE	7 (5.8)	6 (7.2)	1 (2.6)	0.43
HHV8	11 (9.1)	6 (7.2)	5 (13.2)	0.32
Fungal infections	N=43	N=25	N=18	
***Aspergillus* spp**	13 (30.2)	3 (12.0)	10 (55.6)	0.01
***Pneumocystis jirovecii* pneumonia**	12 (27.9)	12 (48.0)	0 (0.0)	0.002
***Candida* spp**	11 (25.6)	7 (28.0)	4 (22.2)	0.74
Cryptococcosis	6 (14.0)	2 (8.0)	4 (22.2)	0.22
Mucormycosis	1 (2.3)	1 (4.0)	0 (0.0)	
Bacterial infections	N=11	N=5	N=6	
Legionella	5 (45.5)	3 (60.0)	2 (33.3)	
***Nocardia* spp**	2 (18.2)	0 (0.0)	2 (33.3)	
Tuberculosis	3 (27.3)	1 (20.0)	2 (33.3)	
Non-tuberculous mycobacteria	1 (9.1)	1 (20.0)	0 (0.0)	
Parasitic infections	N=10	N=7	N=3	
Microsporidiosis	2 (20.0)	2 (28.6)	0 (0.0)	
Cryptosporidiosis	5 (50.0)	3 (42.8)	2 (66.7)	
Toxoplasmosis	3 (30.0)	2 (28.6)	1 (33.3)	

MPS2_4 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN KIDNEY TRANSPLANT RECIPIENTS : A RETROSPECTIVE MULTICENTER NATIONWIDE COHORT STUDY

Adelaide Sanson[1;2], Helene Francois[3], Yannis Lombardi*[4]

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Background: Progressive multifocal leukoencephalopathy (PML) is a rare, serious, opportunistic infectious disease caused by JC virus, which usually leads to death in less than a year. Whether PML frequently occurs in kidney transplant recipients is unclear. Belatacept is an analogue of human immunoglobulin CTLA4, used as an immunosuppressive therapy in kidney transplant. In comparison with calcineurin inhibitors, belatacept is associated with an increased risk in some opportunistic infections such as CMV-associated disease, but the relationship between belatacept and PML is unclear. In this study, we aim to estimate incidence of PML in kidney transplant recipients and to identify a possible association between belatacept and PML.
Methods: We performed a retrospective, multicentric, national study. We contacted all transplantation centres in the country to retrieve cases of PML. We retrieved the number of grafts performed nationwide using registries from regulatory agencies. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR (cerebrospinal fluid and/or stereotactic brain biopsy).
Results: Between 2006 et 2020, 50 160 kidney grafts were performed. We contacted 35 centres, 26 (74%) responded. Collection of cases is still ongoing. To date, we retrieved 28 cases of confirmed PML. First case occurred in 2006, last case in 2022. 11 patients (39%) were men, median age at diagnosis was 68, mean estimated GFR was 41 ml/min/1.73 m², median time from transplantation was 10 years. Immunosuppressive regimen was detailed for 20 (71%) patients. 3 patients (15%) had received an immunosuppressive treatment before transplant. 7 patients (35%) had a history of treated rejection. 7 patients (35%) had received belatacept, mean belatacept exposure time was 33 months. 10 centers gave information on the percentage of belatacept-treated kidney transplant recipients locally: in 9 (90%) centers, less than 5% of recipients received belatacept; in 1 center, 14% of recipients.
Conclusions: In our nationwide study, PML rarely occurred following kidney transplantation. Further analyses are needed to explore a possible association between belatacept exposure and PML occurrence.

MODERATED POSTER

Moderated poster session on infections complications in kidney transplantation

MPS2_6 COMPASSIONATE USE PROGRAMME OF MARIBAVIR FOR ADULT PATIENTS WITH POST-TRANSPLANT REFRACTORY CMV INFECTION

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Background: Maribavir is a benzimidazole riboside that inhibits human CMV replication. Its European indication is “Treatment of adults with post-transplant CMV infection and/or disease who are refractory (with or without resistance) to one or more prior therapy”.
Methods: In France, patients were treated with maribavir prior to the European marketing authorization approval, through the compassionate use program (CUP). To be part of the CUP, patients had to fulfill the eligibility criteria (aligned with the pivotal study inclusion criteria (NCT02931539)) according to the protocol approved by the French health authority. An amendment to this protocol broadened the inclusion criteria in February 2022, with less stringent hematological and renal function cut-off values. The CUP data (from November 3, 2021 to September 30, 2022) at baseline (treatment access request or initiation visit) were analyzed using descriptive statistics to describe patient characteristics, maribavir use, effectiveness and safety data.
Results: The analyses were based on 47 patients with a completed treatment initiation study form. At access request, the median age was 58.6 years (range: 23.9 – 78.8). The majority had a solid organ transplant (n=40, 85.1%), mostly kidney transplant (n= 30, 75.0%). The proportion of patients with severe renal impairment at baseline (i.e. creatinine clearance ≤ 30 mL/min/1.73²) was 14.9% (n= 7). Resistance testing was performed for 44 (93.6%) patients, 30 (68%) of them had an identified mutation. The most frequently identified mutation was UL97, indicating a resistance to ganciclovir/valganciclovir in 23 (76.7%) cases. There were 12 (40%) mutations in the UL54 gene, indicating multidrug resistance to available antivirals.
Conclusions: A considerable effort from 41 French hospitals was undertaken to collect data from patients who enrolled the maribavir CUP in France, resulting in a high data completeness above 95%. In the CUP population compared with the pivotal study maribavir cohort, we observed a higher proportion of patients with SOT and identified antiviral resistance to conventional agent at baseline. Future analysis on effectiveness should provide further data.

MPS2_8 KIDNEY TRANSPLANTATION FROM DECEASED DONORS WITH BACTEREMIA

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Background: Deceased donor bacteremia is a major cause of kidney allograft discard because of the possible transmission of the infectious agent to the recipient. However, the long time on the waiting list renders the optimal use of available organs important.
Methods: A retrospective study that included all deceased donor recipients who underwent kidney transplantation between 1st/2008 and 12th/2021. A total of 102 of 614 recipients (49 male) with a median age of 52[43.5-58] years received a kidney transplant from 82 deceased donors, (45 men), with a median age of 55[46-61] years, with positive blood cultures at the time of organ procurement.
Results: The isolated pathogens were Gram-positive bacteria (64.6%), most frequently coagulase-negative staphylococcus, followed by Gram-negative bacteria (19.5%), and fungi 1.25%. Multidrug-resistant (MDR)/extensively drug-resistant (XDR) bacteria were observed in 18/82 (22%) of donors. Among 10/18 Gram-negative MDR/XDR isolates, *Acinetobacter baumannii* was the most common, followed by *Klebsiella pneumonia*. Two out of the 18 donors had bacteremia caused by *Enterococcus faecium and Staph. aureus*, respectively. Six out of 18 donors had positive blood cultures for gram(-)/gram(+) MDR bacteria. Early appropriate treatment was administered to 62/82 (76.8%) donors for a median of 5 [4-7] days before organ procurement. All recipients received targeted antibiotic therapy starting pre-operatively in 64/102 (62.7%) patients, whereas in 38/102 (37.2%) treatment started post transplantation (median of 4 [3-13] days post transplantation). No evidence of donor pathogen transmission to any recipient was noticed. Delayed graft function occurred in 28(27.5%) recipients. Patient and graft survival rates over 1-year period were 95% and 93 %, respectively.
Conclusions: Kidney transplantation from deceased donors with bloodstream infection is considered safe as long as the pathogen /infectious agent is known, provided that recipients receive appropriate antibiotic therapy. It is preferable that targeted treatment be administered to the donor as well.

MPS2_9 ADVANTAGES OF MONITORING CELLULAR IMMUNE RESPONSE AGAINST CYTOMEGALOVIRUS IN RENAL TRANSPLANTATION

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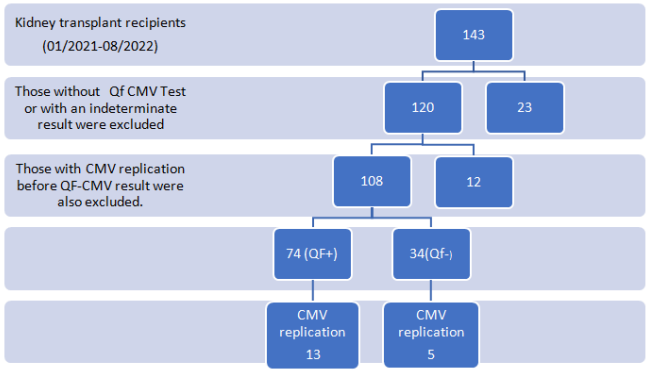
Background: Cytomegalovirus (CMV) infection is common after transplantation. The risk of infection is usually determined by D/R serology and the immunosuppressive regimen. QuantiFERON®-CMV is a test that measures cellular immune response to CMV. Our group has shown that QF-CMV is a predictive marker of CMV replication in renal transplantation. This study evaluates the clinical use of QF-CMV in the incidence of CMV infection/disease in renal transplant patients.
Methods: A prospective, observational study was conducted including all patients who underwent renal transplantation at our center between January 2021 and August 2022. These patients were tested for CMV reactivity using QF-CMV in the immediate post-transplant period. Universal prophylaxis or preemptive therapy was established depending on CMV risk of each patients (low: D+/R+, or high: D+/R- or induction, respectively). Per protocol, prophylaxis duration in high-risk QF-CMV reactive patients was based on the results of the QF-CMV test. The aim of the study was to compeer prophylaxis duration, the percentage of patients with CMV replication and the kind and duration of treatment of these patients (valganciclovir or IV ganciclovir) depending on the QF-CMV status.
Results: 112 kidney transplant patients were included. 68.5% of those (N=74) were QF-CMV reactive; 31.5% (N=34) were QF-CMV non-reactive and 4 patients were QF-CMV indeterminate. The QF-CMV reactive group was compared to the non-reactive group. There were no differences between the two groups in the variables analyzed at baseline. The QF-CMV reactive group had a CMV infection rate of 17.6% compared to 14.7% in the non-reactive group (p=0.73). Prophylaxis duration was shorter in QF-CMV reactive patients than QF-CMV non-reactive (66 days vs. 85 days for QF-CMV non-reactive, P=0.01). There were no differences in requirement for IV ganciclovir treatment (3 QF-CMV reactive patients vs. 1 QF-CMV non-reactive, P=0.8) or in CMV infection treatment duration (mean 19 days in QF-CMV reactive vs. 13 days in QF-CMV non-reactive, P= 0.46).
Conclusions: QF-CMV allows for individualized CMV prophylaxis duration, shortening it in QF-CMV reactive patients without increasing the risk of infection or disease. This would reduce the side effects associated with valganciclovir use and lower drug costs.

Patient Flowchart



	N			108
		QF reactive (N=74)	QF non reactive (N=34)	Statistical significance
Demographic variables	Age, median (p25-75)	58 (47-67)	59(45.5-65)	P=0.5
	Masculine gender	49 (66.2%)	26 (76.5%)	P=0.28
Transplant variables	Induction	56 (75.7%)	24 (70.6%)	P=0.57
	Receptor IgG CMV +	72 (98.6%)	26 (78.8%)	**P=0.01**
	HLA match, median (p25-75)	2(1-2)	2 (1-2)	P=0.39
	HLA mismatch (p25-75)	4 (4-5)	4(3-5)	P=0.23
	Cold ischemia time ,h (p25-75)	13(10-15)	13(10-15)	P=0.32
Replication	PCR CMV >1000 copies	13(17.6%)	5 (14.7%)	P=0.73
Valganciclovir treatment	Valganciclovir treatment	60 (81%)	32 (94.1%)	P=0.077
	Prophylaxis duration, days. median (p25-75)	66 (29-83)	85 (73-110)	**P=0.001**
	Treatment duration (mean, standard d)	19(44)	14 (31)	P= 0.46
Evolution	Nº Hospitalization First year postTx , median (p25-75)	1 (0-2)	1(0-1)	P=0.1
	Indication of Ganciclovir IV	3(4%)	1 (3%)	P=0.8

MPS2_10 LONG-TERM IMMUNE DYSREGULATION AFTER RITUXIMAB INDUCTION IN ABO INCOMPATIBLE LIVING-DONOR RENAL TRANSPLANTATION – IMPACT ON CHRONIC BK VIRUS INFECTION

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Background: We previously described a key role of IL-10 in chronic BK virus infection after renal transplantation. As an increased frequency of BK viremia has been reported after ABOi renal transplantation, we analyzed clinically relevant immune parameters in a prospective renal transplant study up to 5 years posttransplant.
Methods: Mononuclear cell subsets (peripheral blood; regional lymph nodes; protocol biopsies (n=58, 3 months; n=34, 1 year)), intracellular cytokine and in-vitro B cell responses were assessed up to 5 years posttransplant in 85 renal transplant recipients (living donation: n=25 ABO incompatible (ABOi; with rituximab induction) and n=30 ABO compatible (ABOc); deceased donation (DD): n=30, ABO compatible).
Results: The incidence of BK viremia was significantly enhanced in rituximab versus non-rituximab treated patients (P=0.009, 1 year; P=0.029, 5 years). Whereas intracellular IL-10 production was not increased in ABOi patients, IL-10R expression on monocytes was enhanced at 3 months (P=0.009 vs. DD, P=0.037 vs. ABOc) and 5 years (P=0.015 vs. ABOc). Cell subset analysis in protocol biopsies showed rituximab-induced B cell depletion in ABOi patients at 3 months (P<0.001 vs. ABOi and DD), but comparable B cell counts and even enhanced counts of CD3+ T cells (P=0.041), CD68+ macrophages (P=0.021) and CD138+ plasma cells (P=0.033) at 1 year. After rituximab induction in ABOi recipients, peripheral blood B cell subsets were profoundly downregulated for at least 3 years together with impaired B cell responses for 2 years (P=0.010, T-dependent; P=0.053, T-independent). T cell counts were lower in ABOi versus ABOc recipients up to 6 months (CD4+ T cells, 6 months P=0.046; CD8+ T cells, 3 months P=0.011). In regional lymph nodes of ABOi patients, we found a significant rituximab-induced downregulation of CD20+ B cells (P<0.0005), of naive B cells (P=0.031) and short lived plasma cells (P<0.0005) at the time of transplantation.
Conclusions: An increased frequency of BK viremia in rituximab-treated renal transplant recipients may be explained by increased IL-10R expression, downregulated CD4+ and CD8+ T cell counts, a profoundly delayed B cell repopulation together with compromised B cell responses and compromised antigen presentation due to B cell depletion in the graft and regional lymph nodes.

MPS3_1 SAFETY AND EFFICACY OF TIXAGEVIMAB/CILGAVIMAB FOR PRE-EXPOSURE PROPHYLAXIS IN KIDNEY TRANSPLANT RECIPIENTS: A MULTICENTER RETROSPECTIVE COHORT STUDY

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Background: Immunocompromised patients show an impaired vaccine response and remain at high risk of severe COVID-19, despite full vaccination. Neutralizing monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 have been developed for prophylaxis and treatment. No data are available regarding the safety and efficacy of the combination tixagevimab/cilgavimab used as pre-exposure prophylaxis (PrEP) of COVID-19 in kidney transplant recipients (KTRs) during Omicron period.
Methods: Between March 1, 2022, and October 3, 2022, we conducted a multicenter retrospective cohort study including 253 KTRs of whom 98 treated with tixagevimab/cilgavimab 150 mg/150 mg and 155 who received four doses of BNT162b2 mRNA vaccine without prophylaxis [Table 1]. The severity of COVID-19 was classified: no symptoms; mild symptoms (cough, fever, sore throat, asthenia, anorexia, nasal congestion, headache, muscle pain) without radiological findings of pneumonia; moderate/severe symptoms (dyspnea with or without need for oxygen with non-invasive or invasive ventilation, chest imaging showed bilateral pneumonia, shock, multi-organ failure, need for hospitalization).
Results: Only 13.3% of patients developed Sars-Cov-2 infection after the administration of tixagevimab/cilgavimab, (p=0.00013). The largest proportion of infected patients remained asymptomatic (92.3% vs 54.7%), 7.7% had mild symptoms and none of them had severe disease, need for hospitalization or died (p=0.04) [Fig. 1A-B]. Using Kaplan-Meier curves we demonstrated the control group presented an early infection compared to the AZD7442 group (p=0.000014) [Fig. 1C]. Although not statistically significant, the anti-RBD titer at T0EV was lower among infected patients compared to KTRs who did not develop infection [Fig 1D]. No changes in eGFR and proteinuria, assessed before and after the administration, has been observed [Fig 1 E-F].
Conclusions: In conclusion, our study show that tixagevimab/cilgavimab 150/150 mg is effective and safe in preventing infection and severe disease when administered to patients with weak or no response to Covid-19 vaccine.

Table 1 | Patient characteristics

Variables	Tixagevimab/cilgavimab group (n= 98)	Control group (n=155)
Age, yr, median [IQR]	56 [48-64]	62 [52-69]
Sex, n [%]		
Male	60 [61.2]	100 [64.5]
Female	38 [38.8]	55 [35.5]
eGFR (ml/min/1.73 m2), median [IQR]	45.5 [36-60]	52 [39-69.5]
BMI, kg/m2, median [IQR]	25 [22-28]	25 [23-27.5]
Hypertension, n [%]	82 [83.7]	136 [87.7]
Diabetes, n [%]	16 [16.3]	24 [15.5]
Cardiovascular disease, n [%]	33 [33.7]	34 [21.9]
Liver disease, n [%]		
HBV-related	0 [0]	10 [6.5]
HCV-related	2 [2]	5 [3.2]
Malignancies, n [%]	9 [9.2]	23 [14.8]
History of Sars-CoV-2 infection, n [%]	17 [17.3]	26 [16.8]
Type of donor, n [%]		
Deceased	81 [82.7]	142 [91.6]
Living	17 [17.3]	13 [8.4]
Months from kidney transplantation, median [IQR]	14 [7-66]	106 [62.5-187.5]
Retransplantation, n [%]	13 [13.3]	14 [9]
Immunosuppressants, n [%]		
CNI[a]	97 [99]	143 [92.3]
Antimetabolites[b]	81 [82.7]	115 [74.2]
Steroids	94 [95.9]	137 [88.4]
mTORi[c]	8 [8.2]	24 [15.5]

Abbreviations: yr years; BMI body mass index; eGFR, estimated Glomerular Filtration Rate (Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation).
[a]Includes tacrolimus or cyclosporine
[b]Includes mycophenolate mofetil, mycophenolic acid, or azathioprine
[c]mTORi mammalian target of rapamycin inhibitors including sirolimus and everolimus

Figure 1

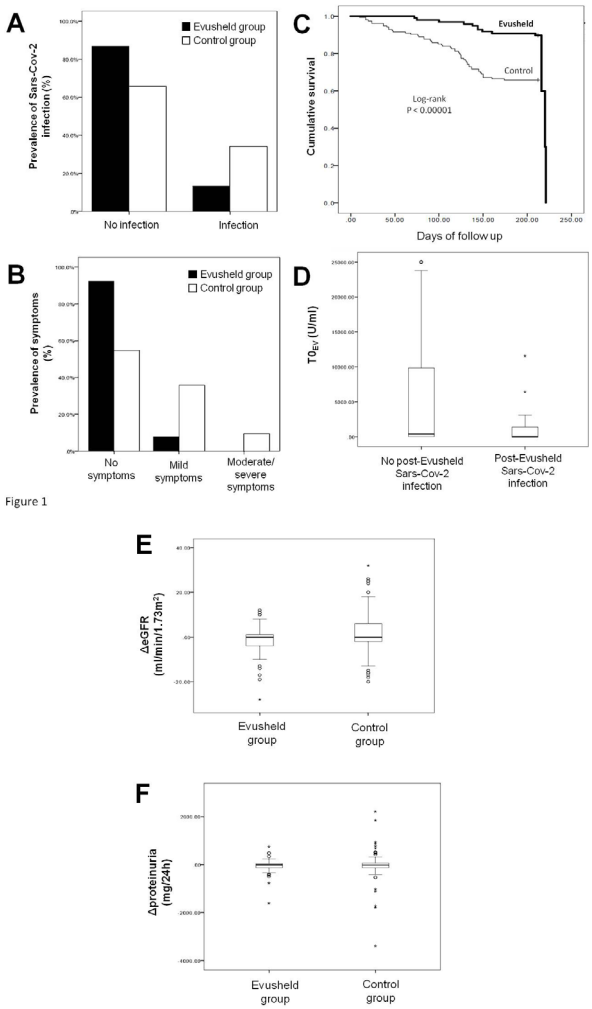

Figure 1

MPS3_2 THE IMPACT OF MONOCLONAL ANTIBODY AGAINST SARS-COV2 AND VACCINATION ON OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS WITH COVID-19

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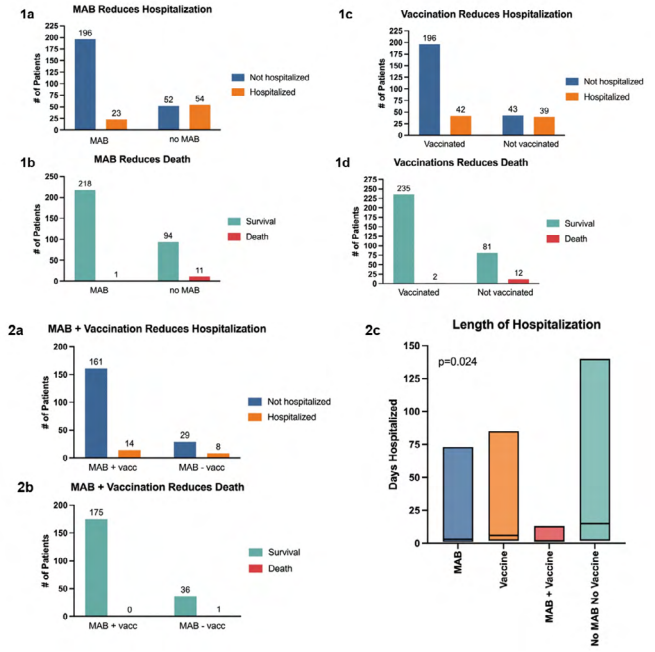
Background: Solid organ transplant recipients are at high risk of morbidity/mortality from coronavirus disease 2019(COVID-19). Studies suggest that monoclonal antibody(MAB) treatment against the SARS-CoV-2 spike protein may decrease hospitalizations. Herein, we report our single center experience with use of MAB for COVID-19 treatment in kidney transplant recipients(KTRs).
Methods: We performed a retrospective review of all KTRs who developed COVID-19 from 7/2020 to 11/2022 at our center. Date of diagnosis, vaccine status, MAB treatment, hospitalization including length of stay and patient outcome was reviewed.
Results: 331 KTRs tested positive for SARS-CoV-2 in the period reviewed. 219(66%) KTRs received MAB treatment. Hospitalization was lower in those receiving MAB (10.5% vs 50.9%, p<0.0001, Fig 1a). KTRs who received MAB had better survival than those who did not (99.5% vs 88.7%, p<0.0001, Fig 1b). SARS-CoV2 vaccination was associated with better survival (98.7% vs 87.1%, p<0.0001, Fig 1d). Hospitalization rate was lower in those vaccinated prior to infection(17.6% vs 41.9%, p<0.0001, Fig 1c). The combination of MAB and vaccination decreased hospitalization compared to unvaccinated KTRs who received MAB (8% vs 21.6%, p=0.014, Fig 2a). Utilizing one-way ANOVA we found that length of hospitalization (LOH) was decreased for KTRs who were either vaccinated, received MAB or both compared to those who were unvaccinated and did not receive MAB (Figure 2c, p=0.024). Median LOH for the unvaccinated/no MAB group was 15 days vs 2 days for those vaccinated and treated with MAB.

Conclusions: MAB treatment for COVID-19 and prior vaccination were associated with improved survival and decreased risk of hospitalization in kidney transplant recipients.

Table 1. Summary of Patients by MAB Treatment, Vaccination Status, MAB + Vaccination Status

	MAB treatment (n=219)	No MAB treatment (n=106)	p	Vaccinated (n=238)	Not Vaccinated (n=93)	p	MAB + Vaccine (n=175)	MAB, no vaccine (n=37)	p
Hospitalized, n (%)	23 (10.5)	54 (50.9)	<0.0001	42 (17.6)	39 (41.9)	<0.0001	14 (8.0)	8 (21.6)	0.014
Not Hospitalized, n (%)	196 (89.5)	52 (49.1)		196 (82.4)	54 (58.1)		161 (92.0)	29 (78.4)	
Survival, n (%)	218 (99.5)	94 (88.7)	<0.0001	235 (98.7)	81 (87.1)	<0.0001	175 (100)	36 (97.3)	0.029
Death, n (%)	1 (0.5)	11 (10.3)		2 (0.8)	12 (12.9)		0 (0)	1 (2.7)	



MPS3_3 REPEATED COVID-19 VACCINATION OF IMMUNOCOMPROMISED KIDNEY TRANSPLANT RECIPIENTS LEADS TO THE INDUCTION OF A FUNCTIONAL T CELL SUBSET ASSOCIATED WITH ANTIBODY PRODUCTION

Yvette den Hartog*[1], Reshwan Malahe[1], Marjolein Dieterich[1], Lennert Gommers[1], Debbie van Baarle[2], Frederike Bemelman[3], Dimitri Diavatopoulos[4], Ron Gansevoort[2], Corine Geurts van Kessel[1], Renate van der Molen[4], Esther Remmerswaal[3], Jan-Stephan Sanders[2], Luuk Hilbrands[4], A. Lianne Messchendorp[2], Marcia Kho[1], Marlies Reinders[1], Rory de Vries[1], Carla Baan[1]

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Background: Spike (S) specific memory T cells play an important role in the control of a SARS-CoV-2 infection. However, the immunogenicity of COVID-19 vaccines is severely hampered in kidney transplant recipients (KTR), and little is known about the phenotype of T cells induced by vaccination. Here, we investigated cytokine profiles that were produced by memory T cells obtained after alternative repeated COVID-19 vaccination strategies of KTRs, and correlated these cytokine profiles to antibody production.
Method: KTRs (n=92) without detectable antibodies after two or three doses of an mRNA-based vaccine were randomized to receive 100 µg mRNA-1273 (n=31), 2x 100 µg mRNA-1273 (n=29) or Ad26.COV2.S (n=32). Whole blood obtained pre and 28 days post vaccination was stimulated with peptides covering the S protein in a commercially available IFN-γ release assay (QuantiFERON, QIAGEN). After stimulation, cytokines (IL-2, -4, -5, -6, -9, -10, -13, -17A, -17F, -22, IFN-γ and TNF-α) were measured in plasma by a multiplex bead assay. Patients were clustered to identify cytokine production profiles via unsupervised clustering. Cytokine clusters and levels of S1 specific binding antibodies were compared pair wise by a Mann-Whitney U test.
Results: Clustering analysis revealed three distinct cytokine profiles. Cytokine profile 1 was characterized by significantly higher concentrations of Th1 (IL-2, IFN-γ, and TNF-α) and Th2 (IL-4, -5 and -13) cytokines in comparison to the other two profiles. This was also significantly associated with higher S1 specific antibody production ($p<0.05$). Cytokine profile 2 and 3 differed in the concentration of IL-2, -6 and -10, but this did not result in a significant difference in antibody production. The identified cytokine profiles were not driven by the type of alternative vaccination strategies due to their even distribution across the profiles.
Conclusions: Repeated vaccination increased SARS-CoV-2 specific memory T cell cytokine responses in KTRs with an initially poor serological response to previous mRNA-based priming. Balanced memory T cell cytokine profiles were associated with a good SARS-CoV-2 specific humoral immune response. However, there was no significant impact of the type of alternative vaccination strategy on differences in memory T cell cytokine responses and profiles.

MPS3_4 INCIDENCE AND SEVERITY OF COVID-19 IN RELATION TO ANTI-RBD IGG ANTIBODY LEVEL AFTER COVID-19 VACCINATION IN KIDNEY TRANSPLANT RECIPIENTS

A. Lianne Messchendorp[1], Jan-Stephan Sanders[1], Alferso Abrahams[2], Pim Bouwmans[3], Frederike Bemelman[4], Rene van den Dorpel[5], Luuk Hilbrands[6], Céline Imhof*[1], Marlies Reinders[7], Theo Rispens[8], Maurice Steenhuis[8], Marc Ten Dam[9], Priya Vart[1], Aiko De Vries[10], Marc Hemmelder[3], Ron Gansevoort[1]

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Background: Kidney transplant recipients (KTRs) elicit an impaired immune response after COVID-19 vaccination, however its exact clinical impact remains unclear. Therefore we analysed the relationship between antibody levels after vaccination and the occurrence and severity of COVID-19 in a large cohort of KTRs.
Methods: All KTRs, living in the Netherlands, were invited to send a blood sample 28 days after their 2nd COVID-19 vaccination by a home-based finger-prick method for measurement of IgG antibodies against the receptor-binding domain of the SARS-CoV-2 spike protein (anti-RBD IgG). Information on COVID-19 was collected from the moment the blood sample was obtained until 6 months thereafter. Multivariable Cox and logistic regression analyses were performed to analyse which factors affected the occurrence and severity (i.e. hospitalization and/or death) of COVID-19.
Results: In total 12,159 KTR were approached of whom 3,828 agreed to participate and 2,885 were included in the analyses. Among those, 1,578 (54.7%) became seropositive (i.e. anti-RBD IgG level >50 BAU/mL). Seropositivity was associated with a lower risk for COVID-19, also after adjusting for multiple confounders, including socio-economic status and adherence to COVID-19 restrictions (HR 0.37 (0.19-0.47), p=0.005). When studied on a continuous scale, we observed a log-linear relationship between antibody level and the risk for COVID-19 (HR 0.52 (0.31-0.89), p=0.02). Similar results were found for COVID-19 severity.
Conclusions: In conclusion, antibody level after COVID-19 vaccination is associated in a log-linear relationship with the occurrence and severity of COVID-19 in KTRs. Therefore higher antibody levels, and not only reaching seropositivity, should be the aim of COVID-19 vaccination in KTRs. Immunosuppressed patients who have no or low antibody levels after vaccination should be offered repeat vaccinations, whether or not via alternative vaccination strategies, or passive immunization.

MPS3_5 TH1-DOMINANT CYTOKINE RESPONSES IN KIDNEY PATIENTS AFTER COVID-19 MRNA-1273 VACCINATION ARE ASSOCIATED WITH POOR HUMORAL RESPONSES

Yvette den Hartog*[1], Reshwan Malahe[1], Wim Rietdijk[1], Marjolein Dieterich[1], Lennert Gommers[1], Daryl Geers[1], Susanne Bogers[1], Debbie van Baarle[2], Dimitri Diavatopoulos[3], A. Lianne Messchendorp[2], Renate van der Molen[3], Esther Remmerswaal[4], Frederike Bemelman[4], Ron Gansevoort[2], Luuk Hilbrands[3], Jan-Stephan Sanders[2], Corine Geurts van Kessel[1], Marcia Kho[1], Marlies Reinders[1], Rory de Vries[1], Carla Baan[1]

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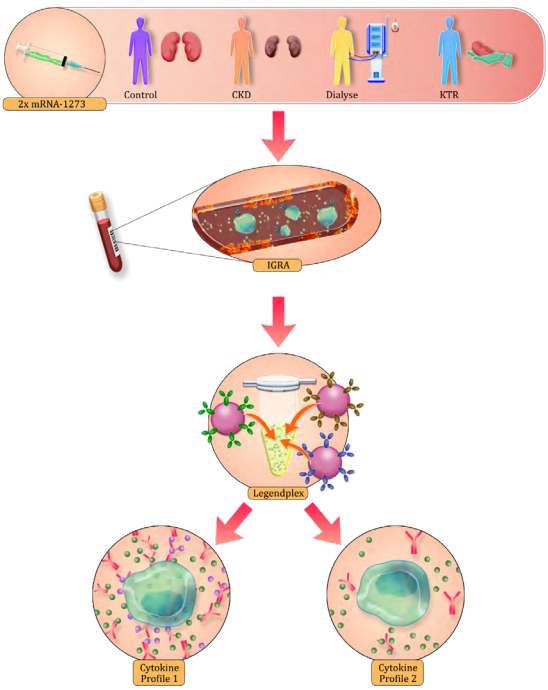
Background: T cells are fundamental in the control and clearance of viral infections and contribute to protective immunity by long-term immunological memory. The mRNA-1273 COVID-19 vaccine-induces durable SARS-CoV-2 Spike (S) specific T cell responses. Cytokines produced by these T cells are regulators of the immune response against SARS-CoV-2. However, little is known about the contribution of cytokine secreting memory T cells to the SARS-CoV-2 specific humoral immune response in immunocompromised kidney patients.
Methods: Patients on dialysis (n=38), with chronic kidney disease (CKD, n=37), kidney transplant recipients (n=67) and controls (n=42) were vaccinated twice with the mRNA-1273 COVID-19 vaccine. Whole blood obtained pre-vaccination, and 28 days post second vaccination, was stimulated with peptides covering the SARS-CoV-2 S protein in a commercially available IFN-γ release assay. After stimulation, cytokines (IL-2, 4, 5, 6, 9, 10, 13, 17A, 17F, 22, IFN-γ and TNF-α) were measured in plasma by a multiplex bead assay. Patients were clustered at 28-days after second vaccination to identify cytokine production profiles via unsupervised clustering.
Results: Unsupervised clustering analysis revealed two distinct vaccine-induced cytokine profiles. The first profile was characterized by high levels of T helper (Th)1 (IL-2, TNF-α and IFN-γ) and Th2 (IL-4, -5 and -13) cytokines, and low levels of Th17 (IL-17A and -22) and Th9 (IL-9) cytokines. This cluster was dominated by patients with CKD, on dialysis, and healthy controls. In contrast, the second cytokine profile contained predominantly KTRs producing mainly Th1 cytokines upon re-stimulation, with lower levels or absence of Th2, Th17 and Th9 cytokines. Multivariate analyses indicated that a balanced memory T cell response with production of Th1 and Th2 cytokines was associated with high levels of S1 specific binding and neutralizing antibodies mainly at 6 months after second vaccination.
Conclusions: In conclusion, seroconversion is associated with the balanced production of cytokines by memory T cells. This emphasizes the importance of measuring multiple T cell cytokines to understand their influence on seroconversion and potentially gain more information about the protection induced by vaccine-induced memory T cells.



MPS3_6 REPEATED COVID-19 VACCINATION ENHANCES MEMORY T-CELL IL-21 AND MEMORY B-CELL RESPONSES IN IMMUNOCOMPROMISED KIDNEY TRANSPLANT RECIPIENTS

Reshwan Malahe*[1], Yvette den Hartog[1], Debbie van Baarle[2], Frederike Bemelman[3], Dimitri Diavatopoulos[4], Ron Gansevoort[2], Daryl Geers[5], Corine Geurts van Kessel[5], Luuk Hilbrands[4], Marcia Kho[1], Ronella de Kuiper[1], A. Lianne Messchendorp[2], Renate van der Molen[4], Alicia Ras[1], Derek Reijerkerk[1], Esther Remmerswaal[3], Jan-Stephan Sanders[6], Rory de Vries[5], Marlies Reinders[1], Carla Baan[1]

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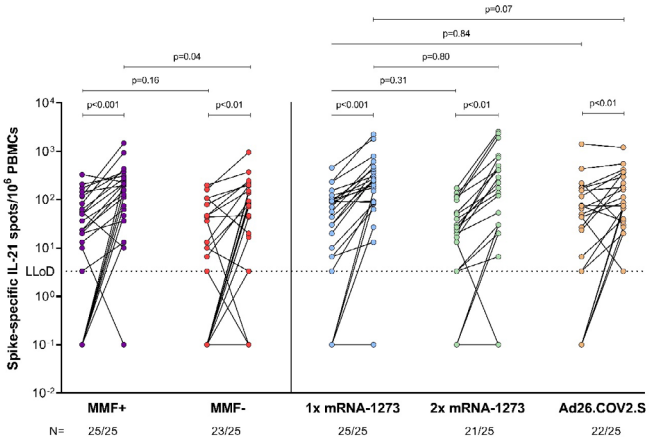
Background: COVID-19 vaccines are poorly immunogenic in kidney transplant recipients (KTR). For the development of virus-specific antibodies, T-cell mediated help to B-cells is required, in which the cytokine IL-21 plays a key role.
Methods: We compared three alternative vaccination strategies to a single dose mRNA-1273 vaccination (control): (1) a double dose of mRNA-1273 vaccination, (2) heterologous vaccination, and (3) temporary discontinuation of the immunosuppressant mycophenolate mofetil (MMF) in KTR with a poor serological response after two or three doses of an mRNA-based vaccine. They were randomized to receive 100 µg mRNA-1273 (n=25), 2x 100 µg mRNA-1273 (n=25) or Ad26.COV2-S vaccination (n=25). In addition, 50 KTR who received 100 µg mRNA-1273, were randomized to continue (MMF+, n=25) or discontinue (MMF-, n=25) MMF treatment for 2 weeks.
Results: All vaccination strategies resulted in a significant increase in the number of SARS-CoV-2-specific IL-21 producing T-cells and memory B-cells (both p<0.01, measured by ELISpot), except for the memory B-cell response in the double mRNA-1273 group. The IL-21 response was higher in the MMF+ group compared with the MMF- group (160 vs 77 spots/10^6 PBMCs, p=0.04), but did not differ between single mRNA-1273 (200), double mRNA-1273, (173), and Ad26.COV2-S (73). Also, the memory B-cell response did not differ between single mRNA-1273 (35), double mRNA-1273 (20), and Ad26.COV2-S (30), nor between the MMF+ (183) and MMF- (295) groups. Furthermore, both cellular responses correlated with the production of neutralizing antibodies (Spearman's ρ 0.52 and 0.86, respectively, both p<0.001).
Conclusions: Repeated vaccination enhances SARS-CoV-2-specific memory T and B-cell responses and antibodies in KTR with an initially poor serological response. A higher dose, a heterologous vaccination, or two weeks discontinuation of MMF were not superior in boosting these responses compared to a normal mRNA based vaccination dose. These findings support the recommendation for repeated vaccination in KTR.



MPS3_7 REAL-WORD EXPERIENCE OF SOTROVIMAB TO PREVENT SEVERE COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS: RESULTS FROM A NATIONAL STUDY

Nizar Joher[1], Kevin Ou[1], Pierre Trémolières[2], Lionel Couzi[3], Nassim Kamar[4], Sophie Caillard[5], Claire Presne[6], Nathalie Chavarot[7], Dominique Bertrand[8], Renaud Snanoudj[9], Philippe Gatault[10], Camille Peti-Hoang[11], Willy Kini Matondo[12], Philippe Grimbert[1], Marie Matignon*[1]

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Background: Sotrovimab, a monoclonal antibody active against the Omicron spike, has been used to prevent severe forms of Omicron induced COVID-19. Clinical data remain scarce in kidney transplant recipient (KTR).
Methods: We conducted a French retrospective multicenter study including all KTR with COVID-19 within the Omicron wave treated with sotrovimab. Study endpoints included occurrence of severe form (death, hospitalization or oxygen therapy) and serious adverse events (SAE) of sotrovimab infusion.
Results: We identified 302 KTR with mild-to-moderate COVID-19 treated with sotrovimab. Median age was 57 years. Table 1 depict patients characteristics. Fifty-six KTR (18.5%) had estimated glomerular filtration rate < 30 mL/min/1.73m2. Anti-Spike immunoglobulin G titer was ≥ 250 BAU in 102 (33.8%) despite vaccination in 266 (88%) KTR. A severe form of COVID-19 occurred in 42 (13.9%) cases with 7 deaths (2.3%) and 35 (11.6%) hospitalizations. Among hospitalized KTR, eight cases required intensive care support. Four deaths were due to a severe respiratory distress syndrome. Acute kidney injury was observed in 28 (9.3%) cases. No SAE of Sotrovimab infusion were reported. Being male, older age, chronic graft dysfunction and administration of Belatacept were associated with evolution to severe COVID-19 in univariate analysis.
Conclusions: Treatment with sotrovimab of mild-to-moderate COVID-19 in KTR in the Omicron BA.1 era prevent severe forms.

Table 1 Baseline characteristics at the time of COVID19 infection

Age (years), median [IQR]	57 [45-67]
Male, n (%)	177 (58.6)
Body mass index ≥ 30 kg/m², n (%)	59 (19,5)
Induction with T-cell depleting antibodies, n (%)	128 (42.4)
Maintenance regimen	
Calcineurin inhibitor + Mycophenolate + Steroid , n (%)	240 (79.5)
Belatacept, n (%)	34 (11.2)
Glomerular filtration rate before COVID-19	
30 > eGFR ≥ 15 mL/min/1.73m², n (%)	49 (16.2)
eGFR < 15 mL/min/1.73m², n (%)	7 (2.3)
Anti-SARS-CoV-2 vaccine doses before COVID-19	
0 doses, n (%)	36 (11.9)
2 doses, n (%)	27 (9)
≥ 3 doses, n (%)	239 (79.1)
Anti-S IgG titer before COVID-19 ≥ 250 BAU/ml, n (%)	102 (33.8)
Casirivimab/Imdevimab before COVID-19, n (%)	52 (17.2)
Tixagévimab/Cilgavimab before COVID-19, n (%)	18 (5.9)

MPS3_8 THE IMPACT OF EARLY THERAPIES FOR COVID IN A GROUP OF KIDNEY TRANSPLANT PATIENTS

Chiara Caletti[1], Elena Conto*[1], Nicolo Cacciatori[1], Stefano Andreola[1], Federica Baciga[1], Carolina Giannini[1], Alessandro Visentin[2], Elda Righi[2], Giovanni Gambaro[1]

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Background: The immunosuppressive therapy normally prescribed to solid organ transplant patients makes this category one of the most at risk for COVID 19 infection. We report the experience of a single kidney transplant centre evaluating 287 patients from March 2020 to January 2023.
Methods: Patients who died from virus unrelated causes, patients participating in the MANTICO single-blind study, and those who became infected with SarsCov2 before the transplant date were excluded. A total of 235 patients were eligible for the study.
Results: We have recorded 117 positive patients in this time frame (49.7 % of total). Among these, 47 patients did not receive early therapy (GROUP A), whereas 70 patients were eligible for monoclonal antibodies therapy (GROUP B). GROUP A patient, who were not eligible for early treatment or who became infected before these drugs were available, on average remained positive for 21 days with longer-lasting symptoms (about one week), reporting 36 surviving patients of whom 6 needed hospitalisation with a positive outcome (12.7%) and 10 patients who died (21% of GROUP A total infected). In GROUP B, on the other hand, we recorded just 3 patients requiring hospitalisation (4.2%) and no deaths. In addition, most of the GROUP B patients reported mild flu-like syndrome symptoms, lasting 3-4 days with an average of 14 days' testing positive (Tab1). No allergic reactions occurred in patients treated with monoclonal antibodies.
Conclusions: The advent of early therapies has drastically reduced mortality, morbidity and time to negative outcome in immunosuppressed patients.

Tab 1: Breakdown by type of monoclonal antibody administered and duration of positive test after therapy

Monoclonal Antibodies	Number of receving patients	Testing positive days average
Sotrovimab	43	12.5 days
Tixagevimab/Cilgavimab	24	12.9 days
Casirivimab/Imdevimab	9	16.9 days
Bamlanivimab/Etesevimab	2	28.5 days
Molnupiravir	1	30 days
Remdesivir	1	40 days

MPS3_9 SERONEGATIVE TRANSPLANT PATIENTS REMAIN AT SIGNIFICANT RISK OF SARS-COV-2 INFECTION AND COMPLICATIONS; WE ARE NOT OUT OF THE WOODS YET

Laszlo Szabo*[1], Verity Brooker[1], Tarique Sabah[1], Mark Ponsford[2], Georgios Koimtzis[1], Stephen Jolles[2], Kathryn Bramhall[2], Soma Meran[3], Usman Khalid[1;3], Ian Humphreys[3], Argiris Asderakis[1;3]

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Background: Our work in a transplant population has shown that, following the 2nd dose of a SARS CoV-2 vaccine, 43% of Astra-Zeneca (AZ) vaccinated patients seroconverted compared with 52.6% of mRNA/Pfizer leaving a considerable number of patients at risk
Methods: Our aim was to assess the impact of subsequent vaccine administration to the antibody (Ab) response (as measured by the Euroimmune assay) and risk of infection in this population. All PCR positive SARS-CoV-2 infections were recorded post 2nd dose and up to the introduction of monoclonal Abs in January 2022. We analysed infections, admissions and ICU stay according to the Ab results
Results: We analyzed 1294 samples in 881 patients. 523 patients had their sample tested after the 3d dose and 167 post the 4th. All but 3 patients received an mRNA vaccine. 380 patients (72.9%) seroconverted after the 3d dose compared to 79% following the 4th. The effect of the type of vaccine (AZ or mRNA) disappeared after the 3d dose, as patients received now an mRNA vaccine. After the 3d dose, 48% of the post 2nd dose Ab-negative patients became positive whilst 8.2% of positive patients became negative. In a multivariate regression analysis increased age (OR 0.96, p=0.001), use of mycophenolate derivatives (OR 0.29, p=0.001), and prednisolone (OR 0.55, p=0.010) had a negative effect on antibody response. Of note, 20/20 patients who were on rapamycin seroconverted following the 3d dose (11/19 post 2nd). Among the 262 patients with PCR confirmed SARS-CoV2 infection, from May 2021 to January 2022, 100 had a recent Ab sample. 63/297 (21.2%) of Ab negative patients got infected during this period compared to 37/513 (7.2%) of seropositive ones (p=0.0001, OR 3.46 CI 2.24-5.35). 17/20 patients admitted (OR 4.2) had no demonstrable Ab response at their latest pre-infection sample. 4/5 deaths and 3 of 4 admissions to ICU were in seronegative patients
Conclusions: 20% of transplant patients remain seronegative even after the 4th vaccine dose. MMF and prednisolone are the strongest predictors of a negative response. Seronegative patients are 3.4 times more likely to get an infection and 4.2 times more likely to be admitted compared to seroconverted patients. Better treatments are essential to protect the small but significant number of transplant patients at risk of severe disease due to SARS CoV-2

MODERATED POSTER

Moderated poster session on COVID-19

MPS3_10 SARS-COV-2 ANTIBODIES RESPONSE AFTER VACCINATIONS IN KOREAN KIDNEY TRANSPLANT RECIPIENTS

Kina Kim[*1], **Soohyun Kim[1], Hyejin Ryu[1], Dohsik Minn[1]**

[1]*Seegene Medical Foundation, Seoul, South Korea*

Background: Patients with kidney-related disease are at high risk of developing severe COVID-19. The risk of death from SARS-CoV-2 infection is particularly higher in kidney transplant recipients than in healthy individuals. SARS-CoV-2 vaccination is especially important in kidney transplant recipients, but antibodies response is limited due to immunosuppression therapy. We assessed the immune response of antibodies production after vaccinations in Korean kidney transplant recipients.

Methods: We included eighty-five Korean kidney transplant recipients who received full SARS-CoV-2 vaccination. We measured binding antibodies against the SARS-CoV-2 spike (S) protein receptor-binding domain and neutralizing antibody levels using surrogate viral neutralization test. Anti-SARS-CoV-2 S titer was quantitatively detected with a double-antigen sandwich-based electrochemiluminescence immunoassay (ECLIA), using the Cobas 8000 e801 (Roche Diagnostics, Mannheim, Germany). Neutralizing antibody levels were measured by ELISA method(R-FIND SARS-CoV-2 Neutralizing Antibody ELISA, SG Medical, Seoul, Korea).

Results: We divided the subjects into 4 groups (< 1, 1–2.4, 2.5–4.9, and ≥ 5-year) according to the time from renal transplantation to vaccination, and the number of patients in each group was 18, 11, 23, and 33, respectively. The means of anti-SARS-CoV-2 S were 3.2 U/mL, 27.8 U/mL, 370.2 U/mL, and 5,094.2 U/mL (P < 0.001), respectively, showing statistical differences. The neutralizing antibody titers (% inhibition rate) were 2.2%, 11.6%, 45.6%, and 93.0% (P < 0.001), respectively and statistically significant.

Conclusions: The shorter the time from transplantation to vaccination, the lower binding antibody and neutralizing antibody titers. The reason for these results is considered to be due to the strong immunosuppression state in the early stage of post-transplantation by the initial introduction treatment.

Moderated e-poster session on pancreas and islet transplantation

MPS4_1 CONTINUOUS VS DISCONTINUOUS HUMAN ISLET PURIFICATION: A MATCHED DONOR COMPARISON

Antoine Buemi[*1,2], **Nizar Mourad[2], Arnaud Devresse[1], Tom Darius[1], Nada Kanaan[1], Pierre Gianello[2], Michel Mourad[1]**

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[2]*UCLouvain Brussels Woluwe, Woluwe-Saint-Lambert, Belgium*

Background: By stopping distribution in Europe of COBE 2991, which is commonly used in standard isolation procedures, alternative purification methods are required without altering the quality and quantity of human islets. The aim of this study was to evaluate the effect of the purification method on the islet function and isolation performance from human organ donors used for research.

Methods: We compared n=4 human isolation procedures using a standard continuous islet purification with COBE 2991 with n=8 procedures using a discontinuous purification with a “bottle” method. For comparison, every pancreas donor of procedures using continuous purification was matched with two pancreas donors of procedures using discontinuous purification with a similar age, BMI and donor category source.

Results: Islet equivalents, purity and dynamic glucose-stimulated insulin secretion were evaluated. A similar islet yield was obtained using continuous purification compared to discontinuous purification (76292,5±40550,44 versus 79625±41484,46 islet equivalents, P = 0.89). Islets from both groups had similar purity (78,75%±19,73% vs 55%±18,16%, P=0,08) and functionality both in terms of stimulation index (3,31±0,83 vs 5,96±3,62, P=0,19) and in terms of insulin secretion (1,26±0,83 vs 1,53±1,40 mean AUC, P=0,73).
Moreover, the size of the islets purified by the “bottle” method was significantly larger than that of the islets purified by COBE purification (19,2%±10,3% vs 45,4%±18,8% of islets less then 100µm, P=0,0097 and 23,7%±5,3% vs 15,6%±5,8 % of 200-250µm islets size, P=0,03).

Conclusions: Discontinuous purification has no negative impact not only on the efficacy of the isolation process but also on the islet secretory function.

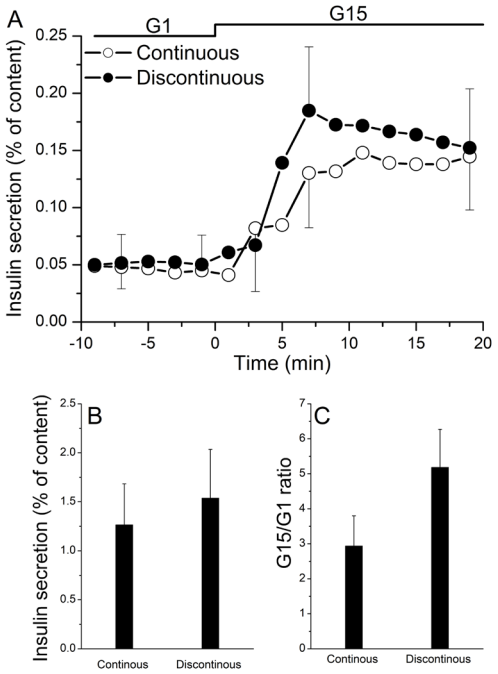


Table 1.
Donor demographics and ischemia times of 4 pancreas isolations using continuous purification matched with 8 pancreas isolations using discontinuous purification according to donor age, BMI and organ source

	Continous Purification (n=4)	Discontinous Purification (n=8)	p *value*
Donor Demographics			
Age, (years)	52,2±20,6	48±10,7	0,64
Gender, n			0,71
Male	2	4	
Female	2	4	
Weight (mean Kg±SD)	77±10,13	82,5±12,08	0,45
Height (mean cm±SD)	171±7,87	175,5±6,84	0,32
BMI (mean±SD)	27±1,8	26,8±3,7	0,8
Donor Organ Source, n			0,99
DBD	1	2	
DCD	3	6	
Cause of Death, n			0,76
CVA	3	5	
Trauma	0	3	
Cardiac Arrest	1	0	
Cardiac Arrest, n	1	4	0,45
Medical History			
HBP, n	1	1	0,62
Diabetes mellitus, n	0	0	0,99
Smoking, n	0	3	0,19
Drug Abuse, n	0	1	0,99
Alcohol Abuse, n	0	2	0,99
Infections	0	4	0,09
Malignancy, n	0	0	0,99
Vasopressor use, n	2	4	0,45
Laboratory Results			
Lipase, (mean U/l)	31±24,57	40,14±33,32	0,71
Amylase, (mean U/l)	171±68,46	81,66±71,98	0,19
Hemoglobine, (mean g/dl)	13,37±1,37	11,01±2,20	0,07
Ischemia time			
Cold Ischemia time, h (±SD)	15,19±5,33	17,33±3,47	0,41
Warm Ischemia time, min (±SD)	18±20,20	9±1,41	0,21
Total Ischemia time, h (±SD)	18,49±5,33	17,54±3,19	0,71

Abbreviations: BMI, body mass index; CVA, Cerebrovascular Accident; DBD, donation after brain death; DCD, donation after circulatory death; HBP, high blood pressure

MODERATED POSTER

Moderated e-poster session on pancreas and islet transplantation

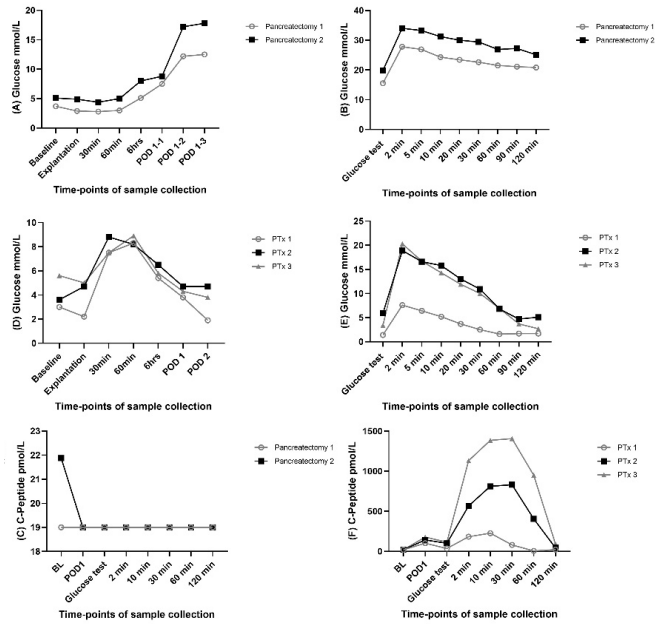
MPS4_2 NORMOTHERMIC EX SITU PANCREAS PERFUSION FOR THE PRESERVATION OF PORCINE PANCREAS GRAFTS

Laura Mazilescu*[1;2], Catherine Parmentier[2], Sangeetha Kalimuthu[3], Markus Selzner[2], Trevor Reichman[2]

[1]University Hospital Essen, Departments of Transplant and General Surgery, Essen, Germany, [2]University Health Network, Ajmera Transplant Centre, Toronto, Canada, [3]University Health Network, Department of Pathology, Toronto, Canada

Background: Pancreas transplantation improves and extends the life of patients with insulin dependent diabetes. Pancreata from extended criteria donors have been increasingly used due to the scarcity of available grafts. Normothermic ex situ pancreas perfusion (NESPP) can keep grafts metabolically active, potentially allowing for assessment and organ repair, and could improve outcomes of marginal grafts.
Methods: A novel NESPP technique was developed and tested. Porcine pancreata were removed after a short period of warm ischemia and subjected to 6hrs of NESPP. Perfusion parameters, potential graft assessment markers and graft injury were measured. Next, pancreata subjected to 3hrs of NESPP were transplanted and animals were followed for up to 3 days. Graft function and injury post-transplantation were evaluated.
Results: Using this novel system of perfusion, pancreata were perfused for an extended period of time with minimal edema. Histology at the end of perfusion showed intact islet cells with only mild signs of tissue injury. NESPP transplanted grafts showed immediate function after transplantation, with glucose levels in normal range.
Conclusions: NESPP maintains a physiologic environment and excellent graft function without causing significant graft injury. Porcine pancreas transplantation is feasible and allows for in vivo graft assessment of pancreas function and injury after NESPP.

Figure 1: Glucose levels after pancreatectomy with/without transplantation and after glucose stimulation test. (A) Glucose levels post-pancreatectomy. (B) Glucose levels after glucose stimulation test in pancreatectomy animals. (C) C-Peptide levels post-pancreatectomy and after the glucose stimulation test. (D) Glucose levels post-transplantation. (E) Glucose levels after glucose stimulation test in transplanted animals. (F) C-Peptide levels post-transplantation and after glucose stimulation test in transplanted animals. POD, postoperative day; POD 1-1, glucose levels on POD1 in the morning; POD 1-2, glucose levels on POD1 at noon; POD 1-3, glucose levels on POD1 in the afternoon. Glucose test, glucose levels before glucose injection; 2 – 120min, glucose levels at different time-points measured from the glucose administration time.



MPS4_3 EFFECT OF RECIPIENT BODY MASS INDEX ON OUTCOME OF PANCREAS TRANSPLANTATION: A SINGLE-CENTER 20-YEAR EXPERIENCE

Samrat Ray*[1], Catherine Parmentier[1], Trevor Reichman[1], Andrea Norgate[1], Zaneta Sawicka[1], Gonzalo Sapisochin[1], Ian Mcgilvray[1], Mark Cattral[1], Markus Selzner[1], Chaya Shwaartz[1]

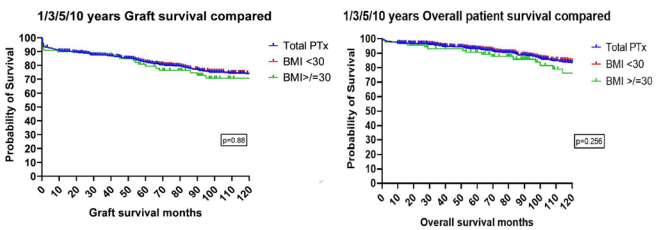
[1]Toronto general hospital, Toronto, Canada

Background: The prevalence of obesity in potential recipients for pancreas transplantation has increased in past decade. However, not much has been detailed in literature about impact of high body mass index (BMI) on short and long-term outcomes of pancreas transplantation. Aim of this study is to analyze the impact of recipient BMI on survival and morbidity following pancreas transplantation.
Methods: All patients undergoing pancreas transplantation (+/- Kidney) between January 2000 and December 2021 were retrospectively reviewed and included in the study and were categorized into 2 groups based on BMI (< 30 and >/=30 kg/m2). Donors and recipients' variables including perioperative variables, survival outcomes were reviewed and compared between the two cohorts.
Results: A total of 595 patients were included in the study period. The mean BMI of the cohort was 25.1 kg/m2 (14.2-45.9). Table 1 shows the comparison of the demographic and peri-operative variables between the 2 groups of the cohort. There was no significant difference in the 90-day mortality between the 2 groups (1.98% vs 2.25%; OR 0.87; p=0.69). Multivariate analysis showed no significant impact of recipient BMI alone on graft survival (HR:0.89; 95% CI: 0.24-1.45; p=0.09). The 1/3/5/10 year pancreas graft survival and overall patient survival were similar in patients with BMI <30 and >/=30 (p=0.88 and p=0.25). Similar results were observed with comparison of overall patient survival (Figure 1).
Conclusions: Obesity alone does not affect graft and overall disease-free survival in pancreas transplant recipients and should not be an exclusion criteria for pancreas transplantation.

Table 1: Pancreas transplant recipients with BMI < and >/= 30 compared

	BMI <30 (n=506)	BMI >/=30 (n=89)	P value
Median Donor BMI (IQR)	23.15 (20.7-25.9)	23.7 (21.1-27.2)	0.31
Males (%)	319 (53.6)	57 (64)	0.89
SPK transplant (%)	369 (73)	64 (72)	0.51
Pre-op Cardiac intervention (%)	181 (32)	34 (38.2)	0.27
Pre-op Infection (%)	42 (8.3)	11 (12.3)	0.22
Median POD 1 amylase (IQR)	13 (59-217)	100 (52-280)	0.77
Early (<1 yr) pancreas graft rejection (%)	34 (6.7)	8 (8.9)	0.49
Delayed renal graft function (%)	10 (1.9)	5 (5.6)	0.06
Portal vein thrombosis (%)	12 (2.4)	3 (3.3)	0.67
Duodenal leak (%)	58 (11.5)	16 (17.9)	0.11
Median Post-op length of stay days (IQR)	9.6 (7.9-13)	9.8 (7.9-13.5)	0.46

Figure 1:



MODERATED POSTER

Moderated e-poster session on pancreas and islet transplantation

MPS4_4 USING DIABETES TECHNOLOGY TO MANAGE HYPERGLYCAEMIA IN PEOPLE WITH TYPE 1 DIABETES AND FAILING PANCREAS TRANSPLANT

Thomas Johnston[*1], **Rebecca Hyslop[1], Dimitra Stathi[1], Janaka Karalliedde[1]**

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Background: Advanced hybrid closed loop systems (AHCLS- 'artificial pancreas') and similar diabetes technology have demonstrated glycaemic control benefits in people with diabetes, however these studies excluded people with end stage kidney disease (ESKD) or post transplant. There is limited clinical experience on using AHCLS and diabetes technology in people with type 1 diabetes who have had simultaneous pancreas and kidney pancreas (SPK) transplants with hyperglycaemia due to failing graft function.
Methods: In this case series, we share our experience of using continuous subcutaneous insulin infusion (CSII) therapy, AHCLS and related diabetes technology in 6 people with type 1 diabetes, who developed significant hyperglycaemia post successful SPK or pancreas only transplant between 2021 and 2022.
Time in range metrics and HbA1c pre and post intervention with diabetes technology was evaluated. All were on multiple daily insulin injections before intervention with diabetes technology. Four people were started on AHCL and 2 people on CSII with 'flash' glucose monitoring. Median (range) duration of follow-up was 15.8 months (1-36 months).
Results: Six people (5 males) aged between 34 and 50 years with mean (±SD) duration of diabetes at 36 years (±6.2). Five people had a SPK transplant and one patient had a pancreas only transplant. Median (range) duration between transplantation and diabetes recurrence was 3.5 years (3-9 years). Median (IQR) time in range (3.9 -10 mmol/l) glucose improved from 37% (24%-49%) to 56.6% (48%-62%) and HbA1c fell from 72.7 (72-79) to 64 (42-67) mmol/mol (p <0.05 for both) without a concomitant increase in hypoglycaemia. In parallel total daily dose of insulin fell and quality of life feedback assessed by questionnaire positive.
Conclusions: Use of 'artificial pancreas' diabetes technology improved glycaemic parameters in people with type 1 diabetes with SPK and failing pancreatic graft function. Early use of such therapies within a multidisciplinary clinic framework should be considered to improve diabetes control in this high-risk cohort.

MPS4_5 EARLY RELAPAROTOMY NEED AND RISK FACTORS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Catarina Cardoso[1], **Bruno Fraga Dias*[2], Patricia Domingues[3], Roberto Calças Marques[4], Catarina Ribeiro[5], José Silvano[5], Jorge Malheiro[5], Manuela Almeida[5], Sofia Pedroso[5], La Salete Martins[5]**

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Background: Simultaneous pancreas-kidney transplantation (SPKT) is a well-established treatment for patients with type 1 diabetes mellitus and end-stage renal disease.1 Despite outcomes have steadily improved as a result of better donor and recipient selection, optimized strategies in immunosuppression and advances in surgical technique, it still displays higher rate of complications and later hospital discharge when compared to kidney transplantation alone.
Methods: We performed a retrospective review of all SPKT conducted in our centre between January 2000 and December 2022. Data from medical records was incorporated. The primary endpoint was defined as the need for relaparotomy after SPKT within the initial hospital stay. Hospital length, graft pancreatectomy and mortality rates were also evaluated.
Results: 263 patients were included. We analysed recipient characteristics, comorbidities and renal replacement therapy at the time of the transplant, as shown in table 1. Sixty-five patients (25%) required at least one relaparotomy within their initial hospital stay. All-cause relaparotomy rate was 2.04 (1.71-2.44) events per each 100 in-hospital-days. The leading cause for relaparotomy was bleeding (26 patients), followed by intra-abdominal infection in 21, graft thrombosis in 17 and anastomotic leak in 4; other causes were found in 16 patients. Peritoneal dialysis (PD) (IRR: 2.053, p<0.001), SPKT performed between 2000-2011 (IRR: 1.507, p=0.031) and a lower body mass index (BMI) (IRR: 0.881; p<0.001) were found to be independent risk factors for all-cause relaparotomy. Considering relaparotomy cause, lower BMI (p=0.045) and PD (p=0.005) were related with thrombosis, PD (p=0.046) with leak and SPKT performed between 2000-2011 (p=0.020) with infection-driven relaparotomy. Relaparotomy increased hospital length (median 28 vs 15 days; p<0.001), graft pancreatectomy (35% vs 2% patients; p<0.001) and 90-day mortality rate (8% vs 0%; p<0.001).
Conclusions: The need for relaparotomy within the initial hospital stay influences short-term prognosis on pancreatic graft and patient survival rates. Efforts should be continuously made to identify and correct potential risk factors. We identified a lower BMI and PD at the time of transplant as independent risk factors for overall relaparotomy.

Table 1 – Recipient and donor baseline characteristics (N=263)

Variable	
Recipient sex (female), n (%)	126 (48)
Recipient age (y), mean (SD)	35.5 (6.3)
Hypertension, n (%)	219 (84)
Diabetes duration, mean (SD)	24.2 (6.1)
Recipient BMI, mean (SD)	22.4 (2.8)
RRT, n (%)	
HD	192 (73)
PD	59 (22)
Pre-emptive	12 (5)
Time on dialysis (mo), median	21
Donor age, mean (SD)	29.3 (10.7)
Donor age ≥ 36y, n (%)	85 (32)

BMI – body mass index; HD – hemodialysis; PD – peritoneal dialysis; RRT – renal replacement therapy

MPS4_6 40TH ANNIVERSARY OF PANCREAS TRANSPLANTATION IN SPAIN. LESSONS LEARNED AFTER MORE THAN 650 CASES IN A SINGLE CENTER

Joana Ferrer-Fàbrega[*1], **Pedro Ventura-Aguiar[2], Mª Angeles Garcia-Criado[3], Alba Torroella[1], Carlos Perez Serrano[3], Miguel Ángel López-Boado[1], Rocío García[1], Antonio J Amor[4], Enric Esmatjes[4], Mireia Musquera[2], Fritz Diekmann[2], Maria José Ricart[2], Laureano Fernández-Cruz[1], Josep Fuster[1], Juan Carlos García Valdecasas[1], Federico Oppenheimer[2], Beatriu Bayés[2], Ramón Rull[1], Frederic Cofan[2]**

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Background: To determine in our institution the results of pancreas transplantations in diabetic recipients in accordance with the evolution of surgical techniques and immunosuppression protocols over a period of 40 years.
Methods: From February 1983 to December 2022, performed pancreas transplants and donor type have been retrospectively analyzed in a prospective database. Pancreatic graft survival and patient survival have been analyzed using Kaplan-Meier curves.
Results: During the study period, 654 pancreas transplants were performed, namely: 579 simultaneous pancreas-kidney (SPK) transplants; 29 pancreas transplants following kidney transplants (PAK); 3 pancreas transplants alone (PTA) and 43 retransplants, in 98% of cases from brain-dead donors. In 2019, the first SPK from a donor in controlled asystole was performed, with a further 12 cases completed to date. Induction therapy and maintenance immunosuppression have been continuously modified over time. The type of exocrine drainage has evolved from bladder diversion to enteric drainage (duodenojejunostomy until April 2016 and duodenoduodenostomy from May 2016). Systemic venous drainage was performed in all cases. Pancreatic graft survival in the most recent period, at 1 and 5 years, was: SPK 91% and 83%, PAK and PA 100% respectively. Patient survival at 1 and 5 years was 97% for SPK and 100% for PAK and PA.
Conclusions: Pancreas transplantation offers promising results in terms of graft and patient survival i.e with a positive impact on quality of life. Advances in surgical technique and clinical management together with the experience of the multidisciplinary team have all contributed to achieving the current results.

MODERATED POSTER

Moderated e-poster session on pancreas and islet transplantation

MPS4_7 RETRANSPLANTATION AFTER PANCREAS GRAFT FAILURE IS IT A VIABLE OPTION FOR SELECTED CANDIDATES?

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Background: Pancreas retransplantation (P-RETX) after graft loss is still a controversial option, although P-RETX improves quality of life, glycemic control and reversal of end organ damage compared to exogenous insulin therapy. In this study we review our single-center experience in P-RETX.
Methods: The study was designed as a retrospective analysis of a cohort of 256 patients who received pancreas transplant evaluating the incidence and causes of pancreas graft failure (PGF) and the indications and outcomes of P-RETX at our Centre between 1991 and 2022. Donor and recipient characteristics, and patient and graft outcome were analyzed in the institutional database.
Results: Among 256 pancreas transplants (241 (94 %) SPK, 10 (3.9%) PAK and 5 (1.9 %) PTA), 46 (17.9%) pancreas grafts were lost and 33 (12.8%) patients underwent graft pancreatectomy. The main causes for PGF were: 17 (6.6%) vascular thrombosis, 8 (3.1%) acute rejection, 7 (2.7%) pancreatitis, 4 (1.5%) enteric fistula, 3 (1.17%) chronic rejection, 1 (0.3%) bowel occlusion and 1 (0.3%) pancreas lymphoma. Overall, 10 P-RETX were performed mainly after early graft loss (median time until retransplant 15.7 months). Demographic and clinical characteristics of the recipients were similar in the first and second transplant cohorts, but donor selection criteria were stricter, with lower PDRI (pancreas donor risk index) in P-RETX. The rate of graft failure was higher in the P-RETX vs first transplant (40% vs 17.9%) Causes of P-RETX pancreas graft loss were 3 thrombosis, 1 pancreatitis. In the P-RETX 1 patient died with functioning graft.
Conclusions: P-RETX is challenging from a surgical and immunological standpoint, but it represents a viable option for recipients who experience PGF with acceptable patients and graft survival. A thorough evaluation of the candidates needs to be carried out considering not only patient comorbidities, surgical viability, immunological status but also patient motivation.

MPS4_8 EVALUATION OF THE EFFICACY OF ANTI-INFLAMMATORY PULMONARY ENTERAL FORMULA IN THE TREATMENT OF PANCREATIC AND LUNG INJURY DUE TO OBSTRUCTIVE JAUNDICE

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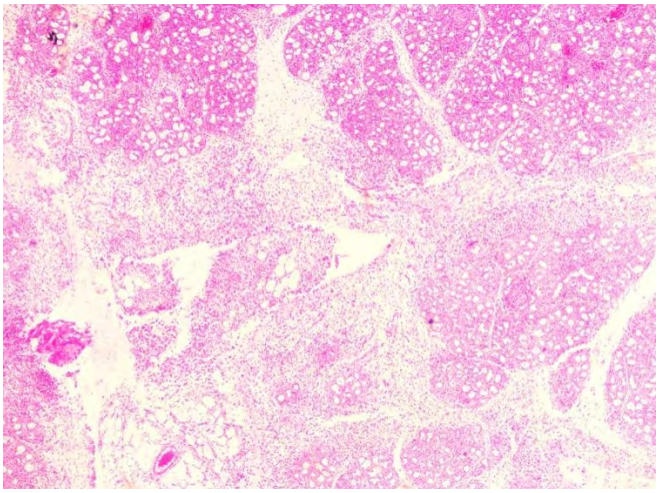
Background: Pancreatic and lung injury are the main complications of obstructive jaundice. The pathogenesis was attributed to excessive inflammation due to bacterial translocation, and endotoxemia. Individuals with obstructive jaundice may benefit from anti-inflammatory pulmonary enteral formula treatment (eicosapentaenoic acid and gamma linolenic acid). This study examined the safety and efficacy of the enteral formula in the treatment of lung and pancreatic injury due to obstructive jaundice.
Methods: 30 Wisteria-Albino rats were randomly assigned to 3 study groups. Group 1 constituted the sham (n=10), Group 2 (n=10) and 3 (n=10) underwent ligation and division of of the common bile duct. The enteral formula was administered to the treatment group (Group 3) for eight days postoperatively. The inflammatory cytokines and markers were analysed in the serum and tissue samples. Histologically lung and pancreas were evaluated and injuries scored. Morphometric documentation for inflammation and acinar necrosis was obtained by mapping the surface of the head of the pancreas into 10 geographical fields and evaluating each field independently. The mean histological score (1-4) was calculated for each variable in each animal.
Results: TNF alpha levels in serum were significantly lower in Group 1 and Group 3 compared to Group 2 ($p<0.001$). IL-6 and C-reactive protein levels in serum did not show any statistical significance between the three groups ($p=0.083$ and 0.130 respectively). Tissue catalase measurements showed no difference among the groups ($p=0.503$). Tissue myeloperoxidase levels were found significantly higher in Group 2 compared to group 1 ($p=0.009$). Malondialdehyde content in tissue didn't differ between the groups ($p=0.496$). TNF alpha tissue levels were higher (190.36pg/ml) in Group 2, as well as IL-6 (37.9 pg/ml) levels ($p<0.001$). Pulmonary injury scores showed significant injury in Group 2 in terms of interstitial thickening, inflammatory cell infiltration and presence of necrosis. Histological assessment of acinar necrosis and inflammation of pancreas revealed severe injury in Group 2 compared to other groups (Figure 1).
Conclusions: Our findings highlighted that anti-inflammatory pulmonary enteral formula alleviated pancreatic and lung injury and inhibited inflammation.



MODERATED POSTER

Moderated e-poster session on pancreas and islet transplantation

MPS4_9 ISLET ISOLATION AFTER NORMOTHERMIC MACHINE PERFUSION OF DISCARDED HUMAN PANCREAS. A PROOF OF CONCEPT STUDY

Catherine Parmentier[*1], **Justin Manuel**[1], **Hongtao Gu**[1], **Xue-Zhong MA**[1], **Samrat Ray**[1], **Jennifer Coleman**[1], **Sujani Ganesh**[1], **Markus Selzner**[1], **Trevor Reichman**[1]

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Background: Pancreas and islet transplantation are both therapeutic options for patients with complicated diabetes. Unfortunately, the availability of pancreas allografts is inadequate to cover the increasing recipient demand. Strategies to expand the number of available grafts are needed. Normothermic ex vivo perfusion (NEVP) is a method that has to potential to assess, and repair organs. The aim of this study was to assess the feasibility of islet isolation after NEVP of the pancreas.

Methods: Two discarded human pancreases were perfused during 4 hours on a NEVP circuit, previously developed by our group. After the perfusion, organs were immediately processed for islet isolation using the Edmonton Isolation Protocol.

Results: Both organs were successfully perfused for 4 hours with posterior islet isolation. Table 1 shows the donor, graft, and isolation characteristics. The islets morphological integrity was proven by insulin staining. A glucose-stimulated insulin secretion test was performed on both cases figure 1. Islets from both donors responded appropriately, secreting insulin at high glucose concentrations. However, case #1 appeared to demonstrate a more robust response than case #2.

Conclusions: Islet isolation after NEVP is feasible using the standard human isolation protocol and could be used to assess and improve the grafts destined for islet isolation. For this study, only the feasibility of the procedure after perfusion was assessed. To our knowledge, this is the first study reporting islet isolation after NEVP in human pancreas. Future studies will focus on improving the perfusion and thoroughly assessing the islets.

Figure 1. A. Pre-purification. B. Post-purification. C. H&E staining D. Insulin staining E. Case 1 glucose-stimulated Insulin secretion test. F. Case 2 glucose-stimulated Insulin secretion test.

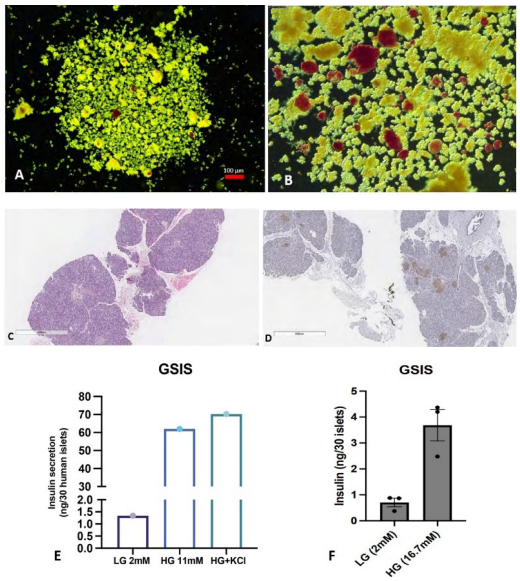

Table 1.

	Donor					Graft					Isolation	
	Gender	Age	BMI	Type of donor	CIT	Wet/dry weight ratio before perfusion (Weight in grams)	Wet/dry weight ratio after perfusion (Weight in grams)	Change in ratio (%)	Final trimmed pancreas weight (g)	Digested pancreas tissue weight (g)	Pre-purification yield	Post-purification yield
Case 1	M	26	22.7	NDD	547	3.5 (270)	4.7 (446)	33% (65%)	NA	NA	NA	NA
Case 2	M	55	19	NDD	383	6.5 (348)	3.1 (362)	-48% (4%)	115.3	60.4	626 204	220 801*

*Only the purest fractions were quantified

MPS5_2 INDIVIDUALIZED HBIG WITHDRAWAL IN AN HISTORICAL COHORT OF LIVER TRANSPLANT RECIPIENTS IN ITALY

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Background: Since the advent of third-generation Nucleoside-Analogues (3-NA), characterized by strong potency and high genetic barrier, the role of long-term HBIG has been questioned. Scientific Societies suggest that HBIG should be used for a finite duration, specifically in compliant patients without Delta co-infection. The same guidance applies to historical patients. Many liver transplant (LT) centres across Europe still prefer continuing with HBIG-NA long term. Aim of this study is to report the results of HBV prophylaxis according to the ELITA Guidelines in a cohort of historical LT recipients.
Methods: 7 LT Italian Centers consecutively included adherent HBV monoinfected LT recipients with regular follow-up in the study. Patients on Lamivudine were shifted to 3-NA before HBIG-withdrawal. A prospective observational Registry for monitoring serological and biochemical paramethers was implemented.
Results: 174 patients were considered for HBIG withdrawal with 3 being excluded, 2 for refusal and 1 for poor-compliance. One additional patient on LAM/HBIG did not tolerate shifting from LAM to Entecavir due to renal tubulopathy. 171 patients stopped HBIG after a median time of 11 years from LT (range 1-27). HBVDNA at LT was positive in 17%, negative in 69% and unavailable in 14% of the cases. 116 and 68 patients have a follow-up of at least 3 and 6 months, respectively with 113 (97.4%) and 66 (97%) being currently HBsAg-ve despite HBIG wirhdrawal. All patients remained HBV-DNA-negative, asymptomatic, with normal liver function tests. Even assuming a very low maintenance dose of 1000 IU every 4 weeks, the cost saving per-patient would be of at least 4.000 Euro for each additional year. For centres who have many patients in follow-up the cost saving would be substantial.
Conclusions: HBIG withdrawal in adherent HBV+/HDV- patients on lifelong 3-NAs is safe and associated with HBsAg negativity in the vast majority of cases. The substantial cost-saving could cover different needs.

MPS5_3 DO DONOR LIVER BLOOD TESTS PREDICT LIVER TRANSPLANT OUTCOMES? UK NATIONAL COHORT STUDY

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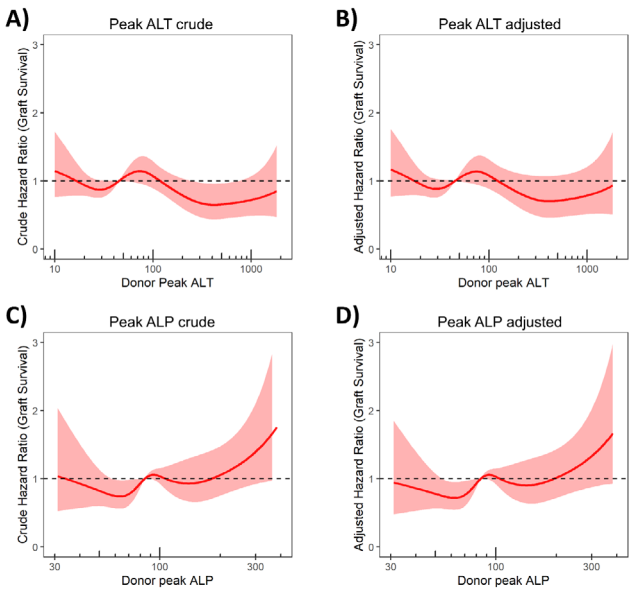
Background: Safely increasing organ utilisation is a global priority. Donor serum transaminase levels are often used to decline livers, despite minimal evidence to support such decisions. We aimed to investigate the impact of donor 'liver blood test' results on transplant outcome.
Methods: This retrospective cohort study used the UK Transplant Registry on adult liver transplantation (2016-2019); adjusted regressions models assessed the effect of donor liver blood tests on outcomes.
Results: 3299 adult liver transplant recipients were included (2530 following brainstem death, 769 following circulatory death). Peak alanine transaminase (ALT) ranged from 6-5927U/L (median=45). Donor cause of death significantly influenced donor ALT; 4.2-fold increase in peak-ALT with hypoxic brain injury versus intracranial haemorrhage (adjusted P<0.001). On multivariable analysis, adjusting for a wide range of factors, transaminase level (ALT or aspartate aminotransferase) failed to predict graft survival (Fig 1), primary non-function, 90-day graft loss or mortality. This held true in all examined subgroups; steatotic grafts, DCD, hypoxic brain injury donors, and donors where ALT was still rising at the time of retrieval. Even grafts from donors with extremely deranged ALT (>1000) displayed excellent post-transplant outcome. In contrast, donor peak alkaline phosphatase was a significant predictor of graft loss (aHR=1.808, 1.016-3.216, P=0.044).
Conclusions: We have found no evidence to support the notion that donor transaminases predict post-transplant outcomes. When other factors are favourable, livers from donors with raised transaminases can be accepted and transplanted with confidence. Such knowledge should improve organ utilisation decision-making and prevent future unnecessary organ discard. This provides a safe, simple and immediate option to expand the donor pool.

Fig 1 - impact of donor ALT/ALP on graft survival (cox regression models with restricted cubic splines)



MODERATED POSTER

Moderated poster session on liver transplantation

MPS5_4 FACTORS AFFECTING SIGNIFICANT DIFFERENCE BETWEEN RADIAL AND FEMORAL ARTERIAL BLOOD PRESSURE IN LIVING DONOR LIVER TRANSPLANTATION

Gaab Soo Kim[1], **Jea Youn Kim**[1], **Hyun Ji Hwang***[1]

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Background: Invasive blood pressure monitoring is essential during liver transplantation. Radial and femoral artery are commonly used, although study about the comparison of blood pressure between radial and femoral artery is scarce. In this study, we aimed to evaluate the perioperative factors related to developing significant differences between radial and femoral arterial blood pressure.
Methods: A retrospective study was performed in adult recipients who underwent living donor liver transplantation (LDLT) in 2021 at Samsung Medical Center. After comparing radial and femoral arterial mean blood pressure (MBP) at 3 phases (dissection, anhepatic, and post-reperfusion), we selected data with the largest differences. We defined the significant differences as the 10% of femoral arterial MBP. The recipients were divided into two groups (with and without significant difference group), and perioperative variables were analyzed in each group at post-reperfusion phase.
Results: A total of 128 adults undergoing LDLT were included in our analysis. The largest difference between the radial and femoral arterial MBP was as follows: The median [IQR] of difference, 9.55 [7.3, 11.93] in dissection phase; 9.19 [5.93, 12.5] in anhepatic phase; and 10.87 [6.59, 15.28] in post-reperfusion phase. The difference was significantly higher in the post-reperfusion phase than in the anhepatic phase (P=0.003), however, the differences was not significantly different between the dissection and post-reperfusion phase (P=0.095). In the post-reperfusion phase, 75 recipients showed a significant difference (≥ 10%) and femoral arterial MBP was higher than radial arterial MBP in 121 of 128 total recipients, and 72 of 75 significant difference group. The units of transfused packed RBC (1 [0, 2] vs. 2 [0, 4], P=0.01), units of transfused fresh frozen plasma (0 [0, 0] vs. 0 [0, 2], P=0.005), and vasoactive inotropic score (5 [0, 14.25] vs. 10 [1.5, 20], P=0.037) were significantly higher in significant difference group.
Conclusions: Radial and femoral arterial MBP can differ significantly during LDLT, and it showed significant association with the amount of transfusion and vasoactive inotropic use. Blood pressure measurement based solely on radial artery has the risk of underestimation during liver transplantation.

MPS5_5 THE MORBIDITY BURDEN AFTER LIVER TRANSPLANTATION – A TREATMENT-BASED ANALYSIS

Joris Couillerot[*1;2], **Guillaume Rossignol**[1;2;3;4], **Breton Antoine**[1;2], **Kayvan Mohkam**[1;2], **Jean Yves Mabrut**[1;2], **Xavier Muller**[1;2;3]

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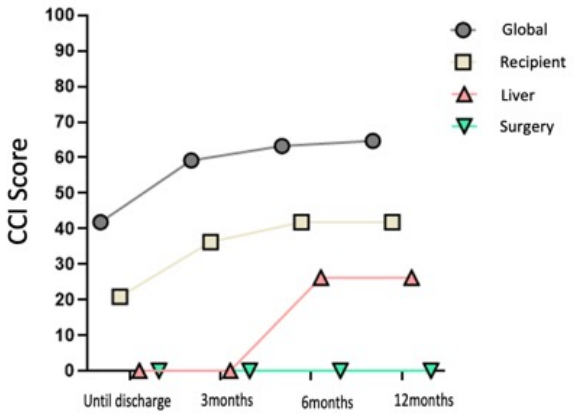
Introduction: Survival after liver transplantation (LT) has improved, now reaching > 90% at 1 year in benchmark cases. However, while post-transplant morbidity remains high, an in-depth analysis of the patient-specific morbidity is currently lacking.
Methods: We retrospectively included all LT performed at our center from 2017 to 2020, except for re-LTs. Complications from the first post-LT year were graded according to the Dindo-Calvien classification and divided into 3 morbidity categories: procedure related (bleeding…) graft related (primary non-function, biliary and arterial complications...) and recipient related (infections, ileus…). The patient specific cumulative morbidity was calculated for each category using the Comprehensive Complication Index (CCI). To test the 3 different morbidity categories, we applied them to low and high-risk donor-recipient scenarios (BAR score<18 and >18).
Results: Out of 287 recipients, 91% had at least one complication during the first post-LT year, including 53% Grade II. While overall and recipient-specific CCI increased from discharge to 1-year, reaching 64,71 and 41,83 points respectively, the graft related CCI only increased after 3 months (26,22 points) mainly including Grade>II complications (Fig 1). The procedure related CCI remained low over the post-LT course but had the highest failure to rescue rate (16,6%). In very high-risk LT scenarios, morbidity increased in all three categories, with the highest increase for procedure related CCI (0 vs 60 points, p<0.001).
Conclusion: Recipient related complications had the highest impact on overall morbidity but transplant related complications had the highest failure to rescue rate. Graft related morbidity only occurred after 3 months with a frequent need of interventional treatment. The proposed morbidity categories may serve as pragmatic study endpoints to validate novel treatment strategies in LT.

Fig 1: Evolution of the CCI score during the first year after TH expressed in median



MODERATED POSTER

Moderated poster session on liver transplantation

MPS5_6 EVALUATION THE SIX MONTH ABSTINENCE RULE PRIOR TO LIVER TRANSPLANT: A CLINICAL PRACTICE GUIDELINE

Joanna Dionne*[1], Simon Oczkowski[1], Susan Abbey[2], Jennifer Chandler[3], Vanessa Gruben[4], Marie-Chantal Fortin[5], Vladimir Marquez[6], Sylvia Carbert[7], Theodore Christou[8], Fatima Dharsee[9], Clay Gillrie[9], Christina Parsons[10], Prosanto Chaudhury[11], Nazia Selzner[2;12]

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Background: Until recently in Canada patients with alcohol associated liver disease (ALD) had to be abstinent from alcohol use for 6-months prior to assessment for liver transplantation (LT). This rule has been called into question from evidence, ethical and legal lenses. The purpose of this clinical practice guideline (CPG) is to guide the assessment and management of ALD and LT.
Methods: A committee including medical and surgical experts in liver transplant, addiction, ethics, law, methodology and patient partners developed a CPG according to GRADE Methodology. The steering committee generated and answered questions in the population, interventions, comparison and outcome format.
Results: Five conditional recommendations (very low certainty of evidence) and 2 best practice statements for patients undergoing LT were made. The recommendations included: 1) To not use the six-month rule as a sole criterion for liver transplant in ALD, 2) The definition of relapse should distinguish between: 1. non harmful relapse (e.g. occasional drinking or slip), 2. harmful drinking (e.g. physical, psychosocial implications, binge drinking/escalation drinking) and relapse monitored by biochemical markers when available, 3. During liver transplant workup, assessment of risk factor associated with post-transplant relapse (presence of uncontrolled psychiatric disease, history of smoking and multiple failed attempts of alcohol treatment) and protective factors (social support and employment) should be part of the holistic multidisciplinary assessment to allow for early intervention to mitigate risk factors, 4) The use of validated screening scoring systems and biomarkers for screening post-transplant relapse, 5) Integrated multidisciplinary teams with psychiatrists, addiction services to prevent relapse pre and post-transplant. The best practice statements included: 1) Listed and transplanted ALD patients should be intermittently screened for relapse pre and post-transplantation and 2) We suggest a holistic assessment for patients being evaluated for liver transplant, that not only take into account risk factors or other screening modalities, but a multi prong, multidisciplinary approach.
Conclusions: This CPG provides evidence-based recommendations for listing and transplanting patients with ALD.

MPS5_7 IMPACT OF DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION (D-HOPE) ON HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION

Federica Rigo'[1], Damiano Patrono*[1], Victor De Donato[1], Ludovico Campi[1], Diana Turturica[1], Nicoletta Petronio[1], Francesco Tandoi[2], Renato Romagnoli[1]

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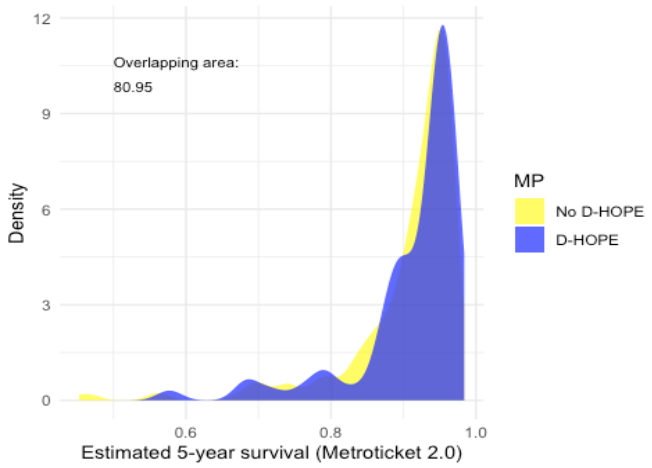
Background: Ischemia reperfusion injury, which is mitigated by machine perfusion, may increase recurrence of hepatocellular carcinoma (HCC) after liver transplantation (LT). We investigated impact of dual hypothermic oxygenated machine perfusion (D-HOPE) on HCC recurrence in LT.
Methods: Single-center retrospective study in the period 01/2016-12/2020. Pre- and postoperative data of HCC patients undergoing LT were analyzed, comparing recipients of a D-HOPE treated graft with those preserved by static cold storage (SCS). Primary endpoint was recurrence-free survival.
Results: Of 326 patients, 246 received a SCS-preserved liver and 80 a D-HOPE-treated graft (DBD, n=66; DCD, n=14). Donors in the HOPE group were older (72 vs 68 years, p=0.003) and had higher BMI (27 vs 25, p=0.001). All DCD donors were treated by normothermic regional perfusion and D-HOPE. The groups were comparable in terms of HCC features, as it was 5-year recurrence-free survival estimated by metroticket 2.0 model (Figure). Immunosuppression was comparable, except that more patients in the D-HOPE group had induction by basiliximab (54% vs 20%, p<0.001). Everolimus was introduced in 71% of patients in each group. 30 (9.2%) patients had HCC recurrence, which was extra-hepatic in 21 (70%). No DCD recipient had recurrence. At Cox regression, HCC recurrence was associated with previous hepatic resection (HR 4.4, CI 1.7-11, p=0.003), microvascular invasion (HR 5.4, CI 2.6-11, p<0.001) and G3-G4 grading (HR 5, CI 2.1-12, p<0.001). HCC recurrence rate was comparable between groups (D-HOPE 10%; SCS 8.9%; p=0.95). D-HOPE did not reduce HCC recurrence, which was confirmed by Bayesan model averaging and competing risk analysis. Excluding DCD recipients did not change results. Recurrence-free survival and other postoperative outcomes, including early (10% vs 10%, p=1) and late (4.5% vs 3%, p=0.145) rejection rate, were comparable, except that in D-HOPE group AST (903 vs 1140, p=0.022) and ALT (496 vs 792, p=0.002) peak was lower.
Conclusions: In our experience, including mainly DBD cases, D-HOPE did not reduce HCC recurrence nor rejection but allowed utilizing livers from extended criteria donors with comparable outcomes. Given low HCC recurrence rate, larger studies may be needed to demonstrate a significant impact of D-HOPE.



MODERATED POSTER

Moderated poster session on liver transplantation

MPS5_8 LIVER TRANSPLANT RECIPIENTS WITH AUTOIMMUNE HEPATITIS IN THE SWISS TRANSPLANT COHORT STUDY HAVE A HIGHER RISK OF GRAFT LOSS AND VASCULAR COMPLICATIONS

Aurélie Rosat[1], Benedetta Terziroli Beretta-Piccoli[2], Linard Hoessly[3], Susanne Stampf[3], Michael Koller[3], Nicolas Goossens[4], Montserrat Fraga[1], Annalisa Berzigotti[5], Nasser Semmo[5], Beat Müllhaupt[6], David Semela[7], Markus Heim[3], Simon Brunner[8], Manuel Pascual[1], Darius Moradpour[1], Julien Vionnet*[1]

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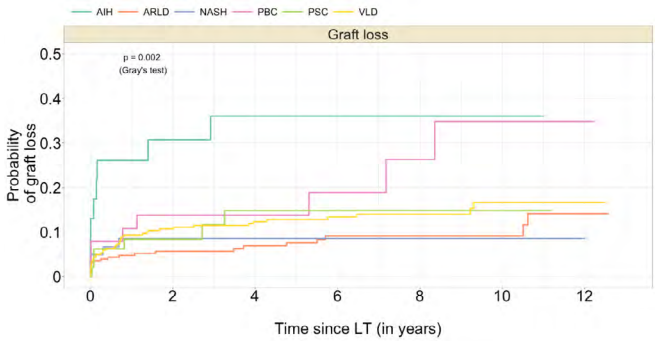
Background: Data suggest that patients transplanted for autoimmune hepatitis (AIH) have a higher post-liver transplantation (LT) mortality compared to other liver diseases.
Methods: All adult patients with a first LT from May 2008 to December 2020 and included in the Swiss Transplant Cohort Study were classified into seven categories according to their indication to LT: AIH, alcohol-related liver disease (ARLD), viral liver disease (VLD), primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), non-alcoholic steatohepatitis (NASH) and other. Patients with AIH were selected based on clinical, immunological and histopathological criteria; patients with unequivocal etiology were classified in the respective categories, patients with mixed or other diagnoses being classified as "other". Primary outcomes were graft and patient survival; secondary outcomes were post-transplant vascular, biliary and infectious complications. Cumulative incidence of graft loss and death were calculated in the different categories and compared with AIH. The p-value was adjusted according to the Bonferroni method. A Cox proportional hazards model was used to investigate the effect of AIH on complications.
Results: 880 LT recipients were included: 23 transplanted for AIH, 254 for ARLD, 303 for VLD, 38 for PBC, 49 for PSC, 61 for NASH, and 152 for other indications. In the AIH group, 65.2% (n = 15) were women, the median age was 49 (IQR 39-58) years and MELD score 20 (15-32); graft loss and death rates were 34.8% (n = 8) and 21.7% (n = 5). There was no significant difference in death rates between AIH and other groups but graft loss was significantly higher in AIH patients (p = 0.002) (Figure). Eighteen (78.3%) AIH patients had a relevant complication, 77.8% (n = 14), 44.4% (n = 8) and 27.7% (n = 5) of them having a vascular, biliary or infectious complication. In multivariate analysis, AIH was independently associated with a higher risk of complications (HR 1.693, 95% CI 1.024-2.799, p = 0.040), along with pre-LT MELD score (HR 1.013, 95% CI 1.002-1.024, p = 0.017), living donation (HR 3.165, 95% CI 2.069-4.841, p < 0.005), and rejection (HR 3.452, 95% CI 2.487-4.791, p < 0.005).
Conclusions: Patients transplanted for AIH have a higher risk of graft loss compared to other etiologies, explained by a higher rate of vascular complications.



MPS5_10 BILIARY COMPLICATIONS FOR HISTIDINE-TRYPTOPHAN-KETOGLUTARATE (HTK) AND UNIVERSITY OF WISCONSIN (UW) PRESERVED DECEASED DONOR LIVER GRAFTS

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Background: Bile duct complications are common in the post liver transplant (LT) period and may be related to the arterial blood supply for the biliary system. Because histidine-tryptophan-ketoglutarate (HTK) is 3-4x less viscous than University of Wisconsin (UW) preservation solution, it has been hypothesized that HTK provides a better flush of the biliary microcirculation. This study reviews the biliary complications in a large number of deceased donor LTs and compares outcomes for HTK versus UW preservation.
Methods: Single center data were extracted using a retrospective review of all liver transplants between 2003 and 2022 for post-transplant biliary complications. Primary outcomes included 1-year post transplant need for imaging, any leak, and stricture formation (anastomotic and intrahepatic). Donation after brain death (DBD) donors were analyzed separately from donation after circulatory death (DCD) donors. The primary preservation solution for our OPO during the study period was HTK, but a large number of UW preserved livers were imported from other OPOs contemporaneously and are utilized as a comparison group.
Results: There were 2396 LTs reviewed. Preservation solution included DBD: 1809 HTK (84%) and 350 UW (16%) and for DCD: 220 HTK (92%) and 18 UW (8%). Any biliary imaging was required for 44% of HTK and 51% of UW DBD LTs (p=0.01), and for DCD 41% HTK and 61% UW (p=0.09). Any leak was higher for UW (7%, 4% DBD, p<0.01 and 6%, 2% DCD, p=0.39). Risk of anastomotic stricture was similar for DBD (34%, 35%, p=0.54) and for DCD (30%, 44%, p=0.20). However, the risk for intrahepatic ischemic-type strictures was much higher for UW preserved grafts (DBD 3% vs 1%, p<0.001) (DCD 22%, 4%, p<0.001).
Conclusions: In this cohort, HTK-preserved livers have significantly less risk of biliary complications, including intrahepatic stricture formation when compared to UW-preserved grafts, including markedly lower risk for ischemic-type strictures in DCD grafts.

Moderated poster session on kidney transplants in children and young people

MPS6_1 DONOR-DERIVED CELL-FREE DNA (DD-CFDNA) AS A NON-INVASIVE BIOMARKER OF KIDNEY ALLOGRAFT REJECTION IN PEDIATRIC KIDNEY TRANSPLANTATION

Julien Hogan[*1;2;3], **Roshan George**[4], **Pamela Winterberg**[4], **Carissa Hayes**[4], **Chris Fan**[4], **Margret Kamel**[5], **Rouba Garro**[4]

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Background: Rejection is the first cause of allograft loss in pediatric kidney transplant (pkTx) recipients. Detection of rejection relies on kTx biopsies performed either because of allograft dysfunction with the risk of late diagnosis or per surveillance protocols allowing early detection of subclinical rejection but resulting in unnecessary biopsies. Dd-cfDNA is a non-invasive biomarker able to improve rejection detection and guide biopsy indications. We aim to assess the association of dd-cfDNA levels with biopsy results in a large cohort of pkTx recipients.
Methods: All pkTx patients with at least one dd-cfDNA assessment at the time of a biopsy were included. Clinical, biological and histological data were collected. Dd-cfDNA were retrospectively measured from plasma samples biobanked at the time of allograft biopsy between 2015 and 2020 or collected in patients receiving dd-cfDNA testing as part as clinical care since 2021.
Results: 170 cfDNA measurements in 132 pkTx recipients were available at the time of a biopsy, including 100 performed for surveillance. Mean age at biopsy was 16 years with a median time from kTx of 21 [11;38] months. Median eGFR was 62 [48;83] mL/min/1.73m^2, median UPCR 0,21 [0,14;0,36] g/g, and 20% had DSA at the time of the biopsy. Biopsy findings included: 109 normal, 30 borderline, 15 TCMR, 11 AMR and 5 mixed rejections. Median cfDNA level was 0,64 [0,31;1,80] %. We found an association between cfDNA levels and active tubule-interstitial and microvascular Banff lesions (Figure 1). cfDNA levels were significantly increased in cases with rejection (Figure 2). Using the proposed cut-off of 0.5%, performances of the test to detect rejection were Se 84%, Spe 51%, PPV 33%, NPV 92%. Among the borderline cases, 17 (57%) had cfDNA>0.5%.
Conclusions: We confirm in the largest pediatric kTx cohort to date, the association of dd-cfDNA levels with allograft rejection and its potential interest as a non-invasive biomarker in children. Further studies are needed to assess the added value of dd-cfDNA monitoring to the current standard of care and its ability to reduce unnecessary surveillance biopsies and improve outcomes.

Figure 1: Association between dd-cfDNA levels and active tubule-interstitial and microvascular lesions

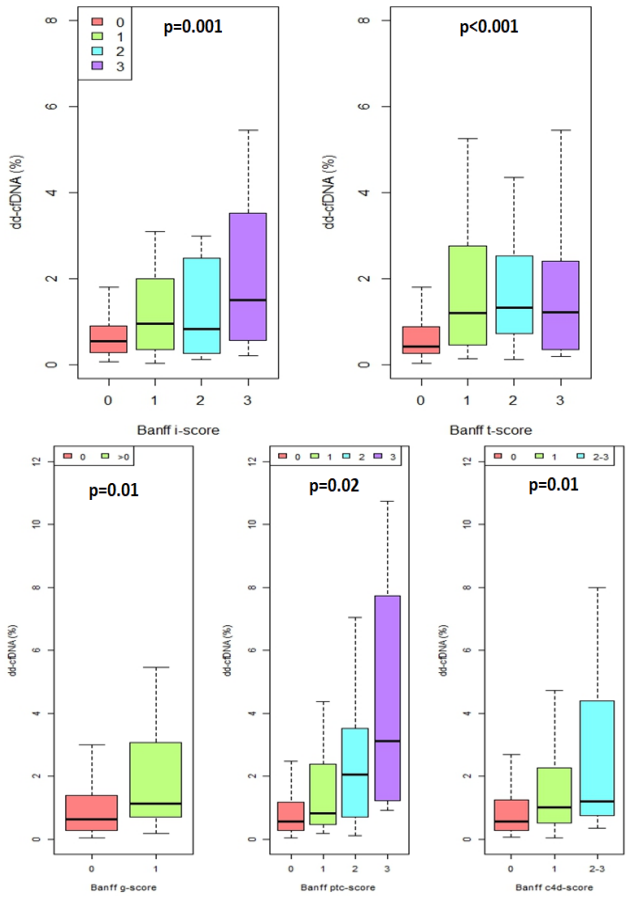
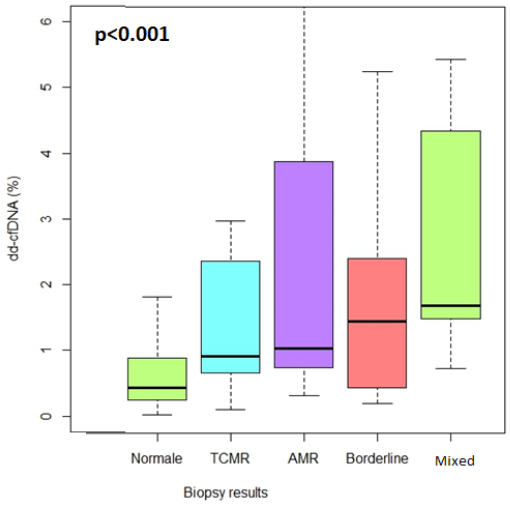


Figure 2: Association between dd-cfDNA levels and biopsy results.



MPS6_2 RENAL ALLOGRAFT SURVIVAL FOR (RE)TRANSPLANTED CHILDREN IN ADULTHOOD; AN ERA REGISTRY STUDY FROM 1978 TO 2019

Evgenia Preka[*1;2], **Marjolein Bonthuis**[1;3], **Stephen D Marks**[4;5], **Anneke Kramer**[3;6], **Vianda Stel**[3;6], **Jerome Harambat**[7], **Kitty Jager**[3;6]

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Background: Knowledge regarding renal allograft survival in (re)transplanted European children followed from childhood into adulthood including factors affecting these outcomes is lacking.
Methods: Using ERA Registry data, we investigated all patients on kidney replacement therapy (KRT) who received their first kidney transplant (KT) before 20 years of age between 1978 and 2019. Graft survival after first, second and third KT were analysed together with their risk factors, using Kaplan-Meier survival analysis and multivariable Cox regression models.
Results: Among 10,012 paediatric KT recipients, 8601, 1962 and 412 received at least one, two and three KTs. Graft survival at 10 years was 65.7% for first, 53.7% for second and 49.5% for third KTs. Factors associated with increased graft failure rates were primary disease of glomerulonephritis or recurrent disease as cause of kidney failure for first KT recipients (aHR 1.24, 95%CI 1.12-1.37 and aHR 1.24, 95%CI 1.13-1.37, respectively). Patients whose first KT lifespan was between 0-30 days or >5 years had lower graft failure rates for their second KT compared to patients whose KT survived between 1-5 years (aHR 0.79, 95%CI 0.64-0.98 and aHR 0.73, 95%CI 0.61-0.88, respectively). Similar results were found for third KT recipients whose second KT survival was >5 years (aHR 0.61, 95%CI 0.41-0.92). Patients who were transplanted for the first and second time before 2007 had 1.5-2x higher graft failure rates compared to patients who received their KT between 2016 and 2019. Pre-emptive KT recipients had lower graft failure rates compared to patients who received dialysis >1 year for first and second KT (aHR 0.89, 95%CI 0.81-0.98 and aHR 0.63, 95%CI 0.51-0.78,respectively). Patients who received a living donor (LD) KT had lower graft failure rates for first and second KT (aHR 0.77, 95%CI 0.7-0.84 and aHR 0.71 (0.6-0.85, respectively). Second LD KT recipients had survival advantage compared to having a second deceased donor KT.
Conclusions: Graft outcomes after pediatric kidney (re)transplantation have improved significantly over time for all recipient subgroups, especially for patients with LD KT, longer previous KT lifespan and pre-emptive KT. Patients with GN and recurrent diseases showed the poorest outcomes, highlighting the requirement for further research.

MODERATED POSTER

Moderated poster session on kidney transplants in children and young people

MPS6_3 REGIONAL OUTCOMES OF PAEDIATRIC RENAL TRANSPLANTATION IN THE UK. A MACHINE LEARNING ANALYSIS

Hemant Sharma[1], **Georgios Koufopoulos*[1;1], Sanjay Mehra[1], Abhishek Sharma[2]**

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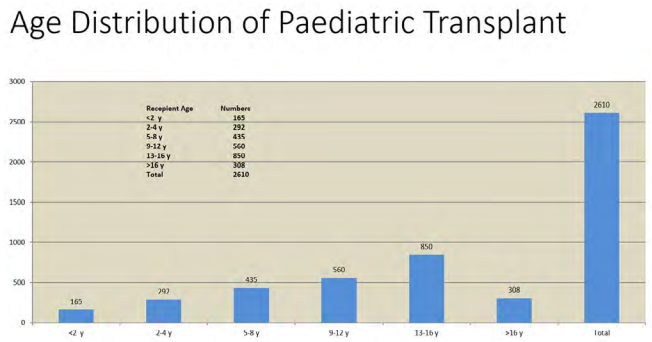
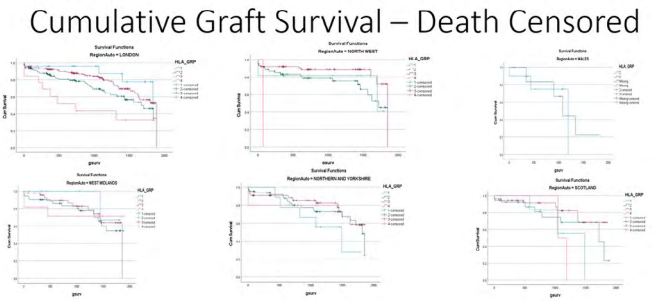
Purpose: <25%of UK children commencing RRT receive a pre-emptive transplant in the UK. Disparities have been reported amongst gender and ethnic groups. Paediatric patients on the waiting list have increased over the last 5 years. This study assesses the paediatric renal transplant rates in the UK since the year 2000 and the regional graft outcomes of paediatric renal transplant in the UK and determine the predictors of survival at 1 year, 3 years, and 5 years.
Methods: We harmonized the NHSBT Data to shortlist the paediatric renal transplants performed in the UK from the year 2000-2019. The Predictors of Transplant outcomes were evaluated by five classifiers including logistic regression, SVM, random forest, K-Nearest neighbour matching, and adaptive boosting. Random Forest Model had the best performance validated by RMSE. Rattle R/ JASP was used to derive Variables of importance. Survival outcomes and predictors data mined from MLA were further mined with Cox Regression.
Results: A total of 2610 paediatric transplants were reported to NHSBT (the year 2000-2019). London region did the maximum transplants (N= 854) followed by Northern and Yorkshire (N=347) and Northern region (N= 340). High Volume center doing living donors had considerably better survival compared to others. On Regression analysis, the better graft survival was correlated to recipient age group >8 years (p <0.001), CIT <12 hr (p= 0.02), Transplant year -2010 onwards (p <0.01), ethnically matched donor-recipient (p= 0.01), HLA NHSBT group 1 and 2 (p=0.04) and high volume centers (> 15 paediatric transplants/ annually).
Conclusions: Superior outcomes were reported from high-volume centers and transplants done after the year 2010. Immunologically well-matched kidneys and low Cold Ischemia time (CIT) predict better survival.





MPS6_4 KIDNEY TRANSPLANTATION IN CHILDREN WEIGHING 10 KG OR LESS: IS IT A CHALLENGE?

Cemile Pehlivanoglu[1], **Erol Demir[2], Ozlem Unlugedik*[3], Emre Arpalı[4], Basak Akyollu[4], Nese Tole[1], Burak Kocak[5], Caner Süsal[2], Ilmay Bilge[1]**

[1]Koç University Faculty of Medicine, Pediatric Nephrology, Istanbul, Turkey, [2]Koç University Faculty of Medicine, Transplant Immunology Research Center of Excellence, Istanbul, Turkey, [3]Koç University Hospital, Department of Pediatrics, Istanbul, Turkey, [4]Koç University Hospital, Koç University Hospital Organ Transplant Center, Istanbul, Turkey, [5]Koç University Faculty of Medicine, Department of Urology, Istanbul, Turkey

Background: Kidney transplantation (tx), which is considered as the most appropriate treatment for children with end-stage kidney disease, is generally applied in children over 10 kg of body weight. Young children represent the vulnerable population in terms of post-transplant fluid-electrolyte and blood pressure management and immunosuppressive treatment. Infections are a significant risk in these patients and may affect graft survival. We aimed to evaluate the clinical outcomes of transplantation in young children, especially infants weighing less than 10 kg, by comparing them with older children.
Methods: Kidney transplant recipients less than 10 kg were included in this retrospective observational study. This patient group was matched with a pediatric control group in the recipient's sex and post-transplant follow-up by the nearest neighbor matching method. The primary endpoint was all-cause mortality and graft loss. The secondary endpoints were the occurrence of allograft rejection, Cytomegalovirus (CMV), BK virus (BKV), and Ebstein-Barr virus (EBV) infections.
Results: Thirty-four kidney transplant recipients were followed for a median of 36 months after transplantation. Although, there were no statistical differences in both groups in terms of BKV (5 vs. 7; p=0.134), CMV infections (8 vs. 11; p=0.166); EBV DNAemia (11 vs. 1; p<0.001) were common in the patient group than the control group. EBV-related Post tx lymphoproliferative disease (PTLD) occurred in 2 children in the patient group.
Conclusions: The survival rates of infants less than 10 kg were %100 at a median three years follow-up. But the frequency of EBV DNAemia in these patients has increased compared to the other pediatric population. Therefore, close follow-up of these patients is required.

MODERATED POSTER

Moderated poster session on kidney transplants in children and young people

MPS6_5 THE EFFECT OF HLA MISMATCHES ON POST-TRANSPLANT OUTCOMES IN PAEDIATRIC RENAL TRANSPLANTATION

Angela Benson*[1], Mikhail Nozdrin[2], Kavyesh Vivek[1], Felix Lui[3], Maria Selyanina[4], Maria Irene Bellini[5], Vassilios Papalois[6]

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Background: Impact of HLA-matching in paediatric transplantations is less known. Our study investigated the effects of HLA matches/mismatches between donors and paediatric recipients of kidney transplantation. To our knowledge this is the first systematic review on the topic.
Methods: Study was registered with PROSPERO. MedLine and Embase were searched through Ovid, Cochrane and Web of Science were also searched systematically. Risk of Bias assessment was performed using NHBLI tools by 2 independent researchers.
Results: Search identified 3033 papers, 4 met the inclusion criteria. Graft survival was not affected significantly if there was 0 or 1 mismatch. Similarly having a match of more than 3 HLA A+B alleles increased the graft survival significantly. Incidence of acute rejection was not correlated with number of HLA mismatches (all types) (P > .05), however it was negatively correlated with number of HLA DR mismatches (P = 0.02).
Conclusions: The Evidence from the papers show that there is no significant difference in graft/recipient survival between 0 or 1 mismatches in kidney transplantation, however a mismatch of 3 or more influences post-transplant outcomes.

Table 1: Effect of HLA matching in paediatric kidney transplantation

Study	Total no. of patients	No. of Patients Mismatch (MM) or Match (M) HLA A+B	HLA DR	Key findings
Rocha 2014	128			Significant difference P=0.025 (univariate analysis) was found between the mean number of HLA mismatches between patients with graft failure at the 10 yr follow up (2.52 ± 1.09 n=27) vs functional grafts (1.95 ± 1.29 n= 101)
El-Husseini 2005	284	Number of matches and (5 yr % survival) 0M: 3 (66.67) 1M:33 (64.64) 2M: 201 (75.45) 3M: 37 (86.24) 4M:10 (83.33) P=0.033 multivariate regression	Number of matches and (5 yr % survival) 1M:261 (73.76) 2M:23 (80.95) P=0.161 Multivariate regression	
McEnery 1992	1558	1+ M (A locus): 1133 1+ M (B locus): 1042	1+ M (DR): 1095	relative risk for graft loss between 1 or 2 matches on the A locus and 0 matches: 1.17 (P=0.25) relative risk for graft loss between 1 or 2 matches on the B locus and 0 matches: 0.79 (P=0.08) relative risk for graft loss between 1 or 2 matches on the DR locus and 0 matches: 0.78 (P=0.06)
Opelz 2010	9209	Number of mismatches and (5 yr % survival) 0MM: 3059 (64.2) 1MM:4833 (64.4) 2MM:1317 (56.0) P=0.12	DR mismatches had no significant effect.	An association between 2 HLA-DR mismatches and non-Hodgkin lymphoma was demonstrated by multivariate analysis (hazard ratio for 2 vs 0-1 DR mismatches 2.04, P=0.021), and the result was consistent for both 10 yr periods.

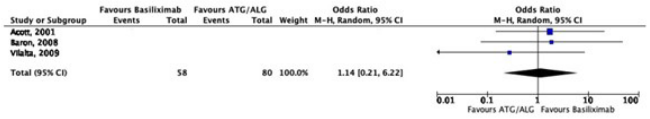
MPS6_6 BASILIXIMAB VS ANTI-THYMOCYTE/ANTI-LYMPHOCYTE GLOBULINS IN PEDIATRIC KIDNEY TRANSPLANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Mikhail Nozdrin*[1], Kavyesh Vivek[2], Angela Benson[2], Maria Selyanina[3], Felix Lui[4], Maria Irene Bellini[5], Vassilios Papalois[6]

[1]Queen's Hospital, London, United Kingdom, [2]Sir Alexander Fleming Building, London, United Kingdom, [3]Barts Health NHS Trust, London, United Kingdom, [4]Yale New Haven Hospital, New Haven, United States, [5]Sapienza University of Rome, Roma, Italy, [6]Hammersmith Hospital, London, United Kingdom

Background: Kidney transplantation is the best treatment for children with end-stage kidney failure. Organ rejection remains the biggest risk factor for graft loss following transplantation. Antibody induction is commonly used to reduce incidence of acute rejection. Lymphocyte-depleting antibodies (ATGAM, alemtuzumab, thymoglobulin) are recommended for use in adults at high risk of rejection, however they increase the risk of infection and PTLD. Basiliximab is a monoclonal antibody, a possible alternative to lymphocyte depleting antibodies with significantly better side effect profile. The aim of our meta-analysis was to compare effectiveness and side effects of Basiliximab vs Lymphocyte depleting antibody induction in pediatric renal recipients. To our knowledge this is the first meta-analysis on the topic.
Methods: Medline, Embase, CENTRAL and Web of Science databases were searched systematically. Risk of bias assessment was performed.
Results: Three studies were included in the meta-analysis. No significant difference was seen in 1 year graft survival between the two treatments (P=0.88) (OR: 1.14 95% CI: 0.21-6.22) (fig 1). Significant reduction in infection incidence was seen in the patients treated with Basiliximab (P=0.03). OR: 0.28 (95% CI: 0.09, 0.90).
Conclusions: Basiliximab was found to be comparable to lymphocyte depleting antibodies in terms of graft survival, however significantly reduced the incidence of infection. Due to the lack of data, further studies need to be carried out to strengthen the recommendation for use of Basiliximab induction in preference to lymphocyte depleting antibodies.

Figure 1: Basiliximab vs Anti-thymocyte/Anti-lymphocyte Globulins 1-year graft survival



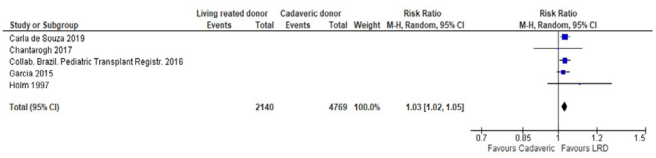
MPS6_7 EFFECT OF DONOR TYPE ON GRAFT AND PATIENT SURVIVAL IN PAEDIATRIC RECIPIENTS OF KIDNEY AND LIVER TRANSPLANTATION

Mikhail Nozdrin*[1], Maria Selyanina[2], Kavyesh Vivek[3], Angela Benson[3], Maria Irene Bellini[4], Felix Lui[5], Vassilios Papalois[6]

[1]Barts Health NHS Trust, London, United Kingdom, [2]Queen's Hospital, London, United Kingdom, [3]Imperial College London, London, United Kingdom, [4]Sapienza University of Rome, Roma, Italy, [5]Yale New Haven Hospital, New Haven, United States, [6]Hammersmith Hospital, London, United Kingdom

Background: Living related donors are the best quality donors in liver and renal transplantation. However, to meet increased demand for organs, extended criteria donors are used. The aim of our meta-analysis was to compare post-transplantation outcomes in pediatric recipients of grafts from living donors and deceased donors in renal and liver transplantation. To our knowledge this is the first meta-analysis investigating the topic.
Methods: Embase, Medline, Cochrane, Web of science were searched systematically. Risk of bias assessment was performed using NHBLI tools, by 2 independent reviewers.
Results: 3003 papers were identified by the search strategy. Thirteen papers were included in the meta-analysis and systematic review. Graft survival was significantly higher in paediatric renal recipients from living related donors (LRDs) compared to cadaveric donors at 1 year (RR 1.03 [95% CI 1.02-1.05]) (*fig. 1*) and 5 years (RR 1.72 [95% CI 1.45-2.05]). Patient survival was significantly higher in paediatric renal recipients from LRDs compared to cadaveric donors at 1 year (RR 1.42 [95% CI 1.03-1.96]) and 5 years (RR 1.63 [95% CI 1.28-2.06]). No significant difference was seen in 30 days graft survival between recipient of liver grafts from LRDs and cadaveric donors (RR 1.30 [95% CI 0.52-3.21]).
Conclusions: Pediatric recipients of renal grafts from LRDs have significantly higher graft and both short- and long-term patient survival compared to recipients from cadaveric donors. No significant difference was seen in short term graft survival between recipient of livers from LRDs and cadaveric donors, however data on liver donor types is limited and a certain conclusion cannot be made. however.

Figure 1: LRD vs Cadaver 1 year graft survival



MODERATED POSTER

Moderated poster session on kidney transplants in children and young people

MPS6_8 STEROID-BASED VS STEROID-FREE IMMUNOSUPPRESSION IN PAEDIATRIC KIDNEY TRANSPLANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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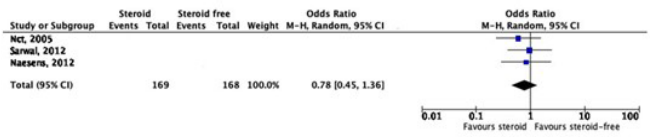
Background: Corticosteroids are the cornerstone of immunosuppressive regimens in kidney transplantation. In pediatric renal transplantation the side-effect profile of steroids becomes crucial as long-term exposure to high dose steroids affects the development and well-being of the child. Steroid free immunosuppressive regimens are an alternative with a better side effect profile, however to date no systematic review has been carried out evaluating corticosteroid free-regimens safety and efficacy in children.
Methods: Medline, Embase, CENTRAL and Web of Science databases were searched systematically. Risk of bias assessment was performed.
Results: Three studies were included in the meta analysis. No significant difference was seen between graft rejection in the steroid-based or steroid-free regimes (P=0.39) (OR: 0.78 (95% CI: 0.45, 1.36) (fig.1) . Cardiac arrest was reported as a side effect in steroid-based regimes whereas atrial flutter and cardiovascular insufficiency were reported in steroid-free regimes. Infections incidence had heterogeneity between studies and the relation to steroid-based or steroid-free regimes. Anaemia was more common in steroid-free and hypertension was more frequent in steroid-based regimens.
Conclusions: Steroid-free immunosuppressive regimens were as effective at minimizing graft rejection when compared to steroid-based regimens. While regimens are comparable in efficacy, side effect profiles differ between regimens.

Figure 1: Steroid-based vs Steroid-free Immunosuppression chronic graft rejection



MPS6_9 CORRELATION BETWEEN CLINICAL OUTCOMES AND QUALITY OF LIFE IN PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

Maura Scott[1], Daniel Johnson[2], Ellen O Connor[1], Nicos Kessaris[1], Stephen D Marks[1;2], Sheila Boyle[1], Zainab Arslan[1;3], Jelena Stojanovic*[1]

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Background: Kidney transplantation is the preferential kidney replacement therapy (KRT) for children with renal failure with well reported physiological and psychosocial advantages over dialysis. There is an abundance of literature regarding clinical outcomes (CO's) associated with KRT but a scarcity of data assessing the impact of these CO's on quality of life (QoL).This study aimed at identifying correlation between CO's and the effect on QoL of paediatric kidney transplant recipients (pKTR).
Methods: Patients attending clinic were offered the opportunity to complete a standardised age-appropriate QoL questionnaire (PedsQL TMv3.0) during clinic attendances in April 2022.Inclusion criteria were pKTR at least three months post-transplant of a single organ (kidney).Questionnaire responses were pseudo-anonymised with QoL scores subsequently matched to individual clinical outcome dataset. The Cronbach alpha co-efficient was calculated for each section of the questionnaire to ensure there was reliable as opposed to error variance.
Results: Of the 46 patients approached to take part, 36 (25% of total post-transplant cohort) met inclusion criteria and completed the questionnaire. The mean patient age and timing post-transplantation were 12.8 years and 5.2 years, respectively. CAKUT (42%) and nephrotic syndrome (22%) were the most common primary renal diagnosis. There was no statistically significant correlation between QoL and number of clinic attendances (p=0.373) or number of medications (p=0.739). There was a statistically significant difference in beliefs regarding the impact of medications on physical appearance between adolescents with a history of rejection and those without (p =0.044).
Conclusions: QoL is subject and patient specific. Clinicians must identify factors impacting QoL and work collaboratively to lessen their impact. Surprisingly medication burden or number of clinic attendances was not shown to affect QoL in this cohort . Adolescents often struggle with compliance, our study has shown a link between history of allograft rejection and a belief that medications negatively impact appearance. At a time of significant social pressures it is important that we address the psychosocial impact of post-transplant medications on self-esteem and positive body image.

MPS6_10 SYSTEMATIC DIGITAL ASSESSMENT OF PATIENT-REPORTED OUTCOMES IN CLINICAL FOLLOW-UP OF PEDIATRIC KIDNEY TRANSPLANTATION PATIENTS: A PILOT STUDY

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Background: Digital and systematized collection of patient history provides additional information in comparison to traditional methods. Measurement of a patient's perception of his/her disease and corresponding treatment without interpretation by a third person (i.e., healthcare personnel) defines Patient-Reported Outcomes (PROs). PROs fill an important gap in chronic kidney disease to achieve optimal disease control, treatment, and well-being. Neither PROs nor digital patient history systems are frequently implemented in clinical routine. This pilot study aimed to develop, implement, and analyze a digital system for collection of patient history and PROs of pediatric patients with kidney transplantation (KTX), in context of their graft function during follow-up.
Methods: Pediatric KTX patients received a tablet with 19 questions collecting their recent history (i.e., since the last visit) and PROs at their regular outpatient clinic visits. We conducted an unweighted, undirected network-based clustering analysis to identify patient history elements and PROs associated with kidney allograft function and other clinical outcome surrogate parameters (e.g., creatinine).
Results: A total of 49 pediatric KTX patients were included in this study, with 67%:33% male:female, a median age of 14 (IQR 11-16) and a median post-transplant follow-up time of 5.3 (IQR 2.7-10) years. 45% were living donor recipients, and maintenance immunosuppression was mainly a triple regimen (tacrolimus, mycophenolate mofetil, steroids). The median graft function at baseline was 100 mL/min/1.72 m² (IQR 70-124). We identified a total of four clusters of which two clearly differentiated between patients with high and low kidney allograft function based on different patient history elements and PROs (e.g., defecation-related questionnaire elements).
Conclusions: With this pilot study, for the first time, we demonstrated a clear differentiation between pediatric patients with high and low kidney allograft function based on different patient history elements and PROs. Longitudinal follow-up of pediatric kidney transplant patients with such digital patient history and ePRO systems could aid in the early identification of complications after successful transplantation and facilitate early intervention.

E-POSTERS

P001 HOW COVID-19 PANDEMY INFLUENCED ON QUALIFICATION FOR KIDNEY TRANSPLANTATION IN POLAND

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Background: COVID-19 pandemy highly influenced on medical services worldwide. A lot of medical procedures has been cancelled or postponed. In some cases access to the physicians was extremely difficult and in very often cases limited to medical advices over the digital communication solutions. One of the most affected medical procedures were qualification for the kidney transplantation, which requires the several medical advices with specialists from different areas and imaging and lab diagnostics on the qualification stage. The aim of the research was check how the numbers of qualified for kindey transplantation patients have been changed in 2020 and 2021 - the years of COVID-19 pandemy in comparison with 2019 data - year without pandemic limitations.
Methods: The official data from Polish Transplant Coordinating Centre Poltransplant bulletin from 2019, 2020 and 2021 has been analyzed in terms of the number of patients registered on the waiting list for kidney transplantation. The number of the kidney Tx provided in the country has been taken into consideration as well.
Results: During SARS-CoV-2 pandemy the number of qualified and transplanted patients significantly decreased. The most worsened data concerns the new qualifications which decreased about 30% in the first year of pandemy as the effect of all restrictions implemented. Second year of pandemy (2021) brought better results of patients newly registered on the waiting list (+11,6%), however still remains on the level lower than in previous years (1178 in 2018 vs. 1160 in 2017). The number of Kidney Tx procedures provided during 2-years pandemy period also decreased significantly and in the second year of the pandemy didn't increased satisfactorily (0,6%).
Conclusions: The period of the pandemic had a great impact on the development of kidney transplantation in Poland. Restrictions caused by pandemic restrictions have deprived many patients of any chance for treatment. We shall focus on the rapid growth in the number of transplants in the years following the pandemic. On the other hand, the community of transplantologists should introduce cooperation with national authorities to implement the best possible procedures of protection the patients reffered for transplantation in case of the future epidemic situation.

P003 IMPACT OF DIFFERENT IMMUNOSUPPRESSIVE PROTOCOLS ON CLINICAL OUTCOMES IN OBESE KIDNEY TRANSPLANT RECIPIENTS: A PROPENSITY SCORE MATCHED ANALYSIS

Lina Maria Serna-Higuita*[1], Andrea Della Penna[2], Martina Guthoff[3], Nils Heyne[3], Sandra Beer-Hammer[4], Silvio Nadalin[2], Peter Martus[5], Alfred Königsrainer[2], Markus Quante[2]

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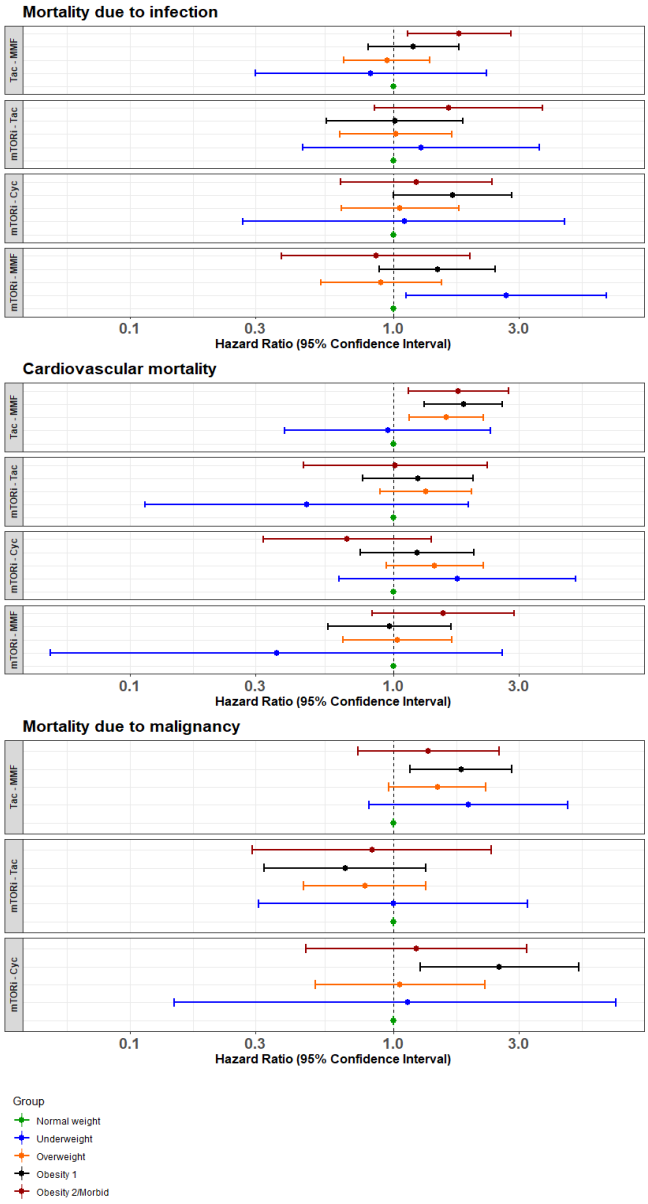
Background: Although obesity has become a relevant clinical problem in the field of transplantation, the impact of different immunosuppressive protocols on clinical outcomes in obese transplant recipients remains unclear. This study aimed to evaluate the obesity-specific impact of calcineurin inhibitor (CNI) or mammalian target of rapamycin inhibitor (mTORi) and its combinations on clinical outcome in kidney graft recipients.
Methods: Data were obtained from the Scientific Registry of Transplant Recipients (SRTR) database. Kidney transplant recipients were categorized to BMI categories and according to immunosuppressive protocols: Tacrolimus/Mycophenolat-Mofetil (Tac-MMF), mTOR-Inhibitor/Tac (mTORi-Tac), mTORi/Cyclosporin (mTORi-Cyc) and mTORi/MMF. Primary outcome was acute rejection within the first year after kidney transplantation, secondary outcomes included eGFR, graft and overall survival. Propensity score matching, binary logistic regression and Cox regression analysis were used.
Results: Among 14,500 patients, graft recipients with advanced obesity (BMI ≥35 kg/m^2) exhibited significantly lower rates of acute rejection (AR) in the mTORi-Tac (6.4%) and mTORi-Cyc (8.2%) group compared to Tac-MMF (10.8%). There was no significant association between obesity and the risk of AR on patients receiving therapy with mTORi-MMF (HR: 1.29, 95% CI 0.69–2.43, p value 0.42) and mTORi-Cyc (HR: 1.55, 95% CI 0.92–2.61, p value 0.097), compared to Tac-MMF. Advanced obesity was associated with a significant risk of graft loss in patients receiving therapy with mTORi-MMF ((HR: 1.50; 95% CI 1.20–1.88; p<0.001) and mTORi-Tac group ((HR: 1.44; 95% CI 1.17–1.76; p<0.001) compared to Tac-MMF, but not for the mTOR-Cyc group (HR 1.11 95% CI 0.92–135, p value 0.28). In the Tac-MMF group, patients with morbid obesity had significantly higher mortality due to cardiovascular disease and infection compared with normal-weight patients.
Conclusions: Combination of mTORi and CNI is associated with lower rejection rates and stable long-term kidney function while reducing cardiovascular side effects linked to CNIs in obese kidney graft recipients. These results are critical for the growing number of obese graft recipients and warrant prospective evaluation.

Figure: Cox regression stratified by BMI



P004 PANCREAS TRANSPLANT ALONE IN UREMIC (PTAU) PATIENTS

Yi-Ming Shyr[*1]
[1]*Taipei Veterans General Hospital, PeiTow, Taiwan*

Background: Theoretically, pancreas before kidney transplant (PBK) could be an option for those waiting for both pancreas and kidney grafts. Outcomes of pancreas before kidney transplant (PBK) have never been reported before.
Methods: In total, 160 diabetes patients undergoing pancreas transplants were included in this study. Clinical data and outcomes were compared between pancreas transplant subgroups.
Results: There were 26 (16%) PBK**.** The rates of pancreas graft rejection were 3.8% in the pancreas before kidney transplant, 16.7% in the pancreas after kidney transplant (PAK), 29.8% in the simultaneous pancreas and kidney transplant (SPK), and 37.0% in the pancreas transplant alone (PTA) groups. There was no chronic rejection in the PBK and PAK groups. Fasting blood sugar and serum hemoglobin A1c levels after PBK were not significantly different from those of other subgroups. Serum C-peptide levels were significantly higher in the PBK than in the other subgroups**.** The 5-year pancreas graft survival was 100% for the PBK and PAK, 97.0% for the SPK, and 77.9% for PTA.
Conclusions: given the inferior patient survival outcome, PTAU is still not recommended unless SPK and PAK is not available. Although PTAU could be a treatment option for patients with diabetes complicated by end-stage renal disease (ESRD) in terms of surgical risks, endocrine function, and immunological and graft survival outcomes, modification of the organ allocation policies to prioritize SPK transplant in eligible patients should be the prime goal.

P005 PANCREAS TRANSPLANT WITH ENTERIC DRAINAGE: EXPERIENCE OF TAIPEI VETERANS GENERAL HOSPITAL

Yi-Ming Shyr[1]
[1]*Taipei Veterans General Hospital, PeiTow, Taiwan*

Background: Insulin-dependent diabetes mellitus (IDDM) eventually leads to nephropathy, neuropathy, retinopathy and angiopathy after 10 – 30 years. Nowadays, pancreas transplantation is the treatment of choice in tight control of blood sugar for IDDM patients. Simultaneous pancreas and kidney (SPK) transplantation would be an ideal treatment option to resolve both uremia and IDDM. We will present our experience in pancreas transplant.
Methods: From September 2003 to Septemberr 2020, 164 cases of pancreas transplant were performed, including 37 SPK, 20 pancreas after kidney transplant (PAK), 78 pancreas transplant alone (PTA), 28 pancreas before kidney transplant (PBK), and 1 pancreas after liver transplant (PAL). The clinical courses including blood sugar, C-peptite and HbA1 C levels and renal function after operation were recorded. The complications and outcomes were also evaluated.
Results: The technique success rate for both pancreas and kidney transplants are 97%. Seven underwent pancreas re-transplant. The most common surgical complication is GI bleeding followed by intraabdominal bleeding. There is 4 surgical mortality. Thew most common infection is CMV infection, followed by pseudomenbraneous colitis. Rejection occurred in 25% including 17% acute and 9% chronic rejection. Rejection occurred most commonly in PTA, acute in 23% and chronic in 14%. Graft loss occurred in 36 cases, with 5 (3%) technique failure, 6 (4%) acute rejection, 11 (7%) chronic rejection, 13 (8%) death with functioning graft, and 2 (1%) unknown reason. Graft loss occurred most commonly in PTA (36%). 1-, 5-, and 10- year pancreas graft survival rate is 96%, 90% and 66% respectively.
Conclusions: Pancreas transplant provided an ideal insulin-free solution with physiological blood sugar control for diabetic patients with and without end-stage renal disease. Pancreas transplant could be even performed simultaneously with, after and also before kidney transplant.

P006 PANCREAS TRANSPLANTATION FOR TYPE 2 DIABETES MELLITUS

Yi-Ming Shyr[*1]
[1]*Taipei Veterans General Hospital, PeiTow, Taiwan*

Background: Pancreas transplantation remains the best long-term treatment option to achieve physiological euglycemia and insulin independence in patients with labile diabetes mellitus (DM). It is widely accepted as an optimal procedure for type 1 DM (T1DM), but its application in type 2 DM (T2DM) is not unanimously acknowledged.
Methods: In total, 146 diabetes patients undergoing pancreas transplantation were included in this study. Clinical data and outcomes were compared between the T1DM and T2DM groups.
Results: Majority (93%) of the pancreas transplantations in T2DM were for uremic recipients. Complications occurred in 106 (73%) patients, including 70 (48%) with early complications before discharge and 79 (54%) with late complications during follow-up period. Overall, rejection of pancreas graft occurred in 37 (25%) patients. Total rejection rate in T2DM recipients was significantly lower than that in T1DM. The short-term and long-term outcomes for endocrine function in terms of fasting blood sugar and hemoglobin A1c levels and graft survival rates are comparable between the T2DM and T1DM groups.
Conclusions: T2DM is not inferior to T1DM after pancreas transplantation in terms of surgical risks, immunological and endocrine outcomes, and graft survival rates. Therefore, pancreas transplantation could be an effective option to treat selected uremic T2DM patients without significant insulin resistance.

P007 REASONS FOR DEATH WITH A FUNCTIONING KIDNEY GRAFT AND REASONS FOR OVERALL GRAFT FAILURE

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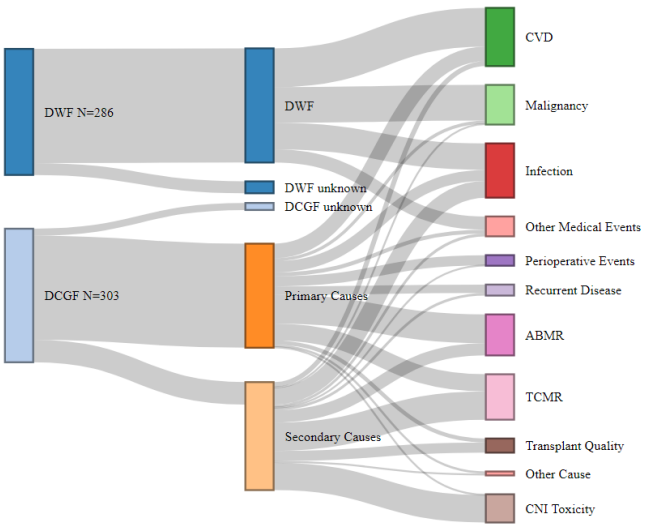
Background: Reported reasons for kidney allograft loss vary widely depending on methods of classification and follow-up duration.
Methods: In this single-center study we included all 1477 adult kidney transplants performed between 1997 and 2017 of which all 286 deaths with a functioning graft (DWF) until the end of observation were analyzed case-by-case by an adjudication committee and causes for death assigned based on pre-specified criteria. Additionally, the results were compared to the causes of 303 death-censored graft failures (DCGF) of the same cohort that have already been investigated, to evaluate the impact of causes on overall graft loss. No patients were lost to follow-up.
Results: The most frequent causes for DWF were cardiovascular disease (CVD) in 30.8%, malignancy in 28.3% and infections in 21%. Only 9.4% of reasons for DWF were unknown. Sudden cardiovascular death occurred in 40% (35/88) of patients classified as DWF due to CVD. While cardiovascular disease was responsible for >50% of deaths in the first month after transplantation, the number of deaths due to malignancy continuously increased and peaked later than for infections and cardiovascular disease around 8 years after transplantation. Overall graft loss was related to the effect of immunosuppression in 36.2% (infection: 20.9% (123/589); malignancy: 15.3% (90/589)) and CVD in 22.4% (132/589) (Figure 1). In 27.4% (161/589) graft failure was associated with under-immunosuppression (rejection). For infections (60 DWF; 63 DCGF) and CVD (88 DWF; 44 DCGF) a considerable overlap was observed between DWF and DCGF. For patients >70 years of age at transplantation, medical events accounted for 78% of overall graft losses and only 6.5% were associated with rejection.
Conclusions: DWF and DCGF share more causes for graft loss than previously reported, and sudden death plays an underestimated role in death with a functioning kidney allograft.

Figure 1: Causes for death with a functioning graft (DWF) and death censored graft failure (DCGF).



P009 METABOLOMICS APPROACH AND GRAFT FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS

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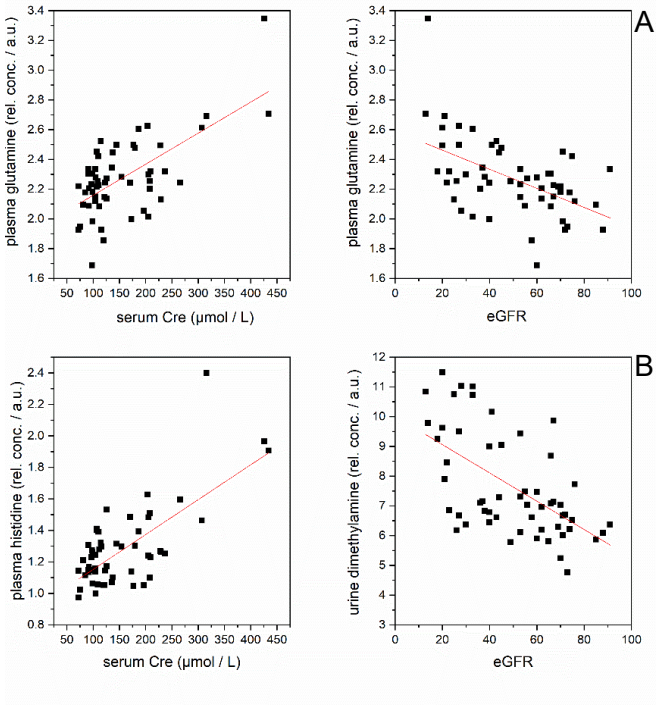
Background: Kidney transplantation is the best treatment modality in patients suffered from terminal renal failure. One-year graft survival reaches more than 90%. However, long term graft survival has not improved in the last decade and it is still an area of interest. There is evidence that many low molecular species are not only intermediate metabolites, but they also work as important regulatory molecules. Non-invasive metabolomics approach might be the option for identification of high-risk grafts for dysfunction.
Methods: In a group of patients after primary kidney transplantation (n = 55) we correlated (Pearson's correlation) relative changes in blood plasma and urine metabolites detectable by NMR spectroscopy with parameters related to graft function: estimated glomurelal filtration rate (eGFR, CKD-EPI) and serum creatinine (Cre).
Results: Positive correlations were found for plasma metabolites levels phenylalanine ($p<0.0005$), glutamine ($p<0.0005$), lysine ($p<0.05$) and histidine ($p<0.0000005$) with Cre. All these metabolites ($p<0.0005$, $p<0.005$, $p<0.05$ and $p<0.005$) as well as acetate ($p<0.05$) and citrate ($p<0.05$) correlated negatively and Branched chain α-keto acids - BCKAs ($p<0.05$) correlated positively with eGFR. In urine, we observed negative correlation of citrate ($p<0.005$), Trimethylamine N-oxide - TMAO ($p<0.05$), dimethylamine ($p<0.00005$) and lactate ($p<0.05$) with eGFR.
Conclusions: Patients after kidney transplantation are challenged with altered metabolomic conditions in blood plasma, where we observed direct relation of particular plasma metabolites to renal dysfunction. Additionally we also observed a close link between urine amines and graft function expressed by eGFR value. Metabolomics approach is very promising in nephrological research, especially in early identification of risk for graft loss.

Figure 1. Correlation between plasma glutamine and creatinine and eGFR (A)
Correlation between plasma histidine and creatinine and eGFR (B)



P011 NEONATAL ORGAN DONATION FOR KIDNEY SHORTAGE; IS THIS THE TIME?

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Background: Renal transplantation is the most successful therapy of end-stage renal failure since it is associated with extended life expectancy and quality of life compared to dialysis. As of January 2022, there were in the US,100,000 patients on the waitlist, with only 24,669 kidneys transplanted the previous year, and an annual death rate of 5,000 patients on the wait-list. Stratagems are sought to expand the donor pool and neonates can be considered a source of kidneys, until now unexplored, since the report by LW Martin in 1969 of the long-term successful transplantation of en bloc anencephalic kidneys to a 17 pound boy.
Methods: To assess the feasibility of neonatal organ donation, we reviewed the neonatal mortality in the US, the physiology of the neonatal kidneys, the ethical, social and medico-legal problems associated with neonatal brain death, and the long-term development of the kidneys after transplantation. The organ procurement and the allocation are also discussed.
Results: Of the 21,000 infants dying in 2020, and taking a conservative approach, 8.600 infants with lethal congenital malformations, 2,380 infants with CNS injuries, and 1,260 infants with respiratory distress could be considered as organs donors. There is ample evidence that en bloc infant kidneys 1- have a catch-up growth, 2- provide excellent long-term function (>25 years) exceeding that of living donor kidneys, 3- are not subjected to hyperfiltration injury, and 4- can be transplanted safely with current techniques at hands.
Conclusions: Ethical, social, medico-legal and technical aspects have been established and are ready for use in neonatal organ donation and transplantation. Policies should be implemented to allow such approach. A simplified allocation system is indicated to avoid long cold ischemia. Neonatal kidneys can improve organ shortage.

P012 VERY LOW DOSE ANTI-THYMOCYTE GLOBULINS VERSUS BASILIXIMAB IN NON-IMMUNIZED KIDNEY TRANSPLANT RECIPIENTS

Christophe Masset[*1], **Clarisse Kerleau[1], Gilles Blancho[1], Maryvonne Hourmant[1], Simon Ville[1], Delphine Kervella[1], Diego Cantarovich[1], Aurelie Houzet[1], Magali Giral[1], Claire Garandeau[1], Jacques Dantal[1]**

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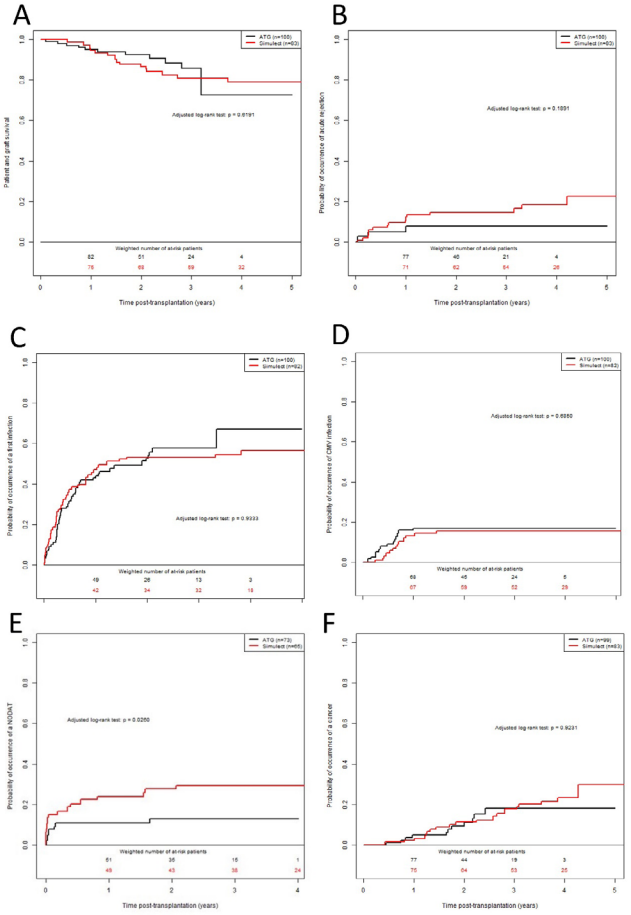
Background: The choice between Basiliximab (BSX) or Anti-Thymocyte Globulin (ATG) as induction therapy in non-immunized kidney transplant recipients remains uncertain. Whilst ATG may allow steroid withdrawal and a decrease in tacrolimus, it also increases the risk of viral reactivations due to a prolonged dose-dependent lymphopenia. We investigated outcomes in non-immunized patients receiving a very low dosage of ATG versus BSX as induction therapy.
Methods: In this monocentric study, we analysed non-immunized patients receiving a first kidney transplant between 2015 and 2020. The study outcomes were patient and graft survival, cumulative probabilities of biopsy proven acute rejection (BPAR), infectious episode, CMV infection, post-transplantation malignancy and post-transplant diabetes (PTD). Cox, logistic or linear statistical models were used depending on the studied outcome and models were weighted on propensity scores.
Results: 183 patients were included: 100 receiving ATG (mean total dose of 2.0 mg/kg) and 83 receiving BSX. Maintenance therapy was comparable between the groups. Patient and graft survival did not differ between groups, nor did malignancies, infectious complications or CMV viremia. There was a trend for a higher occurrence of a first BPAR in the BSX group (HR at 1.92; 95% CI: 0.77; 4.78, p-value = 0.15) with a significantly higher number of BPAR episodes (17% vs 7.3%, p = 0.0152). PTD occurrence was significantly higher in the BSX group (HR at 2.44; 95% CI: 1.09; 5.46; p-value = 0.03).
Conclusion: Induction with a very low dose of ATG in non-immunized recipients was safe and associated with a lower rate of BPAR and PTD without increasing infectious complications.

Figure 2. Confounder-adjusted probabilities of events according to the time post-transplantation and the induction therapy. **A-** patient and graft survival. **B-** cumulative probability of a first episode of acute rejection episode. **C-** cumulative probability of infection. **D-** cumulative probability of CMV replication. **E-** cumulative probability of PTD. **F-** cumulative probability of post-transplantation malignancy



P013 OPERATING THEATRE NURSES´MAIN CONCERNS DURING THE OPERATIVE PROCESS OF ORGAN DONATION- A GROUNDED THEORY

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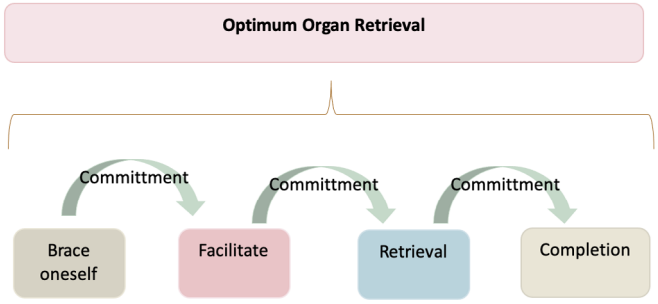
Background: Organ donation is the result of cooperation between many professionals in a chain of events where it is crucial that every professional involved does her/his utmost to facilitate organ preservation and retrieval. The responsibilities for the Operating Theater Nurse (OTN) range from ensuring that the right instruments are in place to safeguarding the donor's dignity and rights. The OTN must be flexible since the donation often occurs during nights and involves unfamiliar surgical teams. Little is known about operating theatre nurses' (OTNs) main concerns during the perioperative organ donation process and how they deal with them. The purpose of this study was to explore OTNs' experiences of caring for the organ donor during operations where organs are retrieved and to answer the question: what is the main concern during this procedure and how do they deal with it?
Methods: A total of ten OTNs, one man and nine women with a mean age of 51.8 years (range 38-63 years) were interviewed in this Constructive Grounded Theory study. No prior theory exists and the grounded theory stem from the participants' own experiences. The informants represent two University hospitals and three regional hospitals in Sweden to reflect a diversity of hospital settings and geographical areas.
Results: A core category emerged during the analysis: Optimum organ retrieval, where the generated grounded theory is present in the four main categories: Brace oneself, Facilitate, Retrieve and Completion. Commitment is the force that binds the OTN to a course of action of relevance for optimum organ retrieval. Respect for and the dignity of the donor is essential.

Conclusions: The first Grounded theory on OTNs main concerns during perioperative care of deceased organ donors is developed and presented. This theory might be useful to support clinical practice in the OR as well as to illuminate what to focus on when educating OTNs in organ donation and perioperative nursing care.



P014 LONG-TERM RESULTS OF AB-INITIO INTRODUCTION OF EVEROLIMUS AFTER LIVER TRANSPLANTATION

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Background: Ab-initio introduction of Everolimus in liver transplantation immunosuppression regimens allows weaning of Calcineurin Inhibitors (CNI) and Mycophenolate levels consequently reducing the common complications associated to their use. The primary aim of our study was the analysis of graft and recipient survival at the 5- and 10-year follow-up timepoints. The secondary aim was to assess the acute and chronic rejection incidence, renal function, and incidence of complications in our cohort.
Methods: Observational retrospective monocentric study analyzing all patients undergoing liver transplantation between September 2009 and March 2020, with a minimum follow-up length of 3 months, in whom Everolimus was introduced on post-operative day 1 along with low-dose CNI and Mycophenolate on a steroid-free protocol.
Results: One-hundred and sixty-six patients [135 (81%) males, mean age 58 y.o. (20-72)] were included. The overall graft and recipient survivals were 70% and 60% at the 5- and 10-year timepoint respectively. The incidence of acute rejection was 3%. In all the 17 (10%) patients suffering from hepato-renal syndrome at transplant [mean Serum Creatinine 0,9 mg/dL (1,6-3,49)] we observed normalization of the renal function. De-novo malignancies incidence and HCC recurrence were 14% and 1% respectively. In 37 (22%) patients, we were able to taper CNIs up to a Everolimus monotherapy.
Conclusions: Ab-initio introduction of Everolimus in liver transplant immunosuppression schemes is safe and associated to a low incidence of acute and chronic rejection. Also, thanks to the reduction of post-operative complications it allows tapering of other immunosuppressants and complete wean-off in 22% of the patients.

P015 RESPONSE TO COVID-19 VACCINATION AND CONTIX-AGEVIMAB-CILGAVIMAB PROPHYLAXIS IN PATIENTS UNDERGOING LIVER AND KIDNEY TRANSPLANTATION: PRELIMINARY STUDY

Domiziana Pedini[*1], **Roberta Angelico[1], Marco Materazzo[1], Andrea Caruso[1], Claudia Quaranta[1], Giulia Bacchiocchi[1], Cristine Brooke Pathirannehalage Don[1], Tommaso Manzia[1], Giuseppe Tisone[1]**

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Background: Liver (LT) and kidney (KT) transplant patients are at high risk of mortality from COVID-19(16-29%, 28%; respectively). Although transplant patients undergo a full vaccination course (3 doses), they are frequently low-responders and long-acting-antibody prophylaxis (LAAB) has been proposed. However, the efficacy of these strategies has not yet been demonstrated in LT and KT. The objective of our study is the evaluation of the antibody response after complete vaccination and the efficacy of prophylaxis with LAAB.
Methods: Since 03/01/2022 all LT and KT patients during follow-up have been enrolled. anti-COVID-19 title was obtained by ECLIA Test (Elyx, Roche). In the case of antibody level <100 IU/ml, patients were invited to prophylaxis with tixagevimab-cilgavimab(AZD7442, AstraZeneca). At three months, a follow-up was performed to assess any COVID-19 infection.
Results: Until 31/03/2022 155 patients were enrolled (58 KT; 57 LT), mean age 59.11 (± 11.61), with mean antibody value 1127.05 and 1701.14 IU/ml and protective value(responder) in 42 (72.88%) and 45 (79.31%) cases, respectively. Among 32 (27.83%) low-responders, 16 (50%) patients underwent LAAB. After LAAB 4 KT contracted COVID-19, 3 in mild/asymptomatic form and one hospitalized which not required oxygen therapy. In the following three months, in reponder patients 83 (72.17%), 6 KT and 8 LT had in mild/asymptomatic COVID-19. No graft-loss, acute rejection, or death have been recorded.
Conclusions: COVID-19 vaccination in KTs and LTs can reduce the mortality of transplant patients. In low-responder patients, LAAB prophylaxis is safe and protective, resulting in reduced complications and hospitalization.

P016 PRE-TRANSPLANT MYCOPHENOLATE MOFETIL MAY BE ASSOCIATED WITH REDUCED INTRAHEPATIC CHOLANGIOPATHY IN ABO-INCOMPATIBLE LIVER TRANSPLANTATION

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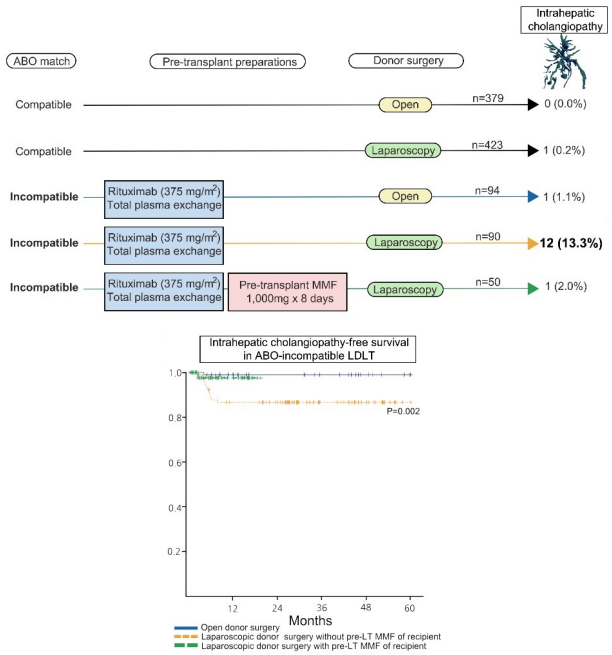
Background: Intrahepatic cholangiopathy is a life-threatening sequela of ABO-incompatible liver transplantation. We analyzed the clinical impact of pre-transplant administration of mycophenolate mofetil in reducing intrahepatic cholangiopathy in ABO-incompatible liver transplantation.
Method: Patients who underwent living donor liver transplantation between 2010 and April 2022 were included. Pre-transplant mycophenolate mofetil was started in November 2020. A comparison between patients who experienced intrahepatic cholangiopathy and who did not among ABO-incompatible transplantation was performed. Recipients of ABO-incompatible transplantations were categorized based on donor surgery into open, laparoscopy without pre-transplant mycophenolate mofetil, and laparoscopy with pre-transplant mycophenolate mofetil groups. Cox analysis of intrahepatic cholangiopathy was performed.
Results: A total of 234 ABO-incompatible transplantations were included. Intrahepatic cholangiopathy occurred in 1.1% (n=1/94), 13.3% (n=12/90) and 2.0% (n=1/50) of patients who received an ABO-incompatible liver with open surgery, laparoscopic donor surgery without pre-transplant mycophenolate mofetil and laparoscopic donor surgery with pre-transplant mycophenolate mofetil. (P=0.001) Multivariable analysis showed that transplantations involving a donor who underwent a laparoscopic hepatectomy and a recipient who did not receive pre-transplant mycophenolate mofetil were associated with a higher risk of intrahepatic cholangiopathy (HR=13.449, CI=1.710–105.800, P=0.02) compared to transplantations from donors who underwent open surgery. Transplantations involving a donor who underwent laparoscopic donor surgery and a recipient who received pre-transplant mycophenolate mofetil resulted in no increased risk compared to transplantations from donors who underwent open surgery. (HR=5.307, CI=0.315–89.366, P=0.25)
Conclusion: Laparoscopic donor hepatectomy was a risk factor for intrahepatic cholangiopathy in ABO-incompatible liver transplantation while pre-transplant mycophenolate mofetil was related to risk reduction of intrahepatic cholangiopathy.



P017 HEPATIC ARTERIAL REVASCULARIZATION IN THE FIRST 72 HOURS FOLLOWING LIVING-DONOR LIVER TRANSPLANTATION: SURGICAL OR ENDOVASCULAR?- A PROPOSED ALGORITHM

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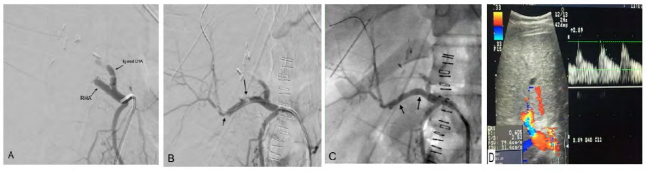
Background: The aim of this retrospective cohort study was to evaluate the feasible treatment modalities for early hepatic artery thrombosis (e-HAT) in the first 72 hours (hrs) following living-donor liver transplantation (LDLT); as well as to design a structured algorithm –based on our 20-year LDLT experience– for management of such a devastating complication during this very early post-transplant period.
Methods: The medical records of 34 patients who developed e-HAT following LDLT between August 2001 and September 2021 were retrospectively reviewed. In all cases, the treatment modalities employed and their outcomes were thoroughly evaluated. Revascularization approaches that were used in the first 72 hrs post-transplant were compared in terms of technical success, procedure-related complications, rebound thrombosis, graft failure and 1-year survival rates. Finally, a structured algorithm for management of e-HAT in the first 72 hrs post-LDLT was designed.
Results: Overall, the definite technical success and 1-year survival rates of hepatic arterial revascularization (Surgical / Endovascular / Both) were 85.3% (29/34 cases) & 61.8% (21/34 cases) respectively. Nineteen patients developed e-HAT in the first 72 hrs post-LDLT (55.9%). Surgical revascularization was carried out in the first 72 hrs post-transplant in 6/34 cases (17.6%) “Group A”; whereas endovascular therapy was carried out within the same time frame in 14/34 cases (41.2%) “Group B”. The definite technical success, rebound thrombosis and 1-year survival rates were 83.3%, 16.7% & 83.3% in group A; and 85.7%, 0% & 57.1% in group B; respectively. Five procedure-related complications were reported in 4 of group B patients (28.6%).
Conclusions: In the first 72 hrs post-LDLT, endovascular therapy –including stent placement (early stenting)– is a feasible and effective treatment option for e-HAT; but is associated with a relatively higher risk of procedure-related complications, compared to surgical revascularization. Hence, endovascular therapy can be reserved as a second-line option for treatment of e-HAT in the very early post-transplant period. It can be carried out –with the use of specific technical precautions– in certain situations where surgical revascularization could potentially be more risky, too complex, or absolutely futile.



Variables	Surgical revascularization in the first 72 hours post-transplant “Group A” (n=6)	Endovascular therapy in the first 72 hours post-transplant “Group B” (n=14)
Timing of development of early hepatic artery thrombosis (e-HAT)		
Postoperative day 1	5 (83.3%)	5 (35.7%)
Postoperative day 2	1 (16.7%)	5 (35.7%)
Postoperative day 3	0 (0.0%)	4 (28.6%)
Intra-arterial thrombolysis (IAT)		
No	4 (66.7%)	1 (7.1%)
Using Streptokinase (SK)	1 (16.7%)	0 (0.0%)
Using Tissue Plasminogen Activator (tPA)	1 (16.7%)	13 (92.9%)
Percutaneous transluminal angioplasty (PTA) & stent placement	0 (0.0%)	6 (42.9%)
Definite technical success rate	5 (83.3%)	12 (85.7%) - IAT + PTA without stenting: 6/7 cases (85.7%) - IAT, PTA & stent placement: 6/6 cases (100%)
Procedure-related complications	0 (0.0%)	4 (28.6%) - Post-thrombolysis bleeding: (n=2) - Anastomotic disruption: (n=1) - Arterial dissection: (n=2)
Rebound thrombosis	1 (16.7%)	0 (0.0%)
Graft failure	1 (16.7%)	4 (28.6%)
Both surgical revascularization & endovascular therapy	2 (33.3%)	1 (7.1%)
One-year survival rate	5 (83.3%) 1/6 patients (16.7%) died of graft failure after failure of arterial revascularization (surgical revascularization & endovascular therapy)	8 (57.1%) 5/14 patients (35.7%) died despite definite technical success of arterial revascularization - Graft failure despite definite technical success of endovascular therapy (n=3) - Acute myocardial infarction (n=1) - Severe autoimmune hemolysis (n=1) 1/14 patients (7.1%) died of graft failure after failure of arterial revascularization (endovascular therapy)

P018 USE OF ECULIZUMAB IN A CASE OF HISTOLOGICALLY PROVEN RECURRENCE OF COMPLEMENT FACTOR H - RELATED 5 PROTEIN NEPHROPATHY TO A KIDNEY ALLOGRAFT

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Background: Human complement Factor H - related 5 protein (CFHR5) nephropathy is a hereditary kidney disease endemic in Greek Cypriots and is the commonest cause of C3 glomerulonephritis (C3GN). Great phenotypic heterogeneity is noted among patients and manifestations can vary from isolated microscopic hematuria to end stage kidney disease (ESKD). CFHR5 protein antagonizes complement Factor H (CFH), which is the main circulating regulator of the complement system. To date there is no specific treatment for CFHR5 nephropathy. Although histologic recurrence of the disease after kidney transplantation is usual, graft outcomes are generally good, using standard immunosuppression regimens. Nevertheless, some transplanted patients lose their grafts due to aggressive recurrent disease, usually at the first post-transplant period. Eculizumab is a long-acting humanized monoclonal antibody targeting complement factor C5. Thus, the cleavage of C5 into C5a and C5b is inhibited resulting in terminal complement system deactivation. Regarding kidney diseases, until now Eculizumab use is only approved for the treatment of atypical hemolytic uremic syndrome.
Methods: We describe the case of a 39 yo male patient with histologically proven recurrence of CFHR5 nephropathy in the renal allograft, two months post-transplant. An allograft biopsy was performed due to non-nephrotic range proteinuria and severe kidney function impairment. The patient’s kidney function deteriorated rapidly, leading to the decision to treat him with Eculizumab.
Results: Proteinuria was improved and kidney function returned to baseline over the next 3 months. The patient is currently in excellent clinical condition, having no adverse effects from the treatment 10 months after initiation of Eculizumab.
Conclusions: To our knowledge, this is the first time that Eculizumab was used as a treatment for CFHR5 nephropathy. Results are promising for kidney transplant recipients with features of clinical and histological recurrence of the disease but also for not transplanted patients with an aggressive form of the disease. Further studies are required to confirm the therapeutic effects of Eculizumab on CFHR5 nephropathy and to identify the subgroup of patients that would benefit from it.

P019 PEDIATRIC ORGAN DONATION: SIXTEEN-YEAR EXPERIENCE OF A PEDIATRIC INTENSIVE CARE UNIT / INTENSIVE CARE UNIT IN A LEVEL 3 HOSPITAL FROM 2006 TO 2021

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Background: Pediatric organ donors represent a small but important portion of the deceased donor pool, helping both children and adults in the transplant waitlist. Despite this, pediatric donation remains an overlooked subject of research.
Methods: Retrospective, single-center, descriptive study. We included all brain death patients under 18 years old who were admitted to the Pediatric Intensive Care Unit (PICU) between January 1st, 2006, and December 31st, 2021, and who were eligible for organ donation.
Results: Between January 2006 and December 2021, 200 children/adolescent died in the PICU and, from those. 62 patients (31%) were considered eligible for organ donation. The mean age of the donors at the time of death was 8,8 years (minimum of 2-month-old and maximum of 17 years-old). Sixty-three per cent were male. The most frequent cause of death was traumatic brain injury (n=35), 20 of which associated with polytrauma. Two hundred fifty organs were collected benefitting 202 persons, both children and adults, with a recipient/donor ratio of 3,3. Kidneys were the most frequent organ donated (n=116), followed by the liver (n=56) and the heart (n=34). The median number of organs donated per child was four, with a minimum of 1 organ and maximum of 9.
Conclusions: Pediatric organ donation represents a small proportion of overall organ donation, but children and adolescents have important impact on the lives they save. PICU teams fulfill a fundamental role in the identification of potential organ donors and asking families to accept donation. The field of pediatric organ donation needs more research to better understand the contribution of the pediatric population to both adults and children who wait for an organ.

P022 ISOLATED GLOMERULITIS IS STRONGLY ASSOCIATED WITH THE ABSENCE OF ANTIBODY-MEDIATED REJECTION BY MOLECULAR DIAGNOSTICS

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Background: According to the 2018 Banff classification, the Molecular Microscope Diagnostic System (MMDx) is indicated in cases when histology is insufficient to diagnose antibody-mediated rejection (ABMR) due to an absence of diagnostic criteria groups 2 and/or 3. The impact of isolated glomerulitis (g>0, ptc0) on the likelihood of ABMR diagnosis by the MMDx appears critical to the implementation of this new biomarker.
Methods: We analyzed 251 kidney allograft biopsies by histology and molecular diagnostics at the University Hospital Zurich from October 2018 to November 2022. Histologic findings were classified concerning the absence of (1) diagnostic criteria groups 2 and 3 (n=18), (2) diagnostic criteria group 2 only (n=18), and (3) diagnostic criteria group 3 only (n=28). In addition, cases with histologically proven ABMR were used for comparison (n=65). High-resolution re-typing was performed from the kidney allograft biopsies if necessary.
Results: The MMDx diagnosed ABMR in 1 of 18 cases (6%) with absent diagnostic criteria groups 2 and 3, 4 of 18 cases (22%) with absent diagnostic criteria groups 2, and 19 of 28 cases (68%) with absent diagnostic criteria groups 3. On the contrary, MMDx confirmed the diagnosis of ABMR in 42 of 65 cases (65%) with histologically proven ABMR but did not in 23 of 65 cases (35%). Among 28 cases with absent diagnostic criteria group 3, only 2 of 19 cases (11%) with ABMR by MMDx but 6 of 9 cases (67%) with no ABMR by MMDx showed isolated glomerulitis (p=0.0048). Among 65 cases with histologically proven ABMR, only 7 of 42 cases (17%) with ABMR by MMDx but 14 of 23 cases (61%) with no ABMR by MMDx showed isolated glomerulitis (p<0.001). Overall, 14 of 65 cases (21%) with isolated glomerulitis showed ABMR diagnosis by MMDx.
Conclusions: Isolated glomerulitis is strongly associated with the absence of ABMR by MMDx not only when diagnostic criteria group 2 is missing but also when diagnostic criteria 3 is missing or ABMR is proven by histology. Our results may help to guide the indication for MMDx in clinical practice. However, the clinical significance of these results needs further investigation.

P023 TAB-CEL FOR EBV+ PTLD AFTER FAILURE OF RITUXIMAB ± CHEMOTHERAPY FOLLOWING SOLID ORGAN OR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT ALLELE

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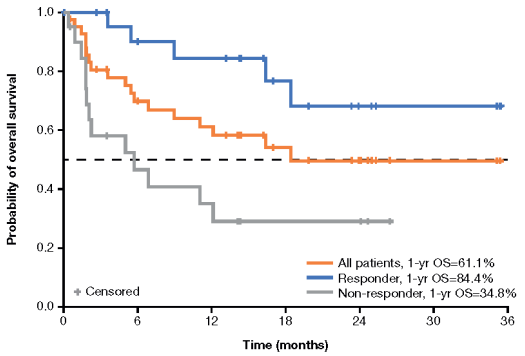
Background: Poor OS in pts with relapsed/refractory EBV⁺ PTLD reveals an urgent unmet need for effective therapies. We previously reported interim data from ALLELE (NCT03394365), an ongoing, phase 3 multicenter clinical trial of tabelecleucel (tab-cel), an investigational, off-the-shelf, allogeneic EBV-specific T-cell immunotherapy for EBV⁺ PTLD after failure of rituximab (R) ± chemotherapy (CT) following SOT or HCT. Here we present updated results with a focus on the SOT cohort.
Methods: Outcomes were assessed in pts with EBV⁺ PTLD following failure of R (HCT [n=14] and SOT1 [n=13]) and failure of R+CT (SOT2 [n=16]). All SOT types were eligible. Pts receive tab-cel at 2x10⁶ cells/kg on days 1, 8 and 15 in a 35d treatment cycle.
Results: Analysis as of Nov 2021 was consistent with previously presented ALLELE data. ORR was 51.2% (22/43) in all pts (BOR of CR [27.9%] or PR [23.3%]), 51.7% (15/29) in SOT overall, 46.2% (6/13) in SOT1, and 56.3% (9/16) in SOT2 (Table). Overall median TTR was 1.0 mo; overall median DOR was 23.0 mo. Estimated 1-yr OS rates were 61.1% overall, 56.2% for SOT overall, 47.6% for SOT1, and 64.3% for SOT2. Responders had a longer 1-yr survival vs non-responders in overall (Fig) and SOT groups. There was no change in safety profile compared with previous data (including no related allograft rejection or GvHD).
Conclusions: Updated ALLELE phase 3 data, with additional pts and longer follow-up, confirm that tab-cel provides consistent clinically meaningful outcomes, including improved ORR and both prolonged DOR and OS, in a pt population with poor survival and no approved therapies. Tab-cel was well tolerated without evidence of safety concerns typically observed with other adoptive T-cell therapies.

Efficacy Outcomes With Tab-Cel in Patients With EBV⁺ PTLD Following SOT or HCT

	SOT1 (n=13)	SOT2 (n=16)	All (n=43)
Responders, n (%) (95% CI)	6 (46.2) (19.2, 74.9)	9 (56.3) (29.9, 80.2)	22 (51.2) (35.5, 66.7)
Best overall response, n (%)			
Complete response	1 (7.7)	5 (31.3)	12 (27.9)
Partial response	5 (38.5)	4 (25.0)	10 (23.3)
Stable disease	2 (15.4)	0	5 (11.6)
Progressive disease	3 (23.1)	4 (25.0)	9 (20.9)
Not evaluable	2 (15.4)	3 (18.8)	7 (16.3)
Clinical benefit rate, n (%)	8 (61.5)	9 (56.2)	27 (62.8)
Median time to response, months (range)	1.6 (1.0–3.0)	1.1 (0.7–4.1)	1.0 (0.7–4.7)
Median follow-up in response, months (range)	2.4 (0.6–21.0)	2.3 (0.8–15.2)	7.0 (0.6–23.3)
Median duration of response, months (95% CI)	NE (0.6, NE)	15.2 (0.8, 15.2)	23.0 (6.8, NE)
Median follow-up, months (range)	6.9 (0.1–35.4)	5.5 (0.4–25.3)	11.0 (0.1–35.4)
Estimated mOS, months (95% CI)	9.0 (1.8, NE)	16.4 (3.5, NE)	18.4 (6.9, NE)
Estimated 1 yr OS rate, % (95% CI)	47.6 (18.2, 72.4)	64.3 (33.8, 83.5)	61.1 (43.7, 74.5)
Responders, n Estimated 1-yr OS rate, % (95% CI)	6 62.5 (14.2, 89.3)	9 85.7 (33.4, 97.9)	22 84.4 (58.9, 94.7)
Non-responders, n Estimated 1-yr OS rate, % (95% CI)	7 33.3 (4.6, 67.6)	7 34.3 (4.8, 68.5)	21 34.8 (14.6, 56.1)

Patients Responding to Tab-cel had Longer Survival



umber at risk (event)

All patients	43 (0)	25 (12)	21 (15)	12 (17)	8 (18)	3 (18)	0 (18)
Responder	22 (0)	17 (2)	15 (3)	9 (4)	5 (5)	3 (5)	0 (5)
Non-responder	21 (0)	8 (10)	6 (12)	3 (13)	3 (13)	0 (13)	

P024 SUCCESSFUL INTERNATIONAL ADOPTION OF A COMPREHENSIVE, INTEROPERABLE, AND SECURE DIGITAL ORGAN OFFERING MANAGEMENT PLATFORM

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Background: It is well understood that costly inefficiencies exist in the current fragmented donation and transplantation ecosystem. Outdated paper processes and systems operating in silos without seamless sharing of key data can lead to errors, compliance issues, time-intensive processes, and patient safety concerns. The implementation of an integrated, real-time clinical workflow platform can alleviate workflow burdens.
Methods: A donation organization responsible for managing country-wide donation and transplant adopted a comprehensive, modern, digital interoperative platform (previously adopted around the world) to manage the donation workflow, shifting from the previous paper process. The platform is a modern web-based system which provides advanced communication tools and has the potential to securely interface with external systems such as hospital EMRs. The donation organization, together with the software provider, coordinated updates to the workflow, processes, and policies, and organized comprehensive training sessions to ensure full compliance and oversee change management of the implementation.
Results: The comprehensive secure donation platform streamlines the clinical workflow by providing: 1) access to the latest chart information across multiple staff; 2) real-time and retrospective data quality tools to flag potential errors; 3) auditing and additional reporting and compliance tools; 4) notifications and alerts to team members upon key case updates; 5) scheduling and assignment coordination; and more.
Conclusions: As the donation organization continues use of the new platform they look forward to upcoming reporting on the qualitative benefits of transitioning to the modern software as well as potentially expanding across the donation-transplantation ecosystem with interfacing capabilities.

P025 THE QUALITY OF LIFE AND QUALITY OF SLEEP SCORE BETWEEN DIALYSIS AND RENAL TRANSPLANTATION

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Background: The health-related quality of life (HRQOL) of patients with renal diseases influences all aspects of their lives. The aim of the present study was to compare the HRQOL and sleep quality of patients who had received a deceased donor renal transplantation with patients on waiting lists for renal transplantation.
Methods: Using a convenience sampling strategy, from our population of renal recipient patients between 2020 - 2022 we identified 100 renal recipients and 96 renal patients on waiting lists. Patients completed two standardized questionnaires to assess sleep quality (PSQI) and health-related quality of life (SF-36). Questionnaires were completed in the Sina organ procurement unit affiliated by Sina Hospital. Demographic information was collected at the same time, including current age, gender, employment status, level of education, marital status, family financial income, and cause of renal failure.
Results: The sample covered a wide range of ages from 18 years to 69 years. The mean age of the respondents was 47 years. Comparing the PSQI scores of renal transplant recipients (4.54 ± 3.57) with the scores of patients on the waiting list (7.75 ± 3.55), the *t* value of student's *t* test was -5.79 (p = 0.001), indicating that the sleep quality of patients on the waiting list was lower than the transplanted patients. There is a significant difference in overall physical dimension (t = 6.65, p = 0.001), and emotional dimension (t = 2.76, p = 0.001) between both groups. The differences of both the physical component (p = 0.04) and mental component (p = 0.01) composite scores were statistically significant between the two groups. The physical component and mental component scores of poor sleepers were significantly lower than the good sleepers' scores.
Conclusions: Renal transplantation can resolve sleep disorders in many patients, but some patients continue to have sleep issues after transplantation. Due to the multifactorial nature of sleep disruptions, clinicians should pay more attention to other factors that may have possible effects on the sleep cycle, such as the psychological state of the patients, physical conditions after transplant surgery, and types of medication as well as side effects of medications in order to achieve a better and more efficacious treatment regimen.

P026 PREDICTORS OF NON ADHERENCE TO IMMUNOSUPPRESSION IN RENAL TRANSPLANT PATIENTS AT A UNIVERSITY TEACHING HOSPITAL

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Introduction: To assess the degree of immunosuppressive medication adherence in kidney transplant patients (KTPs) and to determine the predictors of non-adherence
Methods: From a total of 106 KTPs treated at the RLBUHT, N= 20 (18%) patients were identified as being non-adherent on 2 or more hospital incident episodes identified by continued care clinic, clinicians, and pharmacy Statistical analysis was performed using the student t-test. The predictors were data mined with Cox Regression with time-variable being time to graft dysfunction or Tacrolimus level abnormality > 50% variance of average trough level (6-8 ng/ml).
Results: Non-Adherence was observed in 20 (18.6%) patients, The estimated glomerular filtration rate was significantly lower in the no adherence group (28.52 ± 17.62 ml/min) than in the adherence group (62.43 ± 11.72 ml/min, p < 0.05). With regard to the Tac level, a significant difference was also found between the adherers and the Non adherers (5.10 ± 2.19 vs. 3.06 ± 1.04 ng/ml, p < 0.05). Non-adherers were interrogated during clinical encounters by clinicians and interpreter requirement. Polypharmacy (N=15), (Interpreter requirement) (N=11), young patients age 18-21 (N=05) and old age>70 (N=04) were the predictors of non-adherence. The patients were re-counselled and social services were involved to minimize recurrence.
Conclusion: The KTPs in this study demonstrated that non-adherence was associated with worse graft function and a lower Tac level. Knowledge about the degree of adherence could help the early identification of non-adherent patients and the development of strategies to improve outcomes.:

P027 SUBJECTIVE FRAILTY ASSESSMENT COMPARED TO VALIDATED FRAILTY ASSESSMENT IN DIALYSIS ACCESS/TRANSPLANT SURGERY WORKUP HAS POOR ESTIMATION OF AGREEMENT

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Purpose: Frailty assessment often rely on subjective frailty assessment, such as 'the end-of-the-bed' or 'eyeball' test. These assessments have traditionally been accurate in 40% of cases only. Frailty assessment is a part of our institutional clinical workup. We examined the association between subjective frailty and formal validated score aided frailty estimation in the adult renal failure population.
Methods: A cohort of all renal failure patients presenting for dialysis access/transplant assessment at a satellite unit over one year (December 2020-2021) was analysed. Adult patients aged ≥18 years in the outpatient dialysis access/transplant assessment surgical clinic were rated with eyeball test in routine clinical assessment as either: frail, pre-frail, or non-frail, which was then compared to a formal frailty assessment using a modified version of the Frailty Phenotype. The association between clinician-estimated frailty and formal frailty assessment was examined.
Results: A total of 113 patients were assessed, producing 109 paired frailty assessments. The median age of the patients was 62 years. The Composite Proportions of Agreement of clinician-estimated frailty to formal frailty was poor (0.57). The sensitivity of the Eyeball test was 0.30 & specificity was 0.43. The sensitivity of the Frailty Score was 0.70 & specificity was 0.57. The validated tool has more than twice the odds to estimate frailty OR 2.86 (1.49- 5.46). p=0.002 (2-tailed)
Conclusion: Subjective frailty assessment is not a reliable replacement for formal frailty assessment in adults with renal failure. Validated Frailty Tool provide a uniform frailty estimation.

P028 CHORIOCARCINOMA TRANSMITTED WITH THE TRANSPLANT: CASE STUDY

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Background: Choriocarcinoma is a rare kind of cancer which may be either gestational or non-gestational. Choriocarcinoma is responsible for about a quarter of all documented neoplastic aneurysms. It is a descriptive case report of choriocarcinoma transmission from a donor, following kidney donation. A 45-year-old woman got a kidney from a 25-year-old woman who was taken to the hospital due to a non-traumatic cerebral hemorrhage. She delivered a healthy baby 48 days before her brain death. The transplant was successfully done. Five weeks' post-transplantation, the recipient had pain and erythema in the surgical area. Regarding the high level of B-hCG in her blood, diagnostic tests were performed. Following the confirmation of the cancer, a five-phase chemotherapy plan with various pharmaceutical regimens was initiated. Liver function test values rose after the final round of chemotherapy, and the patient developed hepatic encephalopathy. Considering the thrombocytopenia, dialysis or hemoperfusion, which are normally performed to reduce liver enzymes, were not initiated. Finally, she died due to the hepatic failure and DIC.
Conclusions: Presently, nephrologists do not agree on the best action if this problem occurs, but it seems that a transplanted kidney nephrectomy could have been effective. If this kidney, had a nephrectomy earlier, we would no longer need chemotherapy for micro metastasis. Finally, B-hCG level should be evaluated in the women of reproductive age who have brain death due to unexplained causes of intra cerebral brain hemorrhage and the procurement team should be wary of choriocarcinoma based on the amount of B-hCG in their blood. According to the findings of this descriptive case report, rigorous assessment of the donor and attention to their medical history, as well as adherence to all organ transplantation standards, are critical prior to donation.

P029 PREDICTORS AND ADVERSE OUTCOMES OF ACUTE KIDNEY INJURY IN HOSPITALIZED RENAL TRANSPLANT RECIPIENTS

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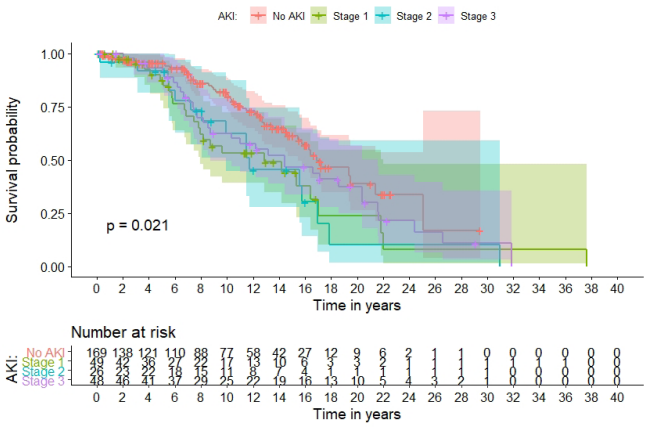
Background: Data about in-hospital acute kidney injury (AKI) in renal transplant recipients (RTRs) is lacking.
Methods: We conducted a retrospective study of 292 RTRs, with a total of 807 hospital admissions between the years 2007-2020, to reveal predictors and outcomes of AKI during admission. AKI was defined as a difference of ≥50% between peak creatinine during admission and baseline creatinine.
Results: AKI during admission developed in 149 patients (51%). AKI in a previous admission was associated with a more than twofold increased risk of AKI in subsequent admissions (OR 2.13, *P*<0.001). Other major significant predictors for in-hospital AKI included an infection as the major admission diagnosis (OR 2.93, *P*=0.015), a medical history of hypertension (OR 1.91, *P*=0.027), minimum systolic blood pressure (OR 0.98, *P*=0.002), maximum tacrolimus trough level (OR 1.08, *P*=0.005), hemoglobin level (OR 0.9, *P*=0.016) and albumin level (OR 0.51, *P*=0.025) during admission. Compared to admissions with no AKI, admissions with AKI were associated with longer length of stay (median time of 3.83 vs. 7.01 days, *P*<0.001). In-hospital AKI was associated with higher rates of mortality during admission, almost doubled odds for rehospitalization within 90 days from discharge (OR 1.95, *P*<0.001), and increased the risk of overall mortality in multivariable mixed effect models.
Conclusions: In-hospital AKI is common in RTRs and is associated with poor short- and long-term outcomes. Strategies to prevent AKI during admission in this population should be implemented to reduce re-admission rates and improve patient survival.

Table 1: Multivariate Mixed Effect Logistic Regression Analysis for Readmission within 90 Days in RTRs

Effect	Odds ratio (95% CI)	P
Admission age	1.01 (0.99-1.03)	0.17
Gender, F vs. M	0.93 (0.62-1.38)	0.72
Hypertension, yes vs. no	1.34 (0.91-1.97)	0.14
In-hospital AKI, yes vs.no	1.95 (1.35-2.81)	<0.001**
SBP min (for every increase of 1 mm Hg)	1.0 (0.99-1.01)	0.93
Albumin min per 1g/dL increase	0.76 (0.53-1.1)	0.15
Glucose max per 1 mg/dL increase	1.0 (0.99-1.0)	0.94
Hemoglobin min per 1 g/dL increase	0.92 (0.85-0.99)	0.02*

Figure 1. | Long-term mortality based on the occurrence and severity of in-hospital AKI in the last admission for each patient.



P030 EVALUATION OF THE CLINICAL EXPRESSION OF IMMUNOSUPPRESSIVE THERAPY IN RENAL TRANSPLANT RECIPIENTS

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Background: Post-transplant immune monitoring in renal transplant recipients (RTRs) is lacking.
Methods: We surveyed 132 RTRs, 38 in the first year post transplant and 94 >1 year post-transplant. A questionnaire administered to these RTRs was divided into physical (Q physical) and mental (Q mental) symptoms.
Results: In multivariable models for the association between Q physical and Q mental scores and different clinical and biochemical variables in the 38 RTRs who filled out the questionnaire 130 times during the first year post-transplant, mycophenolic acid (MPA) and prednisone use increased the mean Q physical score by 0.59 (95% CI 0.21-0.98, p=0.002) and 0.53 (95% CI 0.26-0.81, p=0.00), respectively, while MPA use increased the mean Q mental score by 0.72 (95% CI 0.31-1.12, p=0.001). Among the 94 RTRs who each completed the questionnaire only once, the odds for the mean Q mental score to be above the median value were more than 3 times higher for RTRs treated vs. non-treated with MPA (OR 3.38, 95% CI 1.1-10.3, p=0.03). MPA-treated RTRs had higher mean scores for questions related to sleep disorders (1.83±1.06 vs. 1.32±0.67 for not treated, p=0.037), difficulty falling asleep (1.72±1.11 vs. 1.16±0.5, p=0.02), and to depression and anxiety.
Conclusion: Prednisone and MPA use are associated with an increased Q physical and Q mental scores in RTRs. Routine monitoring of physical and mental status of RTRs should be implemented to improve the diagnosis of overimmunosuppression. Dose reduction or discontinuation of MPA should be considered in RTRs who report sleep disorders, depression and anxiety.

Table 1 | Clinical expression of MPA use in 94 RTRs >1 year post transplant.

	Questionnaire results		
	RTRs on MPA (N=75)	RTRs off MPA (N=19)	
Question	Mean (SD)	Mean (SD)	P value
Fatigue	1.88 (1.13)	1.47 (0.7)	0.183
Muscle weakness	1.51 (0.83)	1.47 (0.96)	0.623
Night sweats	1.24 (0.57)	1.21 (0.92)	0.226
Joint pain	1.45 (0.83)	1.37 (0.83)	0.481
Tremor	1.49 (1.01)	1.16 (0.37)	0.198
Sleep disorder	1.83 (1.06)	1.32 (0.67)	0.037*
Restlessness	1.56 (1.07)	1.21 (0.42)	0.372
Depression	1.59 (1.15)	1.11 (0.31)	0.09
Difficulty falling asleep	1.72 (1.11)	1.16 (0.5)	0.021*
Anxiety	1.45 (0.98)	1.05 (0.23)	0.064

P031 NORMOTHERMIC MACHINE PERFUSION INDUCED REMARKABLE BIOLOGICAL CHANGESOF MARGINAL DONOR KIDNEYS AS DEMONSTRATED BY PROTEOMICS

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Background: Renal normothermic machine perfusion (NMP) is an organ preservation method based on the circulation of a warm (35–37 °C) perfusion solution through the renal vasculature to deliver oxygen and nutrients. However, the biological effects of this technique on the marginal kidneys are unclear. We therefore used mass spectrometry to determine the proteomic profile of kidney tissue and urine from eight organs reconditioned for 120 min using a Kidney Assist device.
Methods: Biopsies were taken during the pre-implantation histological evaluation (T-1), at the start of back table preparation (T0), and after 60 and 120 min of perfusion (T60, T120). Urine was collected at T0, T30, T60, and T120. Multiple algorithms, support vector machine learning and partial least squares discriminant analysis were used to select the most discriminative proteins during NMP.
Results: Statistical analysis revealed the upregulation of 169 proteins and the downregulation of 196 in kidney tissue during NMP. Machine learning algorithms identified the top 50 most discriminative proteins, five of which were concomitantly upregulated (LXN, ETFB, NUDT3, CYCS and UQCRC1) and six downregulated (CFHR3, C1S, CFI, KNG1, SERPINC1, and F9) in the kidney and urine after NMP. Functional analysis revealed that the most strongly upregulated proteins were involved in the oxidative phosphorylation system and ATP synthesis, whereas the downregulated proteins represented the complement system and coagulation cascade.
Conclusions: Our proteomic analysis demonstrated that even brief periods of NMP induce significant metabolic and biochemical changes in marginal organs, which supports the use of this promising technique in the clinic.

P032 ESOT-TLJ 3.0 CONSENSUS ON HISTOPATHOLOGICAL ANALYSIS OF PRE-IMPLANTATION DONOR KIDNEY BIOPSY: REDEFINING THE ROLE IN THE PROCESS OF GRAFT ASSESSMENT

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Background: The European Society for Organ Transplantation (ESOT) TLJ 3.0. consensus conference brought together leading experts in the field of transplantation (pathologists, surgeons, nephrologists) to develop evidence-based guidance on the standardization and clinical utility of preimplantation kidney biopsy in the assessment of grafts from extended criteria donors (ECD).
Methods: Seven emerging themes of interest have been selected by the Steering Committee (4 histopathologists, 4 nephrologists and 2 transplant surgeons) and underwent in-depth analysis after formulation of PICO (patient/population, intervention, comparison, outcomes) questions. After a literature search by the Center of Evidence in Transplantation (CET), the relative statements for each key question were produced and rated according to the quality of evidence using the GRADE approach. The statements were subsequently presented in-person at the kick-off meeting in Prague, discussed and voted.
Results: After two rounds of discussion and voting, all 7 statements reached an overall agreement of 100% on the following issues: needle core/wedge/punch technique representativity, frozen/paraffin embedded section reliability, experienced/ non-experienced on-call renal pathologist reproducibility and accuracy of the histological report, glomerulosclerosis/other parameters (interstitial fibrosis, tubular atrophy, wall/lumen ratio, arteriolar hyalinosis) reproducibility, digital pathology/light microscopy in the measurement of histological variables, special staining methods (Periodic-Acid Schiff, Silver, Picro Sirius Red, Trichrome) / Haematoxylin & Eosin alone comparison in the measurement of histological variables, glomerulosclerosis percentage/interstitial fibrosis, tubular atrophy, arteriolar hyalinosis and cv score reliability to predict transplant outcome.
Conclusions: This methodology has allowed us to reach a full consensus on important technical topics regarding pre-implantation biopsy in the process of ECD graft assessment.

P033 MULTI-CENTRIC ANALYTICAL PERFORMANCE VALIDATION OF AN IVD ASSAY TO QUANTIFY DONOR-DERIVED CELL-FREE DNA FOR SOLID ORGAN TRANSPLANT SURVEILLANCE

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Background: Donor-derived cell-free DNA (dd-cfDNA) has been widely studied as a biomarker for non-invasive allograft monitoring and prediction of rejection risk. Earlier detection of rejection episodes enables more prompt diagnosis and clinical intervention, ultimately improving patient care and outcomes. Implementation of onsite dd-cfDNA testing is a rising area of interest with great potential for clinical laboratories in Europe.
Methods: Analytical performance validation of AlloSeq cfDNA (CareDx) was executed across three independent laboratories. Each site received the same set of 16 blinded samples to perform cfDNA extraction and the entire AlloSeq cfDNA workflow. Results were compared between sites and against expectations from manufacturer validation to evaluate concordance, reproducibility, repeatability, and verify analytical performance metrics.
Results: A total of 247 sample libraries were generated with 10 ng DNA input across 18 runs, with a completion time of <24 hours from sample to result. The first pass rate was 96.0%, highlighting minimal failures. Overall observed versus expected dd-cfDNA results demonstrated good concordance and a strong positive correlation with R^2=0.9982 for the linear fit, and high repeatability and reproducibility within and between sites, respectively, with p>0.05. AlloSeq cfDNA manufacturer validation established LOB as 0.18%, LOD as 0.23%, and LOQ as 0.23%, and results from the independent sites in this study verified those limits. Parallel analyses illustrated no significant difference (p=0.951) between dd-cfDNA results with or without recipient genotype.
Conclusions: AlloSeq cfDNA proved to be a reliable method for efficient, reproducible dd-cfDNA quantification in plasma from solid organ recipients, without requiring genotyping. In-house access to this technology could facilitate more rapid detection of early signals of allograft injury at transplant centers across Europe.

P036 URINARY RETINOL-BINDING PROTEIN 4 IS ASSOCIATED WITH RENAL FUNCTION AND RAPID RENAL FUNCTION DECLINE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Urinary retinol-binding protein 4 (RBP4) has been known as a biomarker of chronic kidney disease. In this study, we evaluated the association of urinary RBP4 with renal function and progression of renal function in kidney transplant recipients (KTRs).
Methods: A total 50 KTRs were included in this study. Proteomic analysis with liquid chromatography-mass spectrometry and tandem mass spectrometry was performed to discover potential urinary biomarkers. Several urinary proteins including RBP4 were identified and then validated by enzyme-linked immunosorbent assay. Rapid renal function decline was defined as estimated glomerular filtration rate (eGFR) decline of >3 mL/min/1.73 m2/year or initiation of dialysis, and 19 (38%) were included in rapid renal function decline group.
Results: Urinary RBP4/creatinine was inversely correlated with allograft function (r = -0.54, P < .001 with eGFR, and r = 0.49, P < .001 with serum creatinine, respectively). Urinary RBP4/ creatinine was higher in rapid renal function decline group than in stable renal function group (184.9 § 156.7 vs 83.1 § 99.9, P=.017). Log-transformed urinary RBP4/creatinine was significantly associated with rapid renal function decline in univariate logistic regression analysis (Odds ratio [OR] 7.59, confidence interval [CI] 2.04-36.70, P=.005). In multivariate logistic regression adjusted with recipient age and sex, donor age, number of HLA mismatch, and acute rejection episode, urinary RBP4/creatinine remained a significant factor for rapid renal function decline (OR 9.43, CI 1.99-65.65, P=.010). Receiver operating characteristic analysis showed that the area under the curve of urinary RBP4/creatinine was 0.747 (CI 0.608-0.886, P < .001) for rapid renal function decline.
Conclusions: Urinary RBP4 levels are associated with renal function and might be used to predict rapid renal function decline in KTRs.

P037 DEVELOPING A STANDARDIZED EDUCATION PROGRAM ON DECEASED ORGAN AND TISSUE DONATION FOR PRE-MEDICAL AND MEDIAL STUDENTS IN KOREA

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Background: It is necessary to deliver essential knowledge on deceased organ donation to medical and premedical students who will play an important role in the field of deceased organ donation in the future. To enhance positive attitude to deceased organ and tissue donation through systematic education, we developed an educational program with delivery pathways for pre-medical and medical students.
Methods: On- and off-line self-learning aids materials on 7 topics on deceased organ donation were generated and posted on the Vitallink Academy YouTube site. Other materials selected from media and literature were also provided. 32 pre- and 15 post-education questionnaires were developed using a web-based survey platform. These surveys were conducted before and immediately after the education process.
Results: A total of 141 pre-medical students in the first grade at the premedical course. Among those, 99 students completed the pre-and 86 students completed the post-education survey. Even though 96% of students had heard about deceased organ-tissue donation, only 2.1% said that they know well. Attitude analysis showed that only 4.0% of students completed registration for deceased organ-tissue donation card. 33.3% of students showed interest in the deceased organ-tissue donation-related issues. Only 24.2% of responders agreed that anyone who was diagnosed with brain death should donate. The proportion of students with positive attitude toward organ-tissue donation was increased from 74.7% to 97.7% (P<0.001). Interest in deceased organ-tissue donation-related issues increased from 33.3%(before) to 84.9%(after) the education(P<0.001). Their attitude toward deceased donation evaluated by expressing willingness to organ-tissue donation also increased from 76.8%(before) to 96.5% after the education (P<0.001
Conclusions: Significant improvements were observed in knowledge and awareness which is enough to bring changes in attitude when we applied our newly developed co-participatory education program to a group of premedical students. The online survey platform provided not only a tool for evaluating the effectiveness of the education program, but also valuable information about the level of public awareness of university freshmen.

P038 TOCILIZUMAB FOR CHRONIC ANTIBODY-MEDIATED REJECTION- 5 YEARS OF EXPERIENCE

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Background: Chronic antibody mediated rejection (cAMR) remains the leading cause of late kidney allograft loss. There is no approved treatment for cAMR. Anti-IL-6 receptor monoclonal antibody tocilizumab (TCZ) is being investigated as treatment for cAMR. Kidney transplant recipients with biopsy proven cAMR were offered rescue therapy with monthly TCZ infusions after standard of care (SOC) therapy.
Methods: We performed a single-center, observational study of kidney transplant recipients who received at least 1 dose of TCZ in addition to conventional therapies for cAMR between January 2018 and January 2023, with follow-up.
Results: 4 patients were identified, all male, aged 35, 42, 30 and 61 at the beginning of the treatment. All received SOC therapy for cAMR. Due to biopsy proven resistant cAMR despite SOC therapy, they also received bortezomib therapy as per local practice at the time, prior to TCZ therapy. All had DSA class II. All 4 patients received TCZ 8 mg/kg (max dose, 800 mg), 6x, monthly. All patients had follow-up biopsies after every cycle (6 doses). The first patient received 24 doses of TCZ with no worsening of renal function, concordant with stationary follow-up biopsies. Upon discontinuation of TCZ, rapid deterioration of renal function occurred, from eGFR 24 ml/min/1.73m^2 to ESRD in 6 months. The second patient received 12 doses of TCZ. His graft function remained stable during treatment, but worsened while the drug was temporarily discontinued due to oral aphthous ulcers. Upon discontinuation of TCZ at eGFR 20 ml/min/1.73m^2, he progressed to ESRD in 6 months. The third patient received 14 doses of TCZ. His graft function remained stable through 2 years of treatment, eGFR 62 ml/min/1.73m^2 with no progression of histological scores, despite high MFI levels of DSA. The fourth patient received 12 doses of TCZ. His graft function remained stable during treatment, eGFR 57 ml/min/1.73m^2, with no adverse events. MFI levels decreased and histology scores improved.
Conclusions: TCZ may be considered as rescue therapy for treatment of cAMR. More studies are needed to determine potential candidates and duration of treatment. Role of bortezomib and potential interaction should be evaluated. Rebound effect and possible accelerated graft loss following discontinuation of TCZ remain a cause for concern.

P039 MAGNETIC RESONANCE IMAGING OF RENAL OXYGEN METABOLISM BY MEANS OF 17O ADMINISTRATION DURING EX VIVO ORGAN PERFUSION

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Background: Renal normothermic machine perfusion (NMP) is a novel strategy to assess pretransplant renal function and injury, but it remains unclear which markers can provide information about renal viability during NMP. Magnetic resonance imaging (MRI) is commonly used to evaluate tissue morphology, metabolism, and function, and recently it has been applied to study ex vivo renal viability. The oxygen-17 (^{17}O) isotope offers a unique tool for the assessment of metabolic rate. By administering ^{17}O to the organ, $H_2{}^{17}O$ is produced and the occurrence of this immediate end product of oxidative metabolism can be selectively imaged and quantified by functional MRI sequences. This project aimed to perform direct ^{17}O MRI sequences on porcine kidneys during NMP to assess the feasibility of ^{17}O imaging over time.
Methods: Viable porcine kidneys were retrieved at a local slaughterhouse, subjected to 30min of warm ischemia (WI), and preserved by hypothermia. Kidneys were subsequently perfused for 3h at 37°C. Initially, oxygenation was administered with 95% O_2 / 5% CO_2. After 1h of NMP, perfusion to the inferior pole of one of the kidneys was blocked for 75min using a balloon catheter and then reperfused for 30min before ^{17}O delivery. ^{17}O was then supplied to the organ and anatomic and dynamic radial $H_2{}^{17}O$ MR images were acquired before, during, and after ^{17}O administration.
Results: $H_2{}^{17}O$ -magnitude imaging displayed that kidneys with partial ischemia had decreased signal intensity in the inferior pole after reperfusion, while kidneys without any additional WIT displayed a well distributed signal intensity over the whole organ. This signal shift after reperfusion could not be visualized with other functional MRI sequences such as T2* mapping, a surrogate to assess tissue oxygenation.
Conclusions: This pilot study showed the first evidence of the quantification of regional production of $H_2{}^{17}O$ in isolated perfused porcine kidneys. With this novel MRI method, we were able to image the impact of ischemic injury on the rate of oxidative metabolism in renal tissue, which could not be visualized by any other functional MRI sequence after reperfusion. This suggests that ^{17}O imaging during NMP could offer a valuable new tool for the assessment of renal metabolism and injury.

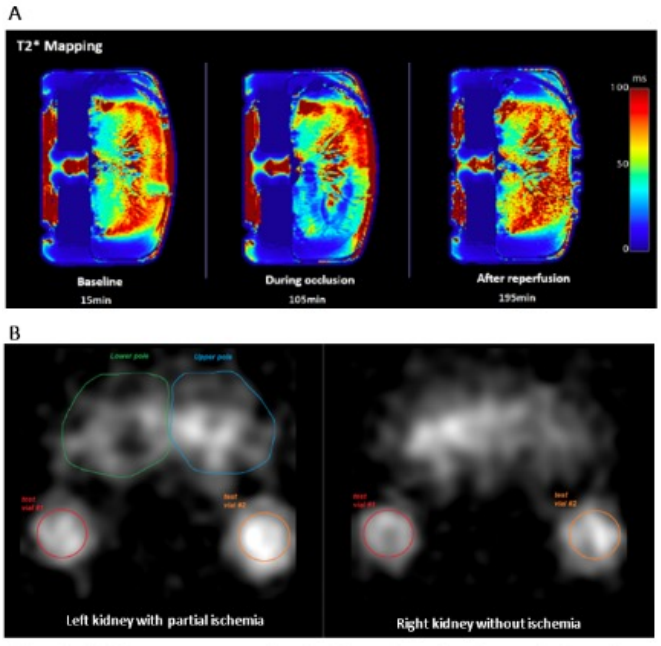

Figure 1: (A) T2 mapping images of renal perfusion showing the absence of perfusion during balloon occlusion of one segmental artery and subsequent homogeneous reperfusion; (B) Transversal view of the time-averaged ^{17}O-magnitude images of the left kidney with 75 minutes of partial segmental artery occlusion and the right kidney without segmental occlusion.*

P040 VOXE: TRANSFORMING CARE IN SOLID ORGAN TRANSPLANT THROUGH THE INTEGRATION OF A DIGITAL PATIENT-REPORTED OUTCOME PLATFORM IN CLINICAL PRACTICE

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Background: As health services shift towards more patient-centred care, the importance of patient-reported outcome measures (PROMs) is increasingly recognized. PROMs can effectively capture patients' perspectives and enable meaningful engagement. This research program aims to improve health outcomes for pediatric solid organ transplant (SOT) patients by systematically implementing PROMs into clinical practice. We have targeted methodological and practical decisions needed to guide effective integration of PROMs into 'real-world' care settings with a phased approach, including a systematic review, key stakeholder interviews, and a consensus workshop. In this study, we designed and tested the usability of an electronic PROM platform called Voxe.
Methods: A user-centred approach in which end-users (i.e., patients and healthcare providers (HCPs)) are central to the design process and usability testing, guided Voxe platform creation. Iterative testing sessions involved participants completing 1) tasks on design wireframes and prototypes to evaluate effectiveness and efficiency, 2) the Microsoft Desirability Toolkit, a system usability scale, and 3) a semi-structured interview to assess satisfaction and gather user feedback. This testing methodology was implemented to 'test, learn and improve' Voxe prior to the full development and launch.
Results: Twenty-five SOT recipients aged 8-17 years and 22 of their HCPs participated. Iterative, and sequential testing rounds demonstrated improved effectiveness as the proportion of successfully completed tasks increased from 74% to 85%. Efficiency improved as time-to-task decreased from 23.2 to 15.8 seconds. Patients described Voxe as "fun", "friendly", "helpful", "easy" and "creative" and remarked "[Voxe] makes you feel like you're welcome in the hospital". HCPs highlighted that Voxe is "intuitive" and enabled "a more patient-centered model of care".
Conclusions: Findings will influence how Voxe looks and operates to drive successful and sustainable adoption. Future research will assess the implementation effectiveness of the Voxe ePROM platform. Ultimately, Voxe leverages eHealth technology as an innovative approach to capture and integrate patients' voices to improve their care experience.

P041 CREATION OF AN ORGAN TRANSPLANT CAREGIVER EDUCATIONAL RESOURCE & LESSONS LEARNED

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Background: Organ transplant caregivers perform an essential and complex role. Their roles comprise informational, instrumental, and emotional support needs and can come with unique challenges. However, limitations remain in the provision of comprehensive educational resources for transplant caregivers.
Methods: Following a call from transplant patients and caregivers, a United States transplantation association formed an Organ Transplant Caregiver Initiative (OTCI). One of the OTCI's primary aims was to develop a multifaceted, comprehensive, and readily accessible educational toolkit for transplant caregivers. A Caregiver Education Subcommittee was formed, consisting of multi-disciplinary transplant professionals and transplant caregivers who collaborated via a multi-step process to outline, develop, and refine educational content. The toolkit was comprised of General content and Organ-specific content sections, with multiple subsections (Table 1). Subcommittee members created section drafts that were shared during virtual review meetings for subcommittee feedback. A final draft was shared with outside reviewers and transplant caregivers for additional feedback and then sent to the association's Board for review.
Results: A comprehensive transplant caregiver toolkit was developed. It was reviewed by the association's Board and is currently undergoing revisions. Once completed, the toolkit will be available online and accessible to caregivers and transplant centers as an educational resource.
Conclusions: A comprehensive educational toolkit was developed by a multi-disciplinary group of transplant professionals and caregivers from across the United States to address a need for caregiver resources. Dedicated leadership, committed project members, and a multi-step review process helped guide toolkit development despite project limitations. Lessons learned included

seeking guidance from others with experience creating similar resources, flexibility in project development amidst unanticipated circumstances, creativity in engaging stakeholders, and routine communication between all entities involved. Involvement of transplant caregivers in the process allowed for added perspectives and contributions, while increasing representation of diverse stakeholders.

Table 1. Transplant Caregiver Educational Toolkit Sections

Domains
A. Generalizable
1. Caregiver Roles and Responsibilities – Information about transplant caregiver roles and responsibilities organized across the different stages of transplant
2. Legal and Financial Considerations for Caregivers – Legal and financial considerations in caregiving including FMLA, advanced directives, power of attorney, and paid leave
3. Caregiver Quality of Life and Self-Care – Information about caregiver stress and caregiver self-care
4. Special Considerations with Caregiving – Cultural, spiritual, and religious considerations with caregiving, end-of-life, and emergency preparedness planning
5. Relationship Dynamics between Patients and Caregivers* - Discussion of relationship issues that may arise during caregiving and role transition after transplant
6. Caregiver Resources* - Practical directory of external resources and links
7. Dictionary of Terms and Transplant Personnel* - Definitions of commonly used terms and descriptions of transplant healthcare providers
B. Organ-specific – Information about specific organ disease and what caregivers should know before, during, and after each organ specific transplant
8. Kidney Transplant
9. Heart Transplant
10. Lung Transplant
11. Liver Transplant
12. Living Donor

*Additional domains added during content development process

P043 THE OUTCOMES OF ADJUSTED IMMUNOSUPPRESSIVE PROTOCOLS DURING DIFFERENT PHASES OF COVID-19 PANDEMIC IN KIDNEY TRANSPLANT RECIPIENTS

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Background: After beginning of the Covid-19 pandemic due to initial reports of high mortality in patients with multiple comorbidities, almost all transplant centres develop different immunosuppressive protocols to decrease the mortality rates in their chronic immunosuppressive kidney transplant patients. In this study, we revealed the outcomes of our immunosuppressive protocols during the different phases of the Covid-19 pandemic.
Methods: In the first phase of Covid-19 due to the high mortality risk of dominant variants until December 2021; the protocol was an increased dose of prednisolone (20mg/day) and complete cessation of calcineurin and MMF. When the dominant variant became Omicron in the second phase, prednisolone 20mg/day, 50% dose reduction of tacrolimus and MMF cessation were applied. The data were evaluated retrospectively in terms of mortality, biopsy-proven rejection, allograft loss, and allograft functions.
Results: Of the 592 follow-up patients at our centre, 132 of them (13.2%) had Covid-19 infection. In the first phase, infection developed in 108 patients (mean age 47.07±12.9 years, 54.6% male, 49% one comorbidity, 9.3% three comorbidities). The mortality rate was 10.2%, Biopsy proven rejection was 3.7%, the need for RRT was 1.9%, and allograft loss was 0.9%. Allograft functions of the patients were well preserved (64ml/min vs. 67.4ml/min GFR, 312.3±766.2mg/dl vs. 435.74±1302mg/dl proteinuria, p=NS). In the second phase of Covid-19 infection, 24 patients were infected (mean age 47±12.98 years, 45.8% male, 46% one comorbidity, 8.3% three comorbidities). Mortality was detected in one patient (4.2%), while biopsy-proven rejection and temporary RRT were required in one patient (4.2%), and allograft loss did not occur. Allograft functions of the patients were well preserved (60ml/min vs. 63.1ml/min GFR, 211.5±366.2mg/dl vs. 116.29±176 mg/dl proteinuria, p=NS)
Conclusions: In the first phase of Covid-19, with aggressive immunosuppressive reduction, lower mortality was achieved in kidney transplant patients than generally reported, while no significant problems were experienced in terms of allograft function and survival. In the second phase, which had a milder course, severe patient and allograft protection could be achieved with moderate immunosuppressive dose reduction.

P044 ARTIFICIAL INTELLIGENCE TOOL FOR KIDNEY PRE-IMPLANTATION BIOPSIES "GALILEO": A STAR IS BORN

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Background: Kidney transplantation pathology is a field with complex diagnostic demands and scarcity of experts. Artificial intelligence (AI) can assist by aiding pathologists with the task of kidney donor assessment. Our aim is to present the AI tool called "Galileo", designed specifically to assist the on-call pathologist with interpreting a pre-implantation kidney biopsy.
Methods: An AI tool called Galileo was created to read pre-implantation kidney biopsy digital pathology slides. The application Suite Create was employed for supervised algorithm training by annotating a case series of pre-implantation kidney biopsy slides by expert pathologists based upon ground truth original pathology reports. To overcome interobserver variability among pathologists we focused only on measurable features, such as number and type of glomeruli and vessels.
Results: The performance accuracy of Galileo improved with increasing number and quality of annotations. The pathologist is not replaced, but remains the protagonist when interacting with this AI-based tool which presents the on-call pathologist with an information on the number and type of glomeruli and vessels. The pathologist can actively dismiss the proposed feature result, edit, and/or validate the information prior to generating a pathology report.
Conclusions: Highly customizable AI solutions are being increasingly developed to address several needs in pathology, such as aiding the interpretation of kidney biopsies in transplant pathology. The AI-based tool called Galileo proved to successfully assist on-call pathologists required to interpret pre-implantation kidney biopsies. Further work is intended utilizing a semi-supervised approach, which would involve training this deep learning model using endpoints such as graft survival over time.

P046 PREDICTION OF HERPES VIRUS INFECTIONS AFTER SOLID ORGAN TRANSPLANTATION: A PROSPECTIVE STUDY OF IMMUNE FUNCTION

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Background: Herpes virus infections are a major concern after solid organ transplantation and linked to the immune function of the recipient. We aimed to determine the incidence of positive herpes virus (cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus 1/2 (HSV-1/2), and varicella zoster virus (VZV)) PCR tests during the first year post-transplantation and assess whether a model including immune function pre-transplantation and three months post-transplantation could predict a subsequent positive herpes virus PCR.
Methods: All participants were preemptively screened for CMV, and EBV IgG-negative participants were screened for EBV during the first year

post-transplantation. Herpes virus PCR tests for all included herpes viruses (CMV, EBV, HSV-1/2, and VZV) were retrieved from the Danish Microbiology Database containing nationwide PCR results from both hospitals and outpatient clinics. Immune function was assessed by whole blood stimulation with A) LPS, B) R848, C) Poly I:C, and D) a blank control. Cytokine concentrations (TNF-α, IL-1β, IL-6, IL-8, IL-10, IL-12p40, IL-17A, IFN-α, and IFN-γ) were measured using Luminex.

Results: We included 123 liver (54%), kidney (26%), and lung (20%) transplant recipients. A total of 2633 herpes virus PCR tests were performed during the first year post-transplantation (Table 1). The cumulative incidence of positive herpes virus PCR tests was 36.6% (95% CI: 28.1-45.1) during the first year post-transplantation. The final prediction model included recipient age, type of transplantation, CMV serostatus, and change in Poly I:C-induced IL-12p40 from pre-transplantation to three months post-transplantation. The prediction model had an AUC of 76.6% (95% CI: 60.9-92.3). Risk scores were extracted from the prediction model, and the participants were divided into three risk groups. Participants with a risk score <5 (28% of the cohort), 5-10 (45% of the cohort), and >10 (27% of the cohort) had a cumulative incidence of having a positive herpes virus PCR test at 5.8%, 25%, and 73%, respectively (p < 0.001) (Figure 1).

Conclusions: In conclusion, the incidence of positive herpes virus PCR tests was high, and a risk model including immune function allowed the prediction of positive herpes virus PCR and may be used to identify recipients at higher risk.

Figure 1

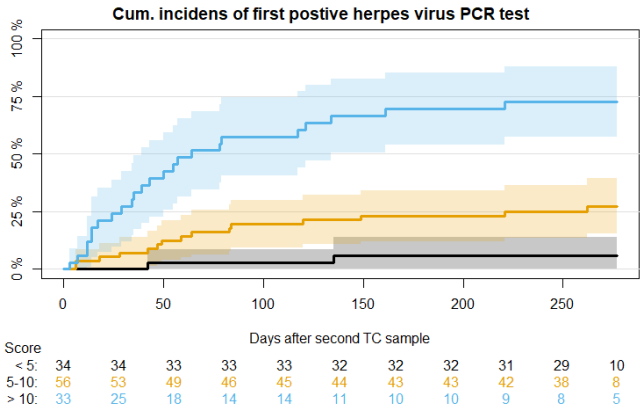

Table 1

	All participants N = 123	Liver transplanted participants N = 67 (54%)	Kidney transplanted participants N = 32 (26%)	Lung transplanted participants N = 24 (20%)
No. of tested participants (%) for				
- CMV	123 (100%)	67 (100%)	32 (100%)	24 (100%)
- EBV	87 (71%)	43 (64%)	20 (63%)	24 (100%)
- HSV-1/2	26 (21%)	6 (9%)	2 (6%)	18 (75%)
- VZV	24 (20%)	2 (3%)	2 (6%)	18 (75%)
Test				
Type of test, n				
- CMV	2099	974	423	702
- EBV	371	168	72	131
- HSV-1/2	106	14	12	80
- VZV	57	7	5	45
Test material, n				
- Blood	2292	1134	501	657
- Airway	307	16	7	284
- Swab	18	4	2	12
- CSF	8	3	0	5
- Other/Unknown[a]	8	6	2	0
Results of tests				
All herpes viruses, n				
- Positive	361	163	67	131
- Negative	2251	990	441	820
- Inconclusive	21	10	4	7
Positive, n (no. participants)				
- CMV	301 (39)	131 (19)	56 (6)	114 (14)
- EBV	41 (10)	30 (4)	5 (2)	6 (4)
- HSV-1/2	15 (5)	1 (1)	6 (1)	8 (3)
- VZV	4 (3)	1 (1)	0 (0)	3 (2)
Cumulative incidence of herpes virus infection	36.6% (CI:28.1-45.1)	32.8% (CI: 21.6-44.1)	21.9% (CI:7.6-36.2)	66.7% (CI: 44.8-85.5)

a: Other/unknown consists of Urine (n=2), Stool (n=1), Unknown (n=5)

P047 PREGNANCY OUTCOMES IN FEMALE ABDOMINAL ORGAN TRANSPLANT RECIPIENTS

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Background: The Transplantation Pregnancy Registry International (TPRI) has been collecting data for over 32 years in all solid organ transplant recipients.

Methods: Data are collected via questionnaires, interviews, online surveys, and review of medical records; retrospective and prospective pregnancy reports are accepted, and recipients worldwide can participate. The figure shows the countries that are represented in the TPRI.

Results: The purpose of this abstract is to present overall outcomes in abdominal organ transplant recipients reported to the TPRI. Results are shown in the table below.Overall outcomes among transplant recipients have remained similar over the last 30 years. The live birth rate is 69-74%, depending on organ transplanted. Each organ group has specific nuances, and it is of utmost importance for recipients to plan pregnancy to avoid mycophenolic acid product exposure as it is a known teratogen and to optimize transplant function in anticipation of pregnancy. The TPRI follows recipients and offspring indefinitely; despite the increased incidences of prematurity and low birthweight, offspring are overwhelming reported healthy and developing well at follow-up. The TPRI has over 250 grandchildren, who comprise a second generation providing the ability to study theoretical concerns about potential effects of in utero exposure to immunosuppressive medications on subsequent generations.

Conclusions: For many recipients, pregnancy after organ transplantation is possible with most of the pregnancies resulting in a healthy live birth. The TPRI is a resource for the worldwide transplant community. Healthcare providers who counsel transplant recipients about parenthood and transplant recipients themselves are encouraged to contact the TPRI.

Organ	Recipients / Total Outcomes	Estimated conception date range	Fetal losses^	Live offspring	Mean Gestational age (wks)	Mean Birth-weight (g)
Kidney	1367/2544*	1967-2022	652	1892 (74%)	35.8	2551
Kidney-Pancreas	84/154	1989-2022	48	106 (69%)	33.9	2128
Liver	400/821	1985-2022	221	600 (73%)	36.8	2778

*includes multiple births, ^includes ectopic, miscarriages, terminations and stillbirth outcomes

P048 EVEROLIMUS POSSIBLY SUPPRESS ANTI-HLA CLASS II PRODUCTION AFTER LIVING DONOR RENAL TRANSPLANTATION

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Background: Production of donor-specific antibody (DSA) is a risk factor for antibody mediated chronic rejection resulting in graft loss. We compared DSA production of everolimus(EVR)-based immunosuppression with mycophenolate mofetil (MMF) based immunosuppression for primary kidney transplant recipients at our single institute.
Methods: From January 2008 to December 2020, 1,231 living donor renal transplant were performed. Among them, 678 recipients who were tested anti-HLA antibody screening in 2021 were enrolled in this study. Pre-DSA patient, and those who received mizoribine were excluded. Immunosuppression included either Tacrolims(TAC) or Cyclosporine(CSA) and either MMF or EVR. All patients received basiliximab and steroids. Rituximab was given in 233 cases for ABO incompatible transplantation. When immunosuppression is converted to other drug, patients are allocated to regimen which is given at least 1 year from Screening test. De novo DSA was identified using LABScreen single antigen beads. Mean fluorescence intensity (MFI) values >1000 was considered positive. P < .05 was considered significant.
Results: There were 445 males and 233 females. Average age was 47.6 years. Distribution of immunosuppression regimens are CSA+MMF 168, CSA+EVR 62, TAC+MMF 382, and TAC+EVR 66. Class I DSA were found in 10 cases and ClassII DSA were found in 39 casas. Incidence of DSA production and MFI values were not statistically different between MMF and EVR. Since recipient age, observation period, and sex distribution were significantly different between MMF group and EVR group, propensity score matched analysis was performed. Then max MFI value against Class II were significantly less in EVR group (111695 in MMF, 2985 in EVR) (p=0.00763). Patients with MFI >6000 was found only 1 in EVR group and 6 in MMF group (n.s)
Conclusions: Even this is limited analysis, immunosuppression regimen including everolimus may possibly suppress production of anti-HLA Class II after living donor renal transplantation.

P049 THE DIFFERENCE BETWEEN ECHOCARDIOGRAPHIC FINDINGS BASED ON THE CAUSE OF BRAIN DEATH: A SINGLE-CENTER STUDY IN SINA ORGAN PROCUREMENT UNIT

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Background: Heart transplantation has been recognized as the gold standard treatment of patients with end-stage heart failure. Based on this study we evaluated the cardiovascular status of confirmed brain death cases by echocardiography and per case coronary angiography or transesophageal echocardiography and compared the result between procured and rejected cases.
Methods: This study was performed on patients who have been registered in Sina hospital after confirmation of brain death based on the advanced neurological assessment. After the diagnosis of brain death and authorization for organ donation was confirmed, donor management was transferred to the echo lab. Based on echocardiographic data, patients were introduced for donation or extraction from the heart donation group. Collected data included, Left and right chambers dimension and function, LVEF (Left Ventricular Ejection Fraction), regional wall motion abnormalities (RWMA), diastolic function, heart valve characteristics and performance, and systolic pulmonary artery pressure (SPAP). The other variable such as demographical data, cause of brain death, and other procedures were gathered from medical records. Data were analyzed by SPSS $_{18}$ Software.
Results: The mean age of the brain death cases was 29.28± 10.59 years. Altogether, the main causes of brain death were 48 (50.5%) resulting from Head trauma, 19 (20%) due to lethal intoxication, ICH 12 (12.6%), tumor 4(4.2%), CVA 3 93.2%), Hanging 2 (2.1%), others 6 (6.3%). From all brain death cases, 59 (60.2%) were eligible for heart donation and 39 (39.8%) were rejected for the procedure mostly due to Low EF at procurement echocardiography assessment. According to the ANOVA test, there were statistically significant differences between the cause of brain death and EF (F= 2.2, P = 0.07), as well as estimated SPAP (F= 2.63, P= 0.05). This test didn't show any significant differences between the cause of brain death and RWMA (P = 0.32).
Conclusions: Based on our results, LVEF and SPAP are the most important predictors for suitable heart for procurement. In addition, successive re-evaluation of borderline cases is recommended according to increase the pool of potential heart donors.

P051 A LOW ABUNDANCE OF HLA IN URINARY EXTRACELLULAR VESICLES HINDERS THE IDENTIFICATION OF DONOR-SPECIFIC VESICLES IN URINE AFTER KIDNEY TRANSPLANTATION

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Background: Urinary extracellular vesicles (uEVs) might reflect the integrity and condition of the kidney allograft. The aim of the present study was to identify donor-specific uEVs based on human leucocyte antigen (HLA) mismatching with the recipient.
Methods: Donor-specific CD9 (tetraspanin, general uEV marker) and HLA-A2 double-positive (CD9+/HLA-A2+) uEVs were quantified from the urine of 12 HLA-A2-positive kidney donors and were compared to urine samples of 12 HLA-A2-negative recipients, using an isolation-free imaging flow cytometry (IFCM) protocol. Paired plasma (positive control) and urine samples collected from 10 healthy controls (HC) were used to investigate the general HLA-class-I+ uEVs (CD9 colocalized) using IFCM, time-resolved fluoroimmunoassay (TR-FIA), or immunogold-staining electron microscopy (IGS-EM). In addition to unprocessed urine samples, uEV isolates were 266-fold concentrated from the HC urine by ultracentrifugation (UC). Lastly, cell-derived CD9+/HLA-class-I+ EVs were spiked into the urine to investigate if the urine matrix (pH, osmotic pressure, ion concentration) affects uEV HLA detection.
Results: CD9+/HLA-A2+ uEV concentrations detected by IFCM could not discriminate HLA-A2+ donor from HLA-A2- recipient urine. In HC plasma, we observed 5.2 ± 4.4 × 10^6/mL CD9+/HLA-class-I+ EVs, while significantly lower CD9+/HLA-class-I+ EVs were detected in unprocessed urine samples from HCs (5.6 ± 1.6 × 10^4/mL, p = 0.0046) and resuspended uEV isolates (1.4 ± 0.8 × 10^4/mL, p = 0.0044). In TR-FIA, the Europium intensity, reflecting HLA-class-I expression of EVs from plasma (5220 ± 2053), was significantly higher than EVs from urine (2077 ± 85, p = 0.001), and the control with only buffer/PBS (2641 ± 48, p = 0.0032). In the IGS-EM, vesicle surface HLA-class-I expression was undetectable in uEV isolates. The spike-in IFCM experiments revealed 4.6 ± 2.3 × 10^6/mL cell-derived CD9+/HLA-class-I+ EVs directly after the spike-in and comparable numbers (3.5 ± 2.1 × 10^6/mL, p = 0.23) after incubation in the urine at 37°C for 8 hours ruling out a matrix effect preventing HLA-class-I detection in urine.
Conclusions: HLA-class I cannot be used to identify donor-derived uEV, likely because HLA-class-I+ EVs are not excreted into the urine under physiological conditions.

P052 IMPROVE ABU DHABI ORGAN DONATION PROGRAM BY APPLYING QUALITY INDICATORS

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Background: Early identification & prevention of organ failure are paramount; however, organ transplantation is the most cost effective treatment for most organ failure patients and the only available treatment for others. Many factors have been identified as contributing to the low number of organ donors, and many studies have highlighted that the lack of consistent processes for the organ donation process is the major limiting factor for organ scarcities. The complexity of the organ procurement process and the caregiver's cultural background are often factors that affect the quality and safety of the procedure. A comprehensive analysis is needed to understand how these factors may affect the organ donation process and improve its efficiency.
Methods: The quality of organ donation after death was evaluated using a dynamic quality framework (JAWDA KPIs) in a selected group of tertiary hospitals (3 public hospitals, and 3 private hospitals) in Abu Dhabi Emirate, served by the Emirates Organ and Tissue Center (EOTC), and compared against specific indicators of the Organ Donation European Quality System (ODEQUS) standards. Therefore, the evaluation includes the structural, clinical procedures, and process outcomes. The data was collected retrospectively from 2019 to 2020, based on ODEQUS's Indicators. Consequently, a comparison was conducted to evaluate the selected hospitals performance against the selected quality indicators of deceased donation after death by neurological criteria.
Results: Structural indicators showed a 97% increase in regards to meeting the standards established by the ODEQUS across the selected hospitals in 2020 compared to 2019. However, process indicators showed a 36% increase and indicators of results showed a 9% increase.
Conclusions: the necessity of developing of quality indicators in identifying gaps and area for improvement in the organ procurement process that should be redesigned or restructured, hence maximizing the number of donors and organs transplanted. The performance increased by 48 percent. However, identification of all possible donors in the ICU, referral of possible DBD donors, patient/ family consent, brain-death identification, conversion rate in DBD donors are areas that need a great opportunity for improvement in order to optimize the process.

P053 ANALYSIS OF TREATMENT PREFERENCES, NEEDS, IMMUNOSUPPRESSANT ADHERENCE, AND MENTAL HEALTH DISORDERS IN KIDNEY TRANSPLANT PATIENTS

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Background: Psychopathological disturbances have been well recognized to impact on graft/patient´s outcomes/survival in kidney transplantation.
Objectives: to quantify mental health disorders prevalence and immunosuppressive adherence, to identify patient´s treatment preferences and resources to face psychological disturbances, to quantify quality of life and to identify patient´s preferences of interventional psychology programs in a kidney transplant cohort
Methods: Transversal-observational study in stable kidney transplant patients. Demographics, social-clinical variables. Validated questionaries applied: Morisky-Green-Levine Test, Depression, anxiety stress scale (DASS-21), Satisfaction with life scale (SWLS), Connor-Davidson Resilience scale (CDRISC-2), Quality of life related with health survey (MOS-SF-36 Health Survey), Ad hoc survey of treatment needs and preferences. Hospital´s ethics committee approval was obtained
Statistical analysis: T-student test, U-Mann-Whitney, chi-square test, Spearman and Pearson correlation coefficients.
Results: A total of 116 kidney tranplants patients were included, 25% had previous mental health pathology before transplant. Mental health disorders prevalence for depression, anxiety and stress were 26%, 27%, and 23% respectively. Life satisfaction screening revealed only 29% of patients very satisfied with life. Patients with lower scores in mental health tests were significatively related to fulfilled criteria for bad immunosuppressive adherence treatment (p=0.004). Treatment preferences identified were how to improve physical condition (47%), information for anxiety and/or depression management (37%), to receive psychological therapy from Nephrology Service (95%).
Conclusions: Mental health disorders prevalence in Spanish kidney transplant patients was high with negative impact in immunosuppressive adherence. This demands a biopsychosocial, interdisciplinary, focused on patient´s treatment preferences approach, individually and in groups from Nephrology Service

P054 CLINICAL EFFECTS OF VALACYCLOVIR-BASED CYTOMEGALOVIRUS PROPHYLAXIS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) infection is a frequent and devastating complication after kidney transplantation (KT). Although guidelines recommend anti-viral prophylaxis with ganciclovir or valganciclovir, there is a demand for alternative regimen for CMV prevention. We investigated the effects of valacyclovir-based prophylaxis for 3 months on CMV infection and clinical outcomes in KT recipients using a nationwide cohort.
Methods: KT recipients from 20 transplant centers registered with the Korean Organ Transplantation Registry were analyzed in this study. The recipients were divided into valacyclovir prophylaxis and non-prophylaxis groups, a 1:3 propensity score matching was performed, and 1,036 recipients (291 and 745 in the prophylaxis and non-prophylaxis groups, respectively) were analyzed. The impact of valacyclovir-based prophylaxis on CMV infection and disease, and clinical outcomes including rejection, graft loss, cardiac events, and all-cause mortality were investigated. Risk factors for the development of CMV infection were also analyzed.
Results: Valacyclovir prophylaxis group showed significantly lower incidence of CMV infection and rejection compared to non-prophylaxis group (3.64 vs. 10.25 events per 100 person-years and 1.85 vs. 7.27 events per 100 person-years, respectively). The risk of CMV infection and rejection was significantly decreased in valaciclovir prophylaxis group compared to non-prophylaxis group. Valacyclovir prophylaxis, donor age, whether deceased donor or not, length of hospitalization after KT, anti-thymocyte globulin usage, and CMV serological mismatch between the donor and the recipient were independent risk factors for the development of CMV infection.
Conclusions: Valacyclovir prophylaxis after KT significantly reduced CMV infection and rejection. Valacyclovir could be considered as an alternative strategy for CMV prophylaxis after KT. Well-designed randomized controlled trials with large sample size are needed.

P055 SELECTION OF SAFE DONORS FOR THE LIVING DONOR LIVER TRANSPLANTATION USING EXTENDED RIGHT LOBE GRAFT

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Background: Extended right lobectomy (ERL) for living donor liver transplantation (LDLT) is selectively performed in many transplant centers and showed excellent recipient outcomes as reported in the previous studies. Yet, there is no universally accepted indication for ERL in respect to donor safety. Current study was designed to stratify risk factors of adverse donor outcome after ERL.
Methods: A total of 79 living donors who underwent ERL for LDLT were included in analysis. Donors were classified as safety and hazard donor groups according to postoperative findings relevant to post-hepatectomy liver failure classification by International Study Group for Liver Surgery.
Results: On multivariable analysis, lateral section volume (LLSV) less than 20% of total liver volume (TLV) and non-preservation of segment 4a (S4a) venous drainage were found to be the independent risk factors impairing postoperative outcomes. Despite the short-term impairment of liver function in hazard donor groups, all donors recovered and showed satisfactory remnant liver regeneration. However, these findings have implications in establishing selection criteria of donors eligible for ERL donation.
Conclusions: In conclusion, LDLT using ERL graft can be safely performed provided that LLSV/TLV is greater than or equal to 20% besides conventional donor selection criteria. Also, efforts to preserve S4a vein must be made in performing ERL graft procurement in LDLT donors.

Table 4. Univariable and multivariable analyses of risk factors of hazard donor

	univariable			multivariable	
Parameters	**Safety group (N=36)**	**Hazard group (N=43)**	**P**	**Odd ratio (95%CI)**	**P**
Height	164.32	167.57	0.08		
BSA > 1.70 m2	10 (27.8%)	18 (41.9%)	0.19		
S4a vein preserved	11 (30.5%)	3 (6.9%)	0.01	0.16 (0.03-0.79)	0.03
SLV (mL)	1153.12	1210.42	0.06		
LLV/TLV (%) < 35	3 (8.3%)	15 (34.9%)	0.05		
LLSV/TLV (%) < 20	6 (12.5%)	25 (58.1%)	<0.01	10.84 (1.93-60.88)	0.01
LLSV/LLV (%)	57.40	54.04	0.06		

Data are presented as number (%)
Abbreviations: BSA, body surface area; LLV, left lobe volume; TLV, total liver volume; LLSV, left lateral section volume

P056 SYSTEMIC IMMUNE-INFLAMMATORY MARKER OF HIGH MELD PATIENTS IS ASSOCIATED WITH EARLY MORTALITY AFTER LIVER TRANSPLANTATION

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Background: The scarcity of deceased donor livers has led to allocation of grafts to only the most seriously ill patients with a high Model for End-Stage Liver Disease (MELD) score, which has resulted in a high mortality rate after deceased donor liver transplantation (DDLT). The aim of this study is to identify risk factors for posttransplant mortality and thereby reduce futile outcomes in DDLT.
Methods: Between 2013 and 2019, 57 recipients with MELD scores ≥30 underwent DDLT in our center. We retrieved data and identified the risk factors for 90-day posttransplant mortality. The perioperative clinical and laboratory parameters of patients who did or did not survive for 90 days were subjected to logistic regression analysis. Twelve patients died within 90 days.
Results: Results of univariate analysis indicated that the differences in patient survival were determined by the amount of intraoperative platelets transfused, the presence of posttransplant septicemia, and systemic immune-inflammation index (SII) at the time of listing with MELD scores ≥30. Multivariate analysis revealed that an SII ≥870 (× 10^9/L) and posttransplant septicemia were independent risk factors for 90-day mortality. Twenty-two patients had SIIs ≥870, and 13 of these patients had posttransplant septicemia. Of the 13 patients, 90-day mortality occurred in 10 cases. However, in 35 patients with SIIs <870, 90-day mortality due to posttransplant septicemia was recorded only in 1 patient.
Conclusions: In conclusion, a preoperative SII ≥870 in a patient with a high MELD score may be a significant risk factor for early posttransplant mortality. Because posttransplant septicemia in patients with high SIIs can lead to fatality, a more intensive effort to prevent infection is needed for patients undergoing DDLT carrying such risk factors to avoid futile liver transplantation.

P057 MALIGNANCY AFTER KIDNEY TRANSPLANT - 50 YEARS EXPERIENCE

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Background: Malignancy after organ transplantation is a leading cause of graft and patient loss. Demography of malignancy occurrence was investigated in a single institute.
Methods: Retrospective cohort analysis was performed in renal transplant recipients for last 50years. Medical charts of patients who underwent living or deceased renal transplant during June 1972 to December 2021 were reviewed.
Results: There were 2,246 cases of living donor renal transplant, 315 of deceased donor renal transplant, 27 simultaneous pancreas kidney transplant, and 5 pancreas transplant after living donor renal transplant. Among them, 213 malignancies in 205 cases (7.9%) were developed. Average period after transplantation was 9.9years (median 7.7years). Average age at onset of malignancy was 56.4-year-old. Five-year survival after malignancy occurrence is 12.0% in pancreatic cancer, 42.1% in PTLD, 47.6% in lung cancer, 58.3% in urinary tract cancer, 36.4% in HCC, 81.3% in renal cancer, 69.9% in colorectal cancer, 87.5% in uterine cancer, 90.9% in prostate cancer, 92.9% in breast cancer, 92.9% in gastric cancer, 94.9% in skin cancer. Post-transplant lymphoproliferative disorder (PTLD) occurred in earlier (8.0years), in young patient (48.3-year-old) and its mortality was very high (55.2%). Survival rate of gastric cancer was very good (100%) compared to national cohort data (67.5% at 5 years) probably due to active screening by gastroscopy. Fecal occult blood test on regularly basis looks also useful to detect early cancer.
Conclusions: Follow-up strategy after renal transplantation should focus on malignancy especially in PTLD and detection of early cancer. We should encourage patients to obtain CT scan and screening gastroscopy on a regular basis. Establishment of multidisciplinary therapeutic approach for malignancy treatment is necessary.

P058 A LOW SURGICAL APGAR IS A STRONG DETERMINANT OF THE RISK OF DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

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Background: The surgical APGAR score (SAS) is a 10-point scale combining 3 intraoperative variables: lowest heart rate, lowest mean arterial pressure, and estimated blood loss. Although SAS is correlated with morbimortality in the context of liver transplantation, little is known about its value during kidney transplantation.
Methods: In a monocentric, retrospective study including all adult patients transplanted with a kidney from a deceased donor between 2016 and 2022, we used CHAA software (GE®) to calculate SAS. A low SAS was conventionally defined as ≤7/10. Delayed graft function (DGF) was defined by the need for dialysis within 7 days post-transplant. DGF was explained by a multivariate logistic model, including variables significant at threshold α=0.20 in univariate logistic regressions.
Results: Among 299 patients, 95 (31.8%) had a low SAS. Recipient age (OR=0.85 per 5 years CI95%=[0.77; 0.94], p<0.001]), recipient BMI (OR=1.05 per 1 kg/m² CI95%=[1.01; 1.10], p=0.029]) and surgery duration (OR=1.03 per 5 minutes CI95%=[1.00; 1.06], p=0.038]) were associated with a low SAS after multivariate analysis. DGF developed in 79 patients (26.4%), including 42 (53.2%) with a SAS>7, and 37 (46.8%) with a low SAS. In multivariate logistic regression, four factors were associated with DGF: a low SAS (OR=2.02, CI95%=[1.11; 3.66], p=0.022), waiting time before transplantation (OR=1.05 per 6 months period, CI95%=[1.01;1.09], p=0.025), cold ischemia time (OR=1.10 per 2 hours CI95%=[1.00; 1.20], p=0.041) and absence of treatment by renin angiotensin inhibitor (OR=2.38, CI95%=[1.28-4.35], p=0.006). After a maximum follow-up of 6 years, and a low mortality (4.1% by year 1), no association was found between SAS and graft or patient survival.
Conclusions: A low SAS during kidney transplantation is a major determinant of the risk of DGF.

P059 PRETRANSPLANT HBA1C AS AN EASY TOOL TO IDENTIFY PATIENTS AT HIGH RISK OF DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION

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Background: Post-Transplant Diabetes Mellitus (PTDM) occurs in 10-40% of kidney transplant recipients and is associated with an increased cardiovascular risk. Early identification of at-risk patients could allow to take timely measures. However, no widely validated risk score exists to predict the risk of PTDM.
Methods: This retrospective study includes 267 adult patients who underwent kidney transplantation at the Antwerp University Hospital between January 2014 and August 2021. PTDM was diagnosed based on the American Diabetes Association definition at 3 months post-transplant. First, a logistic regression analysis was used to identify risk factors for PTDM. Second, criteria to identify patients with a high risk (>35%) of developing PTDM at 3 months were established.
Results: At 3 months post-transplantation, 54 (20.2%) patients developed PTDM. Univariable analysis showed that age, BMI and HbA1c on the day of transplantation were associated with PTDM. However, in a multivariable model with the same parameters, only HbA1c remained statistically significant. An absolute increase in HbA1c with 0.1%, increases the odds for developing PTDM with 28% (95% confidence interval 1.15-1.42). A HbA1c level ≥ 5.3% at transplantation, regardless of age or BMI, is sufficient to identify patients with a PTDM risk of ≥ 35%.
Conclusions: The HbA1c value at transplantation was the strongest risk factor for PTDM at 3 months post-transplant. Furthermore, a pre-transplant HbA1c of ≥ 5.3% showed to be an easy tool to identify patients at high risk of early PTDM in our population.

P060 COMPARING OUTCOMES IN EXTENDED VERSUS STANDARD CRITERIA LIVING DONOR KIDNEY TRANSPLANTATION: A SINGLE-CENTRE ANALYSIS

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Background: Living donor renal transplantation (LDRTx) is considered to be the treatment of choice for treating End Stage Renal Disease (ESRD). Multiple studies have shown the impact of donor and recipient demographics in post-transplant outcomes. We investigated the impact of allocating extended criteria living donor (ECD) renal allografts to extended criteria recipients (ECR).
Methods: We retrospectively analysed all the LDRTx pairs between Apr 2017 and Jan 2022. We defined ECD and ECR, as individuals having at least one of the following: age older than 60, presence of diabetes mellitus (DM), hypertension (HTN), atheroma, body mass index (BMI) above 30. We defined four groups for analysis: ECD to ECR, SCD to SCR, ECD to SCR and SCD to ECR. We documented mortality, return to dialysis, perioperative haemorrhage, surgical site infections (SSI), incisional hernias and latest donor renal and recipient graft function from the respective follow up. Jamovi 2.2.5 was used for statistical analysis.
Results: We identified 149 pairs of LDRTx. Results are in Table 1. Follow up was 5 years for 21,5%, 3 years for 56,4% and 1 year for 22,1% of the LDRTx pairs.
Conclusions: The donor and recipient outcomes of ECD to ECR LDRTx were similar to the other groups which means that extended criteria LDRTx is safe and effective.

Table 1

	N = 149	ECD to ECR (19)	SCD to SCR (60)	ECD to SCR (39)	SCD to ECR (31)	p
Donor characteristics						
Age (mean±SD)	48,1±13,5	58,3±12,8	43,2±10,1	52,9±10,8	42,9±10,8	<0,001
DM	6%	26,3%	0%	10,3%	0%	<0,001
HTN	0,7%	0%	0%	2,6%	0%	0,417
BMI (kg/m²)	28,1±5	31,1±4,4	25,1±3,1	31,8±4,6	24,8±2,6	<0,001
Genetic Relationship	LRD 53%	LRD 36,8%	LRD 50,8%	LRD 53,8%	LRD 56,7%	0,565
Donor single renal vessels	64%	84%	76,7%	71,8%	74,2%	0,677
Recipient Characteristics						
Age	47,3±13,6	63,8±8,1	42,5±10,2	39,4±10,5	56,6±11,8	<0,001
DM	14,1%	26,3%	0%	0%	51,6%	<0.001
Pre-emptive	43,6%	52,6%	45%	38,5%	38,7%	0,733
Previously sensitised	16,8%	21,1%	13,3%	20,5%	16,1%	0,715
CIT (min)	263±106	309±144	226±70,7	223±97	280±115	<0,01
Donor Outcomes						
Last eGFR	71,8±13	68,9±16,9	74,9±11,3	69,9±12,5	71±12,2	0,422
Recipient Outcomes						
Mortality	5	2	1	1	1	0,303
Return to Dialysis	7	2	0	3	2	0,094
Last eGFR	56,4±21,2	51,2±24,8	62,4±17,7	51,7±19,5	51,5±22,6	0,055
Haemorrhage	14	2	5	4	3	0,981
SSI	10	3	4	1	2	0,371
Incisional Hernias	11	3	2	3	3	0,084

P061 PROSPECTIVE ASSESSMENT OF THE NEED FOR AND ADDED VALUE OF MOLECULAR DIAGNOSTICS OF KIDNEY ALLOGRAFT BIOPSIES – AN EVALUATION IN CLINICAL PRACTICE

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Background: The Molecular Microscope Diagnostic System (MMDx) may resolve inconclusive histology findings, as preserved biopsy material can be examined after histology findings have been obtained. The extent to which this approach can be implemented in clinical practice remains unknown.
Methods: We prospectively analyzed 104 consecutive indication kidney allograft biopsies by histology and molecular diagnostics at the University Hospital Zurich from April to December 2022. Pathologists and clinicians with experience in molecular diagnostics assessed the need for MMDx by questionnaire when the histology report was available. Clinicians then assessed the added value of the molecular diagnostics when the MMDx report was available.
Results: 29 of 104 cases (28%) showed rejection by histology, 42 of 104 cases (40%) showed no rejection by histology, and 33 of 104 cases (32%) showed histologic findings insufficient to diagnose ABMR due to an absence of diagnostic criteria groups 2 and/or 3. Pathologists considered molecular diagnostics indicated in 42 of 104 cases (40%), 9 cases to give extra confidence, and 33 cases for diagnostic clarification concerning rejection. Clinicians considered molecular diagnostics indicated in 54 of 104 (52%) cases, 5 cases to give extra confidence, and 49 for diagnostic clarification concerning rejection. In 33 cases with histologic findings insufficient to diagnose ABMR, molecular diagnostics were considered indicated by pathologists and clinicians. Molecular diagnostics allowed the diagnosis of ABMR in 8 of 33 cases (24%). In addition, 11 of 104 cases (11%) showed a discrepancy between the histologic findings and the molecular diagnosis. Clinicians considered adjustment of treatment based on the MMDx report in 3 of 11 discrepant cases. Pathologists and clinicians considered molecular diagnostics indicated in 2 of 11 and 3 of 11 discrepant cases, respectively.
Conclusions: The need for molecular diagnostics goes beyond the recommendation of the 2018 Banff classification for histologic findings insufficient to diagnose ABMR. However, the added value of molecular diagnostics appears to be largely limited to these cases.

P062 EFFECTS OF A QUADRUPLE IMMUNOSUPPRESSANT REGIMEN INCLUDING EARLY ADD-ON EVEROLIMUS AFTER KIDNEY TRANSPLANTATION

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Background: Several studieis have reported that everolimus (EVR), a mammalian target of rapamycin inhibitor, combined with reduced exposure to calcineurin inhibitors (CNIs), has noninferior results for kidney function, acute rejection, and viral infection, compared with current standard immunosuppressive (IM) drugs that use CNIs and mycophenolate mofetil (MMF). Most protocols containing EVR are triple therapy, in which MMF is converted to EVR; IM regimens with MMF and EVR are very few. This study investigated the beneficial effect of a quadruple IM regimen with MMF and EVR after kidney transplantation (KT).
Methods: We evaluated 95 KT patients who used tacrolimus and EVR between May 2014 and December 2020 and followed them for 1-year post-KT. They were divided into two groups by IM regimen: EVR added 7 days after KT (early group; n=52) and EVR added during the stable period (> 3 months post-KT, stable group; n=43). The incidence of acute rejection and infection, adverse events, IM drug dose, CNI trough level, and renal function were retrospectively examined.
Results: Our current IM regimen comprises tacrolimus, methylprednisolone, MMF, and basiliximab, and EVR is administered 7 days post-KT. Before this current regimen, EVR was started when renal function was stable for > 3 months after KT. On average, EVR was started 137.8 days after KT in the stable group. Tacrolimus and mycophenolate mofetil doses were reduced after EVR addition in both groups. One-year post-KT, the mean serum creatinine level in the early vs. stable group was 1.56±1.40 vs. 1.49±0.68 mg/dL (p=0.072), and the estimated glomerular filtration rate was 47.7±19.13 vs. 43.6±16.9 mL/min/1.73 m² (p=0.282), with no significant differences. The incidence of biopsy-proven T-cell-mediated rejection was significantly lower in the early group (p=0.02). There were no significant differences in stomatitis and peripheral edema between the groups. The incidences of cytomegalovirus infection and neutropenia were significantly lower in the early group (p=0.007, both).
Conclusions: Our quadruple immunosuppressant regimen including early add-on EVR yielded acceptable outcomes.

P063 THE IRANIAN EXPERIENCE OF PEDIATRIC ORGAN DONATION

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Background: Child transplantation is a widely accepted life-saving intervention for pediatrics on the waiting list. It can improve the quality of life and prognosis for children with chronic organ impairment, such as renal, lung, or small bowel failure.
Methods: This retrospective, descriptive study reviews pediatric organ donation in Iran. We analyzed the data of all children declared brain dead in Iran between 2018 - 2020, and describe the deceased donor transplants performed in the same period.
Results: During the three years, 349 children, i.e., patients under 18, became deceased-organ donors, all following a diagnosis of brain death. In 51.9%, the etiology of brain injury was trauma, of which 20.3% were due to hypoxia. Comparing different years, significant differences were found in relation to the aetiology of brain death and receipt of defibrillation. The significant differences were found in relation to the etiology of brain death and gender, BMI, and age. 605 kidneys, 308 livers and 62 hearts were transplanted from 349 donors in 2018-2020. During this period, 326 children were listed for a kidney transplant and 138 for a liver. In this period, there were 223, 283 and 307 children on the heart waiting list each year and 21 (2018), 21 (2019) and 18 (2020) transplants performed; so, to clarify for example in 2020 only 6-10 % of children on the waiting list received a heart transplant each year. This indicates a significant gap between the heart transplant waiting list and donor availability, with 78 hearts not donated from deceased child donors in 2020. 1/3rd of children on the transplant waiting list are 'emergency' listed, and while data is incomplete, O is the most prevalent blood group of children on the waiting list. (21.7%) Given the need for matching for some organs, this is the hardest tissue group to match, further limiting organ availability from an already limited donor pool for those requiring small-sized organs.
Conclusions: Organ donation rates are comparatively reasonable, but the lack of specialist centers for children's intensive care is still an issue. The establishment of specialized management centers for deceased donation in children under 18 years are required for donation rates to improve.

P064 PATIENTS' PERSPECTIVE AND UTILITY OF SELF-NARRATIVE BIOGRAPHIES IN THE KIDNEY TRANSPLANTATION PATH

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Background: Waiting for a transplant correlates with trepidation but also emotional distress, a sense of guilt and grief towards the deceased donor, anxiety, and even depression. After a transplant, patients have to cope with uncertainty about outcomes and fear of possible adverse effects. Moreover, organ transplantation is associated with changes in personal identity. Aim of this study was to conduct self-interviews to gather patients' perspectives on significant moments in their transplant journey and experience of sharing related self-narratives.
Methods: Face-to-face and semi-structured interviews were conducted with KTRs from 2020-2021. KTRs were invited to express their opinions and perspectives freely and then received a personal semi-structured interview about the following topics: (1) personal experiences during the waiting-list-period; (2) impact of the transplant on their daily activity; (3) feelings about the post-transplant out-of-hospital routine; (4) description of life changes; (5) opinion on the self-narrative biography utility.
Results: Participants mentioned highly emotional moments: first day of dialysis, telephone call announcing the organ availability, feeling relieved after the transplant surgery and troubles with immunosuppressive medication. Plus, a theme of uncertainty about the outcome emerged. Most KTRs reported sharing their own story verbally with different non-medical figures: it normalizes, allows comparisons with others and relieves the feeling of loneliness; hearing others' narratives appears as a way of gaining knowledge different from the medical standpoint.
Conclusions: Transplant experience is characterized by a non-linear timeline different from the chronological steps foreseen by the medical procedure, overlooked as a "healing moment". Use of creative activities in health care situations, characterized by high intensity, uncertainty and loneliness, can empower people and increase their well-being, self-efficacy and personal growth allowing emotional release. Our study has some limitations: recipients from living donors or who experienced rejection were excluded, it is a monocentric experience and the interviews were conducted only in Italian. More research is needed to study the impact of forms of storytelling as an intervention.

Theme	Illustrative selected quotes
Waiting list	*"I cried with joy when I got the call to show up at the hospital for the transplant."* *"After all the exams and ranking I was over the moon, I saw the light at the end of the tunnel. Then the months start to pass and then a year the joy starts to turn into a nerve-wracking anticipation. Soon after the panic attacks begin... what if they never call me?"* *"My emotions after being listed were a mix of fear, anxiety and not feeling ready."*
After transplant	*"After the transplant I came back to life and felt like a normal person again."* *"Slowly I felt better and better, full of strength. My body began to give the right answers to my desire to do".* *"In the early days I lived with the fear of rejection and I was careful of everything, I didn't exaggerate in my daily routine and I promised myself to live my life much more peacefully, having received a gift".* *"The change was immediately evident given that I no longer did dialysis, being busy three days a week in the hospital away from my family for almost 5 years had a huge impact on my life and not having to do it anymore gave me back a presence in the family that has been missing for too long."*
Outpatient checkups	*"I knew they were necessary for my health even though I have to say I often came home tired."* *"The first few months didn't go well and I was looking forward to visits to see if there was anything new either way."* *"I have always felt serene and confident also because I was aware of the preparation and competence of the medical staff who have been following me for years and who had already saved my life in the past".*
Current life description	*"Now my life is mine. I'm in control of my time again and this gives me an enormous emotional boost."* *"I see everything around me from another perspective, without pessimism."*
Considerations about self-narratives and creative activities as a therapy	*"I think everyone needs a word of support, a voice out of the chorus, which gives meaning to so many things that, seen from our point of view, cannot be explained".* *"We need to share our own story with others who are in the same condition to help those who are less strong to say: you're not alone."*

P065 VITALLINK'S SCHOOL EDUCATION PROGRAM TO NURTURE THE VALUE OF SHARING AND DECEASED ORGAN DONATION FOR TEENAGERS

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Background: In order to form a social consensus on deceased organ donation, it is necessary to nurture the value of coexisting and understand deceased organ donation by school education in one's early life.
Methods: Vitallink, an NGO established by medical professionals in Korea, has built network with school teachers and developed a guidebook of 'The Seed of Hope, the Fruit of Sharing' and built four-hour class program. The guidebook is composed of 14 chapters, the first part of which deals with the value of sharing and the latter part consists of understanding of deceased organ donation. Four-hour 'Respect for Life' program was composed of loving myself, building relationship with empathy, coexisting with others, and practicing sharing. Teachers conducted two to four hour classes of 'Respect for Life' in elementary, middle and high schools since 2021. We collected students' reflections writing what they have learned and felt at the end of the class.
Results: In the 'Love myself' class, students had time to think about themselves and express their thoughts on the questions related to themselves and fullness of life. Under the subject of 'Building relationship with empathy', elementary students created 'our constellation story' by connecting own star and stars of their friends, and the elder students shared their own energy with friends through the 'Energy Ping-pong' game. The third part was to think about what

virtues are necessary for coexistence in nature and society we live in. Students did a group work to express their ideas to preserve nature and make a just and warm community. In the fourth part, students searched for actual sharing cases and made a newspaper or poster to express their thoughts. At the end of the class, the students wrote what they have learned, felt, and would put into practice. The teacher talked with the students while watching the video where life leads to other life in nature and though deceased organ donation. The feedbacks of all students were reconstructed into a keyword map.
Conclusions: Students wrote that through these classes, they have learned the value of themselves and others and that we are living together. Through this experience, when students grow up and become adults, we expect them to have more affirmative attitude toward organ donation after brain death.

P066 DE NOVO CANCER IN LIVER TRANSPLANT RECIPIENTS - A SINGLE CENTER EXPERIENCE

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Background: De novo malignancies following liver transplants are a serious threat in liver transplant recipients. The excess risk of post-LT de novo malignancy occurrence is now well known; the estimated risk for de novo malignancy is 1.4-4.9 times greater in LT recipients compared with the general populations. However, the incidence and type of DNM also depends on different risk factors, including patient demographics, cause of the underlying chronic liver disease, behavior (smoking and alcohol abuse)
Methods: we evaluated 1000 liver transplant recipinets; 206 LT for HCC were excluded.
Results: 42 (5,28%) patients developed *de novo* neoplasms:1pts - 2 types of cancer:- skin and cervix cancer. Interval between transplant and diagnosis of *de novo* cancer (month) were: min 6 month and max 11 years. The cancers were: solid tumors such as pancreatic cancer, lung cancer, colorectal cancer, gastric cancer, esophageal cancer, renal cell carcinoma, bladder cancer, thyroid cancer, oral cancer, brain tumors and laryngeal cancer and non-solid tumors: primarily PTLD/non-Hodgkin Lymphoma (NHL) and leukemia.However, the incidence and type of DNM also depends on different risk factors, including patient demographics, cause of the underlying chronic liver disease, behavior (smoking and alcohol abuse).
Conclusions: All liver transplant recipients should receive counseling on smoking cessation, limitations on alcohol use (complete abstinence in patients with ALD), sun protection and avoidance, regular skin assessments, adherence to routine cancer screening tests, and regular follow-up.

P067 PANCREAS ALLOGRAFT THROMBOSIS AS A POST-COVID-19 COMPLICATION IN DIABETIC PATIENT

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Background: The SARS-CoV-2 pandemic has caused a huge overload onthe healthcare system worldwide [1]. From March 4th 2020 until December, 07th 2021 the total number of COVID-19 cases in Poland reached 3,684,671 million. According to the Polish Ministry of Health 85,700 infected patients died, most of them had been suffering from concurrent disease. [2] The mortality rate from COVID-19 in Polish population is ~ 2.5%. An increase of thrombotic and thromboembolic complications has been associated with COVID-19 in both arterial and venous systems. [3,4] Patients after transplantation suffering from COVID-19 are at a higher risk of mortality (42-24%) and complications than the average population. [5]
Methods: Hospital database analysis and literature search
Results: Recently, in our Center, there was a case of a PTA recipient with diabetes t1 that developed venous and arterial thrombosis 4 months after COVID-19, resulting in graft necrosis and finally in pancreas graftectomy **[figure A-F].** Our 6-year post-PTA patient had no history of thromboembolism or other risk factors apart from diabetes t 1 and a history of COVID-19. Earlier, in 2020 and 2021, 2 cases of infarction of a transplanted kidney in patients suffering from COVID-19 were described. Moreover, both cases occurred in obese transplant recipients with diabetes t 1. The first case - a man with DM t1 13 years after kidney and pancreas transplantation who had a segmental infarction of the kidney [6], and the second case was a woman with DM t1 6, 5 months after kidney transplantation, who lost the graft as a result of a renal artery infarction. [7] Identifiable risk factors linking these cases are the post-transplant status for t1 diabetes and obesity.
Conclusions: Transplant patients who have experienced COVID-19 should be carefully monitored for the occurrence of graft arterial and vein embolism. Early detection of these complications in patients after organ transplantation gives an opportunity to save the organ. Thromoprophylaxis with low molecular weight heparin is highly important and should be continued in high-risk patients (obese, with persistent d-dimer levels> 1000) for a minimum of 2 weeks (preferably 4-6 weeks) after reaching the convalescent status.

P068 TRANSMISIÓN DE VIRUS DE LA HEPATITIS C DE DONANTE VIRÉMICO A RECEPTOR SERONEGATIVO A TRAVÉS DEL INJERTO TEJIDO. UN ESTUDIO PROSPECTIVO

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Background: The transmission of hepatitis C virus (HVC) from viremic donors to seronegative recipients of kidney transplantation is well documented. Pre-transplant administration of direct-acting antivirals prevents viremia, but the seroconversion rate is high. The aim of this study is to assess HCV transmission through the graft tissue.
Methods: In this prospective observational study, we determined the presence of HCV in the tissue of 15 kidneys from 8 deceased viremic donors(D16 transplanted to a seropositive recipient) before transplantation. Tissue samples were extracted in the operating room and Viral RNA determination in donor plasma and tissue was performed with the Xpert HVC viral load quantitative assay (Cepheid)
Results: Plasma viral load in all donors was significant, and in recipients it was undetectable on days 1 and 7 post-transplantation. However, 13 of the 15 recipients (86.6%) had seroconverted within one month. HCV was detected in 9 of the 15 (60.0%) histological samples analyzed. Viral RNA was detected in D5, but not in D6, from the same donor, probably due to the scant sample and borderline viral. Data showed in table
Conclusions: HCV was detected in a large proportion of kidney grafts from viremic donors, which could facilitate its transmission to recipients.

Donor	Recipient	Donor Load (UI/mL)	Recipient Plasma Viral Load (UI/mL)		Kidney Viral Load	Seroconversion
			DAY 1	DAY 7		
D 1 D 2	R1 R 2	4.000	Undetectable Undetectable	Undetectable Undetectable	Undetectable Undetectable	Positive Positive
D 3 D 4	R 3 R 4	470.000	Undetectable Undetectable	Undetectable Undetectable	Undetectable Undetectable	Positive Positive
D 5 D 6	R 5 R 6	1.400.000	Undetectable Undetectable	Undetectable Undetectable	Detectable Undetectable	Negative Negative
D 7 D 8	R 7 R 8	1.300.000	Undetectable Undetectable	Undetectable Undetectable	Detectable Detectable	Positive Positive
D 9 D 10	R 9 R 10	180.000	Undetectable Undetectable	Undetectable Undetectable	Detectable Detectable	Positive Positive
D 11 D 12	R 11 R 12	1.300.000	Undetectable Undetectable	Undetectable Undetectable	Detectable Detectable	Positive Positive
D 13 D 14	R 13 R 14	4.500.000	Undetectable Undetectable	Undetectable Undetectable	Detectable Detectable	Positive Positive
D 15 D 16	R 15 R 16	450.000	Undetectable	Undetectable	Undetectable	Positive

P070 17B-ESTRADIOL AND METHYLPREDNISOLONE ASSOCIATED EFFECTS ON RENAL INFLAMMATION INDUCED BY BRAIN DEATH IN FEMALE RATS

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Background: Brain death (BD) causes hemodynamic and hormonal impairment, compromising organ quality. Hormone replacement therapies, using thyroid hormones and cortisol, have shown positive results. After BD, female kidneys tend to present higher inflammation in comparison to male. This was associated with the rapid decrease in female sex hormones, like estradiol (E2), considering that E2 plays an important role in female response to stress. In that context, we aimed to investigate the role of E2 and its association with methylprednisolone (MP) in kidneys of female rats after BD.
Methods: Female Wistar rats were submitted to BD by rapid inflation of an intracranial balloon catheter and maintained for 6h. Rats received MP (MP, 4 mg/ml i.v–2 ml/h) or MP and E2 (MP/E2, 50 ug/ml i.v–2 ml/h) after 3h of BD until the end of experiment. Sham-operated (S) rats were used as controls. After 6h, plasma and kidney tissue samples were collected for further analyses.
Results: In kidney homogenate, IL-6 (S:26.97±8.52; BD:74.87±25.65; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.0076) and VEGF (S:2.45±2.32; BD:23.45±28.72; MP/E2:2.75±2.99; MP:3.18±4.95 pg/mg/protein - p=0.024) were increased after BD, and both molecules were reduced after treatments. Regarding TNF-α, there was no difference between S and BD, but there is a significant reduction with both treatments (S:$1.07x10^{-3}$±2x10-3 ; BD:1.03x10-3±$17x10^{-3}$; MP/E2:0.03x10-3±$2x10^{-3}$; MP:0.02x10-3±$2x10^{-3}$ pg/mg/protein - p=0.025). Plasma measurements showed no difference in urea after BD and a reduction with MP (S:131.4±14.24; BD:133.3±15.19; MP/E2:119±20.8; MP:79.36±10.96 mg/dL - p=0.069). A slight increase of creatinine levels was observed after BD in comparison to S (S:2.44±0.89; BD:5.85±1.98; MP/E2: 5.45±1.65; MP:4.16±1.15 mg/dL - p=0.276). Regarding relative gene expression, there was no difference in IL-1β, IL-6, IL-10, TNF- α and KIM-1.
Conclusions: Results suggest that both treatments are able to reduce kidney acute inflammation. These data indicate that MP and its association with E2 has a potential beneficial effect in inflammation triggered by BD in kidneys from female donors, suggesting that this treatment may improve organ quality.
This study was financed by 2020/11211-6, Fundação de Amparo à Pesquisa do Estado de São Paulo-FAPESP

P071 FIRST ROUTINE CLINICAL APPLICATION OF MOLECULAR MICROSCOPE (MMDX) IN EUROPE

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Background: Although molecular assessment of kidney allograft biopsies has been recommended by Banff guidelines for the last decade, its routine clinical application has been missing in Europe due to lack of approved technologies. In August 2022, the MMDx® was licensed and established into the routine clinical practice at the Institute for Clinical and Experimental Medicine in Prague. The MMDx results are available within 28 hours allowing clinicians to modify the treatment avoiding unnecessary delays.
Methods: One of the performed biopsies was immersed in RNAlater for eventual MMDx assessment, indicated the same day based on histology describing DSA negative ABMR, borderline inflammation, unexplained graft dysfunction, or in cases non-fulfilling criteria for adequacy. The MMDx reports were compared with histology and clinical outcomes.
Results: Since implementation of MMDx assessment, 71 out of 278 biopsies performed (25.5%) have been processed so far, with molecular rejection in 38 cases (54%) including 3 histologically marginal samples. The rejection by histology was confirmed by MMDx in 26/35 cases (74%, Fig.1A). Contrary, MMDx revealed no-rejection in 33 biopsies. From those, 3 cases were classified by histology as chronic TCMR, and 1 as TCMRIA. In one case, two sequential biop sies were classified by histology as DSA negative acute ABMR however with negative molecular rejection scores and finally diagnosed as monoclonal gammopathy of renal significance. In 2 cases with chronic active ABMR and 1 case with chronic mixed rejection by histology, MMDx found only atrophy-fibrosis with no rejection. Moreover, other histological findings suspicious of alloimmune response were classified as no rejection by MMDx (Fig. 1B). In 29/33 patients classified by MMDx as no rejection, the antirejection therapy was not indicated.
Conclusions: MMDx in real-life settings provides the benefits of more precise diagnostics of kidney allograft pathologies and, more importantly, reduces costs for prolonged hospitalization and non-necessary antirejection treatment in suspicious histology findings. The safety of this approach needs to be further validated.

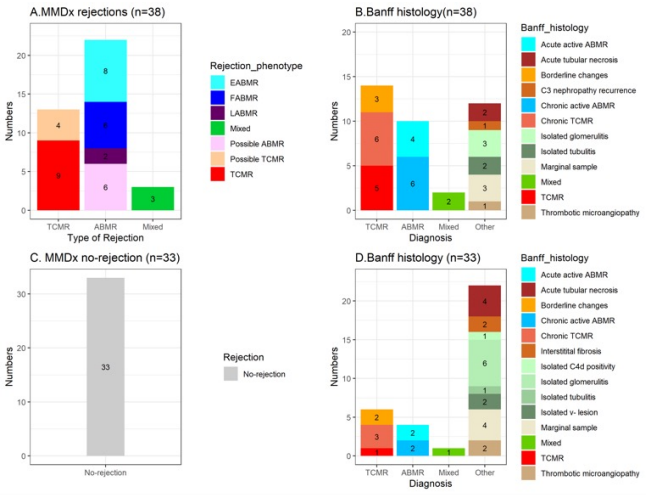

Figure 1. Comparison of MMDx-rejection and non-rejection phenotypes with histopathology.
TCMR, T-cell mediated rejection; ABMR, antibody-mediated rejection; E, early; F, fully-developed; L, late.

P072 PERFORMANCE OF A NOVEL NGS ASSAY SUITABLE FOR MONITORING DD-CFDNA FOLLOWING KIDNEY TRANSPLANTATION

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Background: One severe complication following solid organ transplantation is antibody- and/or cell mediated rejection of the graft. Early detection of rejection is therefore of paramount importance to improve outcome of solid organ transplantation. The present study was conducted to determine the analytical performance of the Devyser kit designed for sensitive detection of dd-cfDNA (donor-derived cell free DNA) following kidney transplantation.
Methods: Three artificial dilution series mimicking recipient and donor were manufactured to determine the analytical performance of the assay. The DNA samples were fragmented to correspond to cell free DNA (~166 bp) using NEBNext dsDNA Fragmentase (New England Biolabs) according to manufactures instructions. The dilution points for each dilution series were the following; 0.05%, 0.1%, 0.2%, 0.3% 0.4%, 0.5%, 1%, 10%, 20% and 30%. A total of 443 samples were amplified and sequenced using the Devyser kit. All NGS-data were analyzed and visualized employing the ADVYSER software. The stability of the cfDNA in plasma collected in two different kinds of collection tubes were also evaluated prior and post plasma isolation. The integrity of cfDNA was evaluated using Agilent TapeStation Cell-free DNA ScreenTape Analysis.
Results: All samples were tested and sequenced on three different Illumina MiSeq instruments and the fastq files were analyzed using the ADVYSER software. The following analytical parameters were established during the study; Limit of Blank (LOB), Limit of detection (LOD), Limit of Quantification (LOQ), Linearity, lot-to-lot uniformity, within-and between run. Even in samples with low DNA concentration, ddcfDNA as low as 0.1 % was detected.
Conclusions: The present study shows that a novel assay for solid organ transplantation based on NGS, exhibits excellent sensitivity, accuracy and precision and is suitable for monitoring dd-cfDNA.

P073 A MULTI-CENTRE STUDY TO ASSESS THE TOLERABILITY AND EFFECTIVENESS OF EXTENDED-RELEASE TACROLIMUS (LCPT) IN DE NOVO LIVER TRANSPLANT PATIENTS

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Background: Available tacrolimus formulations exhibit substantial inter- and intra-individual variability in absorption and metabolism. The present non-interventional cohort study aimed to assess the tolerability and effectiveness of the once-daily tacrolimus formulation, LCPT, in hepatic allograft recipients in real life.
Methods: This study was conducted in Austria and the Czech Republic between 07/2016 and 08/2019. Patients aged ≥18 years received LCPT per the approved label and local clinical routine. All the participants provided informed consent. Patients newly treated with tacrolimus (*de novo*) directly after transplantation were observed for six months. The relevant clinical variables were tacrolimus trough level (TL), total daily dose (TDD), number of dose adjustments, kidney and liver function, and tolerability.
Results: Of the 70 analysed patients,72.9% were male and 85.7% were aged <65 years. The mean (SD) time to achieve tacrolimus target TL was 6.4 (4.6) days after 4.4 (4.0) dose adjustments; thereafter, TL remained stable throughout observation at approximately 8 ng/mL. The LCPT TDD at initiation was 8 mg, and decreased by a median of 41.4% to 5 mg at six months. Liver function continuously improved, and kidney function remained stable. LCPT was well tolerated with 24 adverse events in eight patients (17 related to immunosuppression, mostly mild renal insufficiency, and hematological adverse events); two serious unrelated adverse events were reported (atrial flutter and liver dysfunction).
Conclusions: TL was rapidly attained with few dose adaptations after LCPT initiation in *de novo* liver transplant patients. Liver function rapidly improved, whereas kidney function remained normal. LCPT was well-tolerated in this population.

P074 FROM PEN TO CLOUD – INTRODUCTION OF A DIGITAL DOCUMENTATION PLATFORM FOR ORGAN DONATION COORDINATORS

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Background: In the context of digitalisation, the analogue National Coordination paper protocol, where all telephone calls and allocation decisions are documented, should be replaced by a cloud-based digital solution. This should improve traceability, minimise errors during transfer (e.g. readability of entries) and simplify cooperation between team members, especially in the home office and in shift work with duty handover. Cooperation with the local coordinators is also to be facilitated by the introduction of a status terminal. The status terminal with all important time points is to be filled in real time, directly from the protocol, without duplicate entries.
Methods: Advantages and disadvantages of paper documentation and digital documentation were collected and compared. Technical options were looked at and a budget was created. After the analysis, we found that there is a need for different roles with different permissions for all stakeholders involved in organ donation.
Results: In several sprints (each sprint approx. 4 weeks), the protocol was programmed and finally introduced by an external company after the needs of the national coordination, represented by a specialist project manager. Improvements are constantly being made to simplify the protocol and make the status terminal more interesting for the coordinators in the hospitals. Data protection aspects were also taken into account during implementation.
Attention was also paid to who should have access rights to the status terminal and what type of access (read only or read/write).
Conclusions: The digital protocol was introduced over a year ago. It has simplified the cooperation, the handover to colleagues is faster and more error-free. The protocol also serves as a checklist and processes can be standardised. Digitalisation has also proved its worth in the case of queries about organ donations that took place some time ago. The introduction of the real time status terminal supports the coordinators in the hospitals. The issue of data security was somewhat underestimated at the beginning, but it is very important and must be reassessed and tested continuously.

P079 HYPERTENSION AFTER LIVING DONOR KIDNEY DONATION IN THE ERA OF EXTENDED DONOR ELIGIBILITY CRITERIA

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Background: Hypertension represents a deviation from the ideal living donor kidney evaluation study protocol. It has been considered to be a contraindication for live kidney donation because it is associated with or can promote the onset of cardiovascular and renal diseases. To date, few articles have been published regarding the long-term follow-up of these donors.
Methods: Between January 2016 and December 2021, 121 living donor kidney transplants were performed at this Kidney Transplant Unit. Demographic characteristics (age, BMI, sex, renal function, presence or absence of hypertension) of the potential donors were collected. Of these, 27 (22%) had pre-donation hypertension (≥140/90 mmHg) under medical therapy with 1 (85%) or 2 drugs (15%). The 121 donors were divided into two groups (hypertensive and normotensive donors) before the donation.
Results: Results at 1, 2 and 3 years after donation were analyzed. The hypertensive and normotensive donors did not differ in BMI (p=n.s.), nor in renal function (p=n.s.) but did differ in age (p=0.00) since the hypertensives were older than the normotensives. In addition, 9 (9.6%) pre-donation normotensive donors developed hypertension and 3 (15%) pre-donation hypertensive donors had increased antihypertensive medications. After the donation, the creatinine and filtrate values (eGFR) of the hypertensive donors were comparable to those of the normotensive donors at 1, 2 and 3 years (p=n.s.). These results are confirmed by the multivariate analysis (logistic regression model) performed.
Conclusions: A non negligible proportion of donors develop *de novo* hypertension after donation. In most cases, hypertension in live kidney donors was not associated with a greater increase in blood pressure nor a relevant decrement in filtration rate after donor nephrectomy. Pre-donation hypertension without organ damage should not be considered an absolute contraindication for live kidney donation. However, long follow-up with serial monitoring of blood pression and renal function is mandatory for these donors.

P080 PLASMA CELL-FREE DEOXYRIBONUCLEIC ACID AND SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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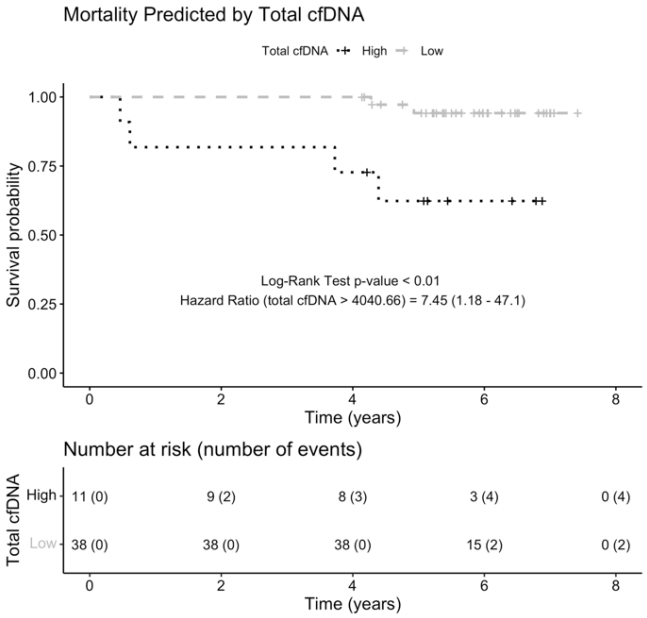
Background: Studies investigating the role of cell-free deoxyribonucleic acid (cfDNA) in kidney allograft dysfunction have primarily focused on the ability of donor-derived cfDNA (ddcfDNA) to detect rejection. Higher plasma ddcfDNA levels have been shown to be diagnostic of antibody-mediated rejection (ABMR). As ABMR is an established determinant of long-term graft outcomes, we hypothesised that higher levels of ddcfDNA would associate with poorer outcomes. We aimed to examine the long-term prognostic value of plasma ddcfDNA and total cfDNA, measured immediately prior to indication kidney transplant biopsies.
Methods: A retrospective review was performed of kidney transplant recipients (KTRs) who underwent prospective cfDNA quantification by droplet digital polymerase chain reaction, at the time of transplant indication biopsy between 2014 and 2017. Absolute (copies per millilitre, cp/mL) and relative (%) ddcfDNA levels, and total cfDNA concentration, were analysed against long-term survival outcomes.
Results: Of 49 unique KTRs (mean follow-up 5.8 years), there were 6 deaths and 6 failed grafts. Total cfDNA was higher (4736.6cp/ml vs 1639.91cp/ml, p=0.04) and relative ddcfDNA was lower (0.21% vs 0.52%, p=0.047) in KTRs that died. The optimal cutpoint (by Youden's index) for mortality was 4040.66cp/mL (area under the curve, AUC 0.76) for total cfDNA, and 0.31% (AUC 0.75) for relative ddcfDNA. On multivariate analysis, increased KTR mortality was predicted by total cfDNA above the cutpoint (hazard ratio, HR 7.45, 95% CI 1.18-47.1), and by relative ddcfDNA below the cutpoint (HR 20.53, 95% CI 1.4-299.8). Total cfDNA was lower in KTRs with death-censored allograft failure (912.43cp/ml vs 1803.09cp/ml, p=0.02). All cases were identified by total cfDNA below the optimal cutpoint of 1304.68cp/mL (AUC 0.81). Absolute ddcfDNA was not associated with survival outcomes.
Conclusions: Death was significantly associated with higher total cfDNA and lower relative ddcfDNA. Allograft failure was significantly associated with lower total cfDNA. These associations are a novel finding in KTRs. Relative ddcfDNA has been used to identify transplant rejection, but cfDNA and ddcfDNA may indicate prognosis more widely.



P081 REVISED USUAL INTERSTITIAL PNEUMONIA DIAGNOSES IN EXPLANT LUNGS AFTER THE CURRENT INTERNATIONAL GUIDELINES: A 17-YEAR BICENTRIC EXPERIENCE

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Background: Usual interstitial pneumonia (UIP) pattern is associated with Idiopathic Pulmonary Fibrosis (IPF) but is also frequently detected in other clinicopathologic settings such as Connective Tissue Diseases (CTD) and fibrotic Hypersensitivity Pneumonitis (f-HP). Improved knowledge has highlighted the importance of additional histological and clinico/radiological features for the diagnosis of UIP/non IPF patients. Several recent studies have shown a different post-transplant outcome of patients with fibrosing interstitial lung diseases other than IPF with a better outcome in the group of f-HP. The main goal of this study was a multidisciplinary revision of explanted lungs with a diagnosis of UIP/IPF obtained from patients undergoing LTx from 2002 to 2018 in two referral Centres, according to the current statements.
Methods: All cases with diagnosis of UIP/IPF in the explanted lungs, complete clinical information and available HRCT images, were included (81 patients). Histological and radiological review were independently performed and each case was categorized as "UIP", "Probable UIP", "Indeterminate for UIP", "Alternative diagnosis" following the current guidelines. In addition, pathologists quantified key histological features (e.g. lymphoid follicles, lymphocyte/plasma-cell ratio, vessel remodelling, peribronchial metaplasia, granulomas/giant-cells) helpful in identifying non-IPF diagnoses, according the recent literature. Clinical data were also reviewed, and all cases were categorized after multidisciplinary team discussion (MTD).
Results: In 39/81 (48%) of patients the final diagnosis of IPF was made, after MTD. The remaining 42/81 (52%) was categorized as follows: 12% IPF likely, 9% indeterminate for IPF, 10% IPF likely/non-IPF and 21% non-IPF. After MTD, 64% of cases were finally categorized as IPF, 11% as f-HP, 9% as CTD, 12% as other diseases and 4% remained unclassifiable.
Conclusions: In conclusion, the rate of IPF diagnoses appears to have been overestimated and this is crucial as f-HP patients are good candidates for LTx for the best survival rates. A precise diagnosis of native lung diseases may influence the post-transplant outcome and management, for example limiting the exposure factors responsible of f-HP and avoiding possible relapsing disease.

P082 CLINICAL OUTCOMES AND QUALITY OF LIFE IN CHILDREN WITH METHYLMALONIC ACIDAEMIA AND END-STAGE KIDNEY DISEASE; A PROMISING FUTURE

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Background: Methylmalonic Acidaemia (MMA) is characterised by accumulation of methylmalonic acid in body tissues due to defects in Methylmalonyl-Coenzyme (CoA) mutase or Cobalamin (Vit B12). It leads to end stage kidney disease (ESKD) and severe neurological deficits. To minimize disease-related complications and improve quality of life, isolated Kidney (KT), Liver (LT) or Combined Liver-Kidney Transplantation (CLKT) can be considered. This is the first study reporting correlation of these transplant strategies on quality of life (QoL) and clinical outcomes.
Methods: This single centre, retrospective observational study, evaluated the clinical outcomes and QoL of children with MMA and ESKD, comparing transplanted and non-transplanted patients from 2015 onwards. Percentage change in serum MMA, Creatinine and e-GFR were analysed using IBM SPSS software. Statistical significance was considered at 95% confidence level ($p<0.05$). Mann Whitney U test was used to compare current clinical outcomes and QoL between transplanted and non-transplanted groups. Validated PedsQL Transplant Module and End Stage Renal Disease Module questionnaires were used. Scores were calculated and compared using a scale from 0 to 100, with higher values representing better QoL.
Results: This study included 5 girls and 4 boys with MMA; median age of 10 years. Transplantation was performed in 6 out of 9 children (2 KT, 2 LT, 2 CLKT); median age of 6.5 years. A statistically significant difference in mean percentage reduction in serum MMA was observed between transplant and non-transplant groups (63.21% Vs 0.18%, $p<0.05$). In the transplantation subgroups, CLKT demonstrated the highest percentage reduction in serum MMA levels (93.32%), followed by LT (58.74%) and KT (37.58%). CLKT showed the highest percentage improvement in serum creatinine (71.43%). PedsQL mean score values of 75 and 74.7 were observed in non-transplanted patients and transplanted patients respectively.
Conclusions: Children with MMA and ESKD benefit from transplantation, with reduced MMA-levels post-transplant and subsequently reduced toxic effects on all organs. CLKT should be considered as the first choice type of transplant in children with established ESKD. Short term follow up identified no statistically significant improvement in QoL in this cohort.

P085 FUROSEMIDE ATTENUATES TUBULOINTERSTITIAL INJURY AND ALLOWS FUNCTIONAL TESTING OF PORCINE KIDNEYS DURING NORMOTHERMIC MACHINE PERFUSION

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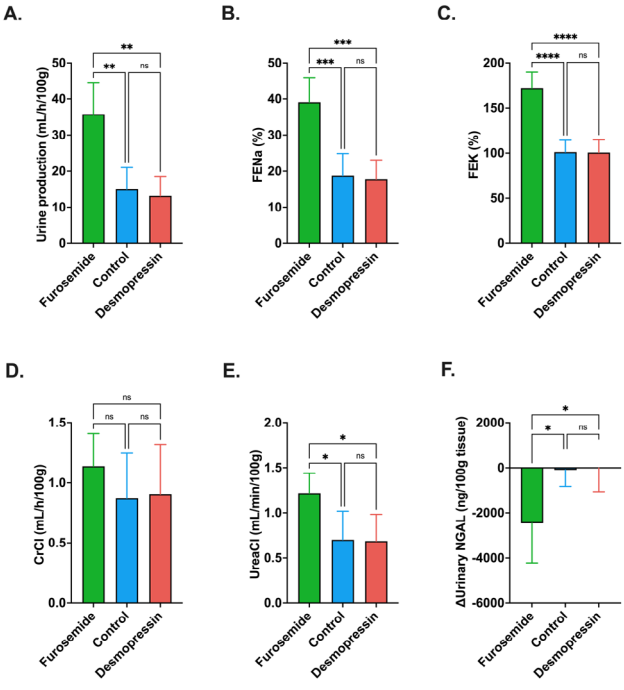
Background: Normothermic machine perfusion (NMP) is a promising pretransplant kidney quality assessment platform, but it remains of crucial importance to increase its diagnostic potential whilst ensuring minimal additional injury to the already damaged kidney. Interventions that alter tubular transport could influence renal function and injury during perfusion. This study aimed to determine whether furosemide and desmopressin can affect renal function and injury during NMP.
Methods: Eighteen viable porcine kidneys (n = 6 per group) sustained 30 min of warm ischemia and 3-5 hours of oxygenated hypothermic perfusion before being subjected to 6 hours NMP. Each organ was randomized to receive either no drug, furosemide (750 mg), or desmopressin (16 µg) during NMP.
Results: Compared to other groups, the addition of furosemide resulted in significantly increased urine output, fractional excretion of sodium and potassium, and urea clearance during NMP (Figure 1). Urinary neutrophil gelatinase-associated lipocalin levels decreased significantly with furosemide supplementation compared to other groups. The addition of desmopressin did not result in any significantly different outcome measurement compared to the control group.
Conclusions: This study suggests that adding furosemide could affect renal function while attenuating tubulointerstitial injury during NMP. Therefore, furosemide supplementation may provide renal protection and serve as a functional test for pretransplant kidney viability assessment during NMP.

Figure 1. Urine production (A), fractional excretion of sodium (B) and potassium (C), creatinine clearance (D), urea clearance (E), and delta urinary neutrophil gelatinase-associated lipocalin (F) during normothermic machine perfusion. Means and standard deviations are shown. Deltas are the differences between the end and the start of perfusion. CrCl, creatinine clearance; FEK, fractional potassium excretion; FENa, fractional sodium excretion; NGAL, neutrophil gelatinase-associated lipocalin; UreaCl, urea clearance. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001.



P086 REPROGRAMMING MITOCHONDRIAL METABOLISM TO REDUCE ORGAN TRANSPLANT ISCHEMIA REPERFUSION INJURY

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Background: Oxidative damage from ischemia/reperfusion injury (IRI) in organ transplantation is initiated by a burst of reactive oxygen species (ROS) generated by reverse electron transport (RET) in mitochondria. RET is driven by succinate dehydrogenase (SDH)-mediated oxidation of the mitochondrial metabolite succinate, which accumulates extensively in ischemic tissues. We use translational models of kidney transplantation to identify conserved metabolic changes between mice, pigs, and humans, and examine the efficacy and mechanism of protection afforded by inhibition of SDH by disodium malonate (DSM).
Methods: Mouse and pig kidney IRI (bilateral renal pedicle clamping) and pig and human *ex vivo* normothermic machine perfusion models were used to temporally quantify changes in succinate metabolism. Further mouse experiments examined key metabolic pathways and the impact of DSM treatment, through untargeted metabolomics analysis and bulk RNA sequencing.
Results: Kidney succinate metabolism was highly conserved between mice, pigs, and humans during IRI. DSM treatment prior to kidney IRI in mice inhibited complex II and was protective, reducing elevations in serum creatinine and oxidative markers. DSM treatment rapidly reprogrammed metabolism, reducing ROS generation upon reperfusion. Over-representation analysis of differentially expressed genes between untreated and DSM treated mice indicated global cellular changes including in the activity of the PI3k/Akt/mTOR, integrated stress response, and interleukin signalling pathways.
Conclusions: DSM not only ameliorates oxidative damage through inhibition of ROS production but may also pharmacologically precondition kidneys by rewiring their metabolism in a protective fashion. Whether these transcriptomic changes are solely attributable to DSM-mediated SDH inhibition is unclear, however these analyses identify key enzyme targets for further investigation. Together, these data increase our understanding of the mitochondrial mechanisms underpinning IRI and facilitate clinical translation of DSM as a safe and effective therapy in organ transplantation.

P087 A PROPOSED EXTENDED REALITY SYSTEM FOR SURGICAL PRACTICE AND TRAINING

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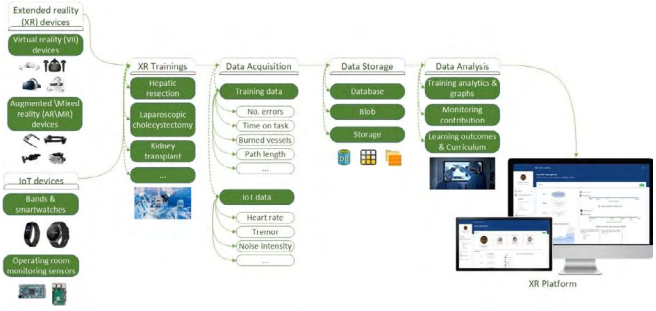
Background: Virtual reality (VR) technologies are rapidly developing, with a range of applications in gaming, educational purposes, and healthcare. In the field of healthcare, VR technologies are being used in surgical education and training, making it possible to explore surgical pathways and skills in a safe and cost-effective manner. They could act as a cognitive enhancers in the field of surgical education and practice, however, there is a lack of VR training in the field of organ transplantation.
Methods: A 5-layered system of low-cost XR devices (VR, AR, mixed reality and internet of things) is designed to foster surgical training, with a focus on co-designing and co-creating virtual and augmented surgical training. This system will facilitate the collection of data from heterogeneous sources, which will be uploaded on a cloud-based infrastructure and stored in a suitable database for analysis. Training analytics based on the analysis of the aforementioned data will offer an overview of the course and allow the user to evaluate the impact of stressors on their performance. Transplant surgical procedures, such as open and laparoscopic donor nephrectomy, are used as examples.
Results: The framework consists of five layers. The first layer includes low-cost VR and AR, IoT, and Arduino and Raspberry devices for data acquisition. The second layer focuses on co-designing and co-creating virtual and augmented surgical training. The third layer involves a big data acquisition system, along with an AI system, to assess the quality of surgical procedures. The fourth layer involves programming biosensors and uploading them to a cloud-based infrastructure. The fifth layer focuses on creating a platform that graphically presents training analytics and the course of surgeries, as well as analysing additional factors such as noise and fatigue to create new approaches to medical errors.
Conclusions: VR technologies in the field of healthcare have the potential to revolutionize surgical practice, providing a safe and cost-effective way to explore pathways and skills. With careful consideration and cost-effectiveness analysis, XR systems have the potential to revolutionize healthcare, providing a new way to ensure effective and safe procedures.



P088 KINETICS OF POST-TRANSPLANTATION DIABETES MELLITUS IN A LARGE COHORT OF KIDNEY TRANSPLANT PATIENTS

Julie Olabe[1], Bruno Pereira[2], Cyril Garrouste[3], Anne Elisabeth Heng[*3;4]

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Background: Kidney transplantation is the best treatment for End Stage Renal Disease (ESRD). However, post-transplant diabetes mellitus (PTDM) occurred in 15% of cases. To better prevent PTDM, we studied its prevalence at different time points, its dynamics of occurrence, and influencing factor.
Methods: We used data from the French national Astre database, including patients transplanted between 2008 and 2017. The occurrence of PTDM was defined by fasting blood glucose ≥1.26g/L or HbA1c ≥6.5% or the use of antidiabetic treatments. The remission of PTDM was defined by normal fasting blood glucose and HbA1c and no more need of antidiabetic treatments.
Results: the prevalence of PTDM among the 2898 transplants was 27.3% at 3 months (M3); 21.3% at 1 year; 19.8% at 2 years; and 19.9% at 3 years. The trajectory analysis used to study the dynamics changes was based on 1825 transplants and revealed 4 groups: 67% with no PTDM, 6% with late PTDM developed after M3, 10% with PTDM remission after M3, and 17% with early and persistent PTDM. Early and persistent PTDM was associated with higher BMI at transplantation time and lower rejection-free survival. Late PTDM was associated with a history of cardiovascular disease or higher BMI. Weight gain is associated with PTDM at 1 year. Corticosteroid are associated with early, persistent and late PTDM. Used or change immunosuppressive drug between tacrolimus and cyclosporine did not influence PTDM evolution.
Conclusions: This study confirmed the high prevalence of PTDM in post-renal transplantation and emphasized the importance of the first-year post-transplant, which seems to be decisive for the progression of PTDM to onset or remission. Corticosteroid use and weight gain before or after transplantation have to be restricted to avoid PTDM.

P089 JEJUNAL OR ILEAL EXOCRINE DRAINAGE IN PANCREAS TRANSPLANTATION? GASTROINTESTINAL IMPACT

Jaimee Tan[*1;2], Daniel Doherty[1;3], Robert Mcfarlane[3], Jennifer Kingston[1], Zia Moinuddin[1], Hussein Khambalia[1;3], Titus Augustine[1;3], David van Dellen[1;3]

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Background: Pancreas transplantation (PT) is performed for restoration of endocrine function in type 1 diabetes mellitus and amelioration of diabetic sequelae. However, PT can have serious complications requiring salvage pancreatectomy and surgical approaches should be carefully considered. Enteric anastomoses to jejunum or ileum are most often employed. We compare outcomes between these techniques.
Methods: A retrospective analysis of simultaneous pancreas and kidney transplant recipients (SPK) was performed at Manchester University Hospitals NHS Foundation Trust between 2013 and 2015. Follow up was completed until 2020.
Results: 86 SPK were performed. 59.2% were male with mean age of 41.5yo (SD±8.4). 72.4% (n=55) were donors after brain death and 98.7% (n=75) were receiving first PT. 43 SPK were performed with ileal anastomosis, 33 jejunal. There were no significant differences in demographics of recipients, donors, immunosuppression regimens, overall patient and graft survival or frequency of GI complications. Length of hospital stay was higher with ileal anastomosis (median 14 v 19 days, $p<0.05$), as was cold ischaemic time (median 8:48 v 9:31 hours, $p<0.05$). Salvage pancreatectomy and loop ileostomy formation was performed in the ileal group in three cases for graft pancreatitis with intra-abdominal sepsis, enteric anastomotic leak, and haemorrhage from mycotic aneurysm.
Conclusions: Long term outcomes between groups were comparable in this cohort. Catastrophic complications occur in the minority requiring salvage surgery. Here, more occurred with ileal anastomosis, but this allows graft pancreatectomy and formation of loop ileostomy, avoiding a more proximal stoma in a clinically unstable patient. Further powered studies are required to rigorously examine the impact of enteric anastomosis site.

P090 LONG-TERM RESULTS OF HEART TRANSPLANTATION IN RECIPIENTS WITH PRIMARY CARDIAC SARCOMA

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Background: Primary cardiac sarcoma is an aggressive cardiac tumor that is very rare in the general population. The only effective treatment is radical surgical removal of the malignancy. However, if sarcoma removal cannot be performed, orthotopic heart transplantation (OHT) becomes the only treatment option. Globally, such operations are performed in a small number and this is the lead reason of difficulties with postoperative curation of these patients. Our investigation presents the successful experience of OHT in recipient with cardiac sarcoma and ways of the treatment and postoperative care.
Methods: We have studied the clinical case of recipient with cardiac sarcoma about 340 ml in volume with myocardial infiltration and without metastasis. The diagnosis has been verified in 2021 by using CT-guided needle biopsy of the heart tumor. In 2021 the patient underwent bicaval OHT.
Results: On November 27, 2021, the patient underwent bicaval OHT, which proceeded typically. In this case, a triple immunosuppressive therapy was used, which included a combination of calcineurin inhibitors, antimetabolites, and corticosteroids. Heart transplant function was satisfactory. After discharge from the clinic, target therapy was initiated. Given the patient's history of cardiac sarcoma, immunosuppressive therapy was converted with exchange the antimetabolites on proliferation signal inhibitors regimen. According to control investigations, there was no evidence of graft dysfunction, the target values of the immunosuppressive drugs were achieved.
Conclusions: Cardiac sarcoma is one of the most rarely detected malignant heart tumors with the most aggressive course and unfavorable prognosis in patients. OHT is the only radical method of treatment in these patients. The OHT could be successful in these recipients, but the close observation and treatment selection are obligatory.

P091 HEALTH-RELATED QUALITY OF LIFE IN OLDER RECIPIENTS: THE BRIGHT SIGHT OF LIFE FIVE YEARS AFTER KIDNEY TRANSPLANTATION

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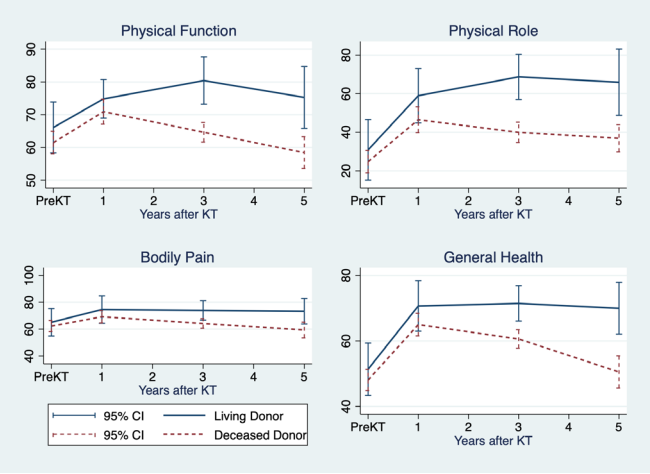
Background: In older patients with end-stage renal disease recent studies report similar long-term survival between receiving a kidney transplant (KT) or remaining on dialysis. Health-related quality of life (HRQOL) improves early after KT, but the long-term impact of KT on HRQOL in the elderly is not known. In a population of older recipients, we aimed to investigate the longitudinal HRQOL development from waitlisting until five years after KT.
Methods: Patients ≥ 65 years, who were enlisted for KT between January 2013 and November 2016 were included. Self-reported HRQOL was assessed using the Kidney-Disease Quality of Life Short Form version 1.3 (KDQOL-SF) survey. After enrolment, scores were obtained every 6 months until KT, with the last value representing baseline. Post-KT scores were obtained at 6 months and at 1-, 3- and 5-years. Linear mixed-effect models were used to detect HRQOL changes over time and to identify predictors of long-term HRQOL outcomes.
Results: Among 289 enrolled participants ≥ 65 years, 222 (77%) received a kidney transplant. By December 2022, 84 recipients had completed the five years follow up questionnaire. Mean age at time of answering the questionnaire was 76.2 years, 60 (71%) were males, and 22 (26%) received a living donor kidney. HRQOL substantially improved during the first year after KT, thereafter showed a decreasing trend at three and five years. At five years, the observed HRQOL benefit persisted for half of the generic, and kidney specific domains, compared to the pre-KT values. Recipients of living donor transplants experienced the most favorable outcomes and trended to improve in their HRQOL scores (Figure).
Conclusions: KT offers a long-term HRQOL benefit also in older recipients. Living donor transplantation is associated with a sustained HRQOL improvement and should be preferred, if possible.

Figure: Health-related quality of life development until 5 years after kidney transplantation. Comparison between recipients of living donor versus deceased donor transplants



P092 EFFECT OF BASILIXIMAB INDUCTION IN PEDIATRIC KIDNEY TRANSPLANTATION. A SYSTEMATIC REVIEW AND META-ANALYSIS

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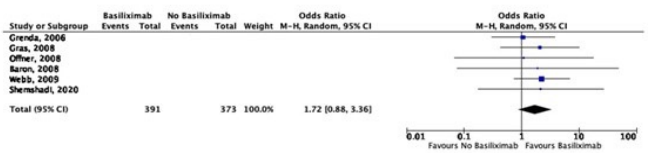
Background: Renal transplantation is the curative treatment for ESRD with significantly better outcomes than dialysis. In pediatric transplant recipients it is crucial to optimize immunosuppressive therapy to extend the graft lifespan and minimize harmful side effects from the regimen. Negative effects of high dose corticosteroid use in children are well known. Basiliximab is a monoclonal antibody used for immunosuppression induction in adults and decreases incidence of acute rejection, however its efficacy and safety in children is less well known. The aim of our study was to evaluate use of basiliximab immunosuppressive induction in pediatric kidney transplant recipients.
Methods: Medline, Embase, CENTRAL and Web of Science databases were searched. Risk of bias assessment was performed. Study was registered with PROSPERO.
Results: Our search identified 3003 papers; 7 papers were included in the study. Basiliximab had no effect on 1 year graft survival (fig.1) OR: 1.72 (95% CI: 0.88, 3.36), chronic graft rejection OR: 0.99 (95% CI: 0.61, 1.62), post-transplant lymphoproliferative disorder (PTLD) incidence OR: 0.69 (95% CI: 0.29, 1.66). The systematic review found comparable recipient survival rates, serum creatinine concentrations and viral infection incidences in patients treated with and without basiliximab.
Conclusions: No statistical benefit was found in patients using basiliximab. However, the current evidence on basiliximab is limited and further studies are needed as a possible benefit in graft survival and decrease in PTLD may exist.

Figure 1: Basiliximab vs No Basiliximab 1-year graft survival



P093 OPTIMAL TACROLIMUS LEVELS FOR PREVENTING MALIGNANCY AS WELL AS GRAFT FAILURE IN KIDNEY TRANSPLANT PATIENTS

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Background: Tacrolimus is the main immunosuppressant in kidney transplantation (KT) patients. Too low tacrolimus levels increase risk for rejection and graft failure, whereas too high tacrolimus levels could increase risk for malignancy. We aimed to determine balanced tacrolimus levels for preventing malignancy as well as graft failure.
Methods: This single-center study analyzed 1,616 adult KT patients that used tacrolimus-based immunosuppression between 1979 and 2017. We calculated mean tacrolimus trough concentration between the first 6th month and 1 year after KT and investigated association of tacrolimus levels with malignancy and death-censored graft failure using Cox regression analysis.
Results: Overall, malignancy occurred in 120 (7.4%) KT patients. Tacrolimus levels ≥ 7.0 ng/mL had a higher risk for malignancy compared to tacrolimus level < 5.5 ng/mL (Hazard ratio [HR] 1.899, 95% confidence interval [CI] 1.015-3.517) and tacrolimus level between 5.5 and 7.0 ng/mL (HR 2.324, 95% CI 1.150-4.697). However, there was no difference in risk for malignancy between the low tacrolimus group (<5.5) and the intermediate tacrolimus group (5.5 ≤ < 7.0). Graft failure occurred in 248 (15.3%) KT patients. Tacrolimus levels < 5.5 had a higher risk for graft failure compared to tacrolimus levels ≥ 7.0 (HR 0.661, 95% CI 0.468-0.935) and tacrolimus levels between 5.5 and 7.0 (HR 0.609, 95% CI 0.390-0.950). However, there was no difference in risk for graft failure between the high tacrolimus group (≥ 7.0) and the intermediate tacrolimus group (5.5 ≤ < 7.0). Low tacrolimus level < 5.5 increased graft failure risk, whereas high tacrolimus level ≥ 7.0 increased malignancy risk. To minimize risk of malignancy and graft failure simultaneously, the intermediate tacrolimus levels (5.5 ≤ < 7.0) seemed to be balanced target. In parallel, the intermediate tacrolimus group had a tendency of lower risk for mortality compared to both the low tacrolimus group (HR 0.442, 95% CI 0.159-1.229) and the high tacrolimus group (HR 0.556, 95% CI 0.283-1.094), although there was no statistical significance.
Conclusions: Tacrolimus levels between 5.5 and 7.0 is the optimal level between 6 months and 1 year after KT to minimize risk of both malignancy and graft failure.

P094 CHALLENGES EXPERIENCED BY ADULT LIVER DONORS AFTER LIVING DONOR LIVER TRANSPLANTATION: AN INTEGRATIVE REVIEW

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Background: Living donor liver transplantation (LDLT) is a complex experience that can challenge health and quality of life of donors. With the growing demands to LDLT worldwide, it is timely to review the current state of knowledge regarding challenges and experiences of the living donors following LDLT. Therefore, this integrative review aimed to describe challenges experienced by living donors following LDLT.
Methods: Using Whittemore and Knafl's methods, we searched 5 databases (Pubmed, Embase, Web of Science, CINAHL, PsycINFO) to identify studies that explored post-LDLT experience of living donors. Inclusion criteria were studies (1) relevant to post-transplant phase of the adult-to-adult LDLT; (2) published in peer-reviewed journals; (3) written in English; and (4) presented one or more of the following variables: (a) psychological outcomes (e.g., anxiety), (b) physical outcomes (e.g., pain), (c) social outcomes (e.g., employment), or (d) needs (e.g., information needs). Study findings were further synthesized using a qualitative-led synthesis.
Results: Of 1171 articles, 26 studies were included for review (21 quantitative and 5 qualitative studies). Living donors reported varying challenges to their physical and mental health, which were beyond the challenge of post-surgical complications (e.g., wound infection). Identified challenges were fatigue, anxiety, depression, altered body image, changes in employment/income, relationship with recipients, etc. Major factors associated with these challenges were recipients' health outcomes and uncertain prospects for donor's own health.
Conclusions: Findings of this review highlight the current state of the science in physical and psychosocial challenges of living donors after LDLT. Future studies are warranted with more robust methods, such as longitudinal cohort studies, to enhance understanding and supports for living liver donors, a growing but under-researched population.
Keywords: Living donors, Liver transplantation, Adult, Physical, Psychosocial, post-transplant outcomes

P095 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: IS THERE A CURATIVE TREATMENT FOR DISSEMINATED RECURRENCE?

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Background: Liver transplantation (LT) is the best treatment in selected patients with both cirrhosis and hepatocellular carcinoma (HCC). Despite strict adherence to accepted selection criteria for transplantation, HCC still recurs in 6-18% of patients post LT, and it is associated with significantly lower survival in these patients compared to those without recurrence. Currently, the clinical management of HCC recurrence is challenging as standardized protocols for post-LT surveillance and consensus treatment guidelines are lacking.
Methods: A retrospective observational study was carried out on patients undergoing LT for cirrhosis and HCC between January 2010 and December 2022, selecting patients with recurrence of the HCC.
Results: 117 patients were transplanted for HCC, all with subsidiary liver cirrhosis. The most frequent cause of cirrhosis was enolism (40.4 %). During follow-up, 4 patients (3.41%) developed recurrence of hepatocarcinoma. The mean age of the 4 relapsed patients was 58.8 ± 6.4 years. Two were male (50%) and two were female (50%). All recurrent patients were included for LT according to the Milan criteria. Average time from HCC diagnosis to transplant was 12.43 ± 5.52 months. In this period, 100% of the patients received adjuvant treatment. The surgery was uneventful in all cases. The median time from LT to HCC recurrence was 17 months (ICR 14 - 37.5). During this time, 2 patients had acute graft rejection and were treated with corticosteroid therapy and increased doses of immunosuppression. All cases were presented as disseminated peritoneal disease. No significant differences were found in terms of tumour marker values at the time of transplantation and at the time of recurrence. As for the treatment of recurrence, two cases were treated palliatively and died within two months due to rapid progression. Two patients remain alive on systemic treatment with tyrosine kinase inhibitors (sorafenib), one of them with tumour progression and the other with stable disease.
Conclusions: There is a clear benefit in terms of survival with the current criteria for candidate selection, although the recurrence rate is not negligible and its treatment is still a challenge. So far, the goal for disseminate recurrence is to prolong survival and treatment is for palliative intent, rather than pursuit of cure.

P096 SELF-MANAGEMENT ASPECTS IN ADULTS AFTER SOLID ORGAN TRANSPLANTATION: A SCOPING REVIEW

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Background: Solid Organ Transplant (SOTx) recipients face lifestyle changes beyond adherence to a medical regimen requiring adequate self-management (SM). Specific post-transplant SM is complex and may differ from other chronic diseases. Due to inadequate knowledge and skills, many recipients experience challenges in diverse life areas that make it difficult to carry out necessary SM tasks and to cope with the new situation. To date, there has been no overview or clear conceptualization of SM across all SOTx types thus hindering a more holistic SM support specifically for SOTx recipients. Therefore, we aimed to synthesise evidence on *aspects* of SM for adults after SOTx to develop a comprehensive conceptualization.
Methods: A scoping review of international scientific literature published in English and German was conducted. Following piloting, six databases (without date limits) and three study registers were searched to September 2021. Searches were supplemented by hand searches, reference checking, and expert recommendations. All types of scientific articles were included. Data were analysed descriptively and using qualitative content analysis via MAXQDA software in accordance to principles of framework synthesis based on an a-priori developed conceptual model.
Results: 34,045 records were identified. After screening of titles, abstracts and full-texts, data from 742 unique included publications were extracted. Bibliographic analysis indicated frequency of publications have risen since 2016, with kidney transplant as the most commonly researched organ type. Findings supported the underlying conceptual model domains of the medical regimen, managing emotions and adaptation of everyday-life. However, the nuances of the domains were extended significantly. For example, authors identified several new tasks and competences, including adapting to a new normality or internal strategies.
Conclusions: Scoping review findings demonstrate depth and breadth of existing data specific to SOTx recipients and SM aspects. Findings may improve the understanding of the concept of SM after SOTx and inform future interventions recognising the complexity of tasks and necessary competences for recipients.

P097 HYPOTHERMIC OXYGENATED MACHINE PERFUSION IN EXTENDED CRITERIA DONORS, A SPANISH EXPERIENCE

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Background: In the Spanish scenario of high donation rate and short waiting list, introduction of new graft preservation strategies is controversial. We present our experience with D-HOPE (dual hypothermic oxygenated perfusion) protocol for ECD (extended criteria donors) since October 2021.
Methods: We present a retrospective descriptive study of the use of hypothermic liver machine perfusion in the period between October 2021-October 2022. Indications: 1 ECD: DCD (death cardiac donors) or DBD (brain death donors): age over 65 years, BMI (body mass index) over 30Kg/m^2, UCI (intensive care unit) more than 7 days, Sodium 155 mmol/l, liver enzimas (AST 150 UI/ml, ALT 170 UI/ml), cardiac arrest, macrovesicular steatosis (biopsy) 30%
2 Prolonged hepatectomy**.** We reproduce a usual technique for organ procurement, static cold storage for transport and backtable surgery, with posterior connection to the perfusion system, with a goal of perfusion time of 2 hours.
Results: We transplanted 7 patients with livers from 7 brain death donors with median age of 81 years. Recipient characteristics: median age 63, BMI 25, MELD-Na 19, preoperative portal vein thrombosis 2/7 (28%). Transplant duration 395 minutes; cold ischaemia time including D-HOPE 400 min; all cavectomy technique (no piggy-back), no portocaval shunt, no Kehr drain. No PNF (primary non function). Median postoperative ICU stay 6 days, length of stay 33 days. Peak ALT 614 U/L, AST 535 U/L, INR 7th day 1,25. 2 reoperations because of postoperative arterial thrombosis: one biliary anastomotic stricture with NAS in one of them.
Conclusions: The technique is feasible; the principal drawbacks are that one member of the surgeon team must prepare the device before the arrival of the organ and the implantation surgery can be delayed one hour. The results observed show the complications of liver transplantation technique, none of them attributable to the perfusion procedure. Older donors may have more atherosclerosis and in our recipients more arterial thrombosis, related with problems in arterial suture. It´s important the assessment of the organ in the retrieval and a good matching donor-recipient to avoid complications. We need more experience to have statistically significant data.

P098 ORGAN DONATION IN PATIENTS ON VENOARTERIAL ECMO SUPPORT - SINGLE CENTER EXPERIENCE

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Background: The use of extracorporeal membrane oxygenation (ECMO) has been increasing in past years. Anyhow, the mortality of these patients remains high. These patients entity could represent a significant source of organ donors. We have focused on the subgroup of ECMO cardiopulmonary resuscitation patients considered as brain dead donors (DBD).
Methods: We have retrospectively analysed the organ donors treated with venoarterial VA ECMO fulfilling the criteria of brain death in years 2018-2022. The donor characteristics, AKIN stage and time on VA ECMO is reported. The kidney transplant function was evaluated in terms of presence of delayed graft function (DGF), and glomerular filtration rate (GFR) in 3 months, 1 year and 3 years after transplantation.
Results: In the period of 2018 to 2022 7 DBD donors on VA ECMO (8% of total 84 DBD donors). Acute kidney injury was present in 4/7 donors. Average time on VA ECMO support was 44 hours. Over all 12 kidneys and 1 liver were transplanted (2 kidneys were discarded because of donor renal cell carcinoma). DGF was present in 4/12 recipients (33%). No graft failure was reported during a follow up. In 10 transplant recipients 3 year follow up was completed. The mean GFR in 3 months, 1 year and 3 years after transplantation was 57±13 ml/min; 62±15 ml/min and 65±17 ml/min respectively.
Conclusions: Kidney donation in donors on venoarterial ECMO is safe and does not affect the outcome in terms of graft survival eventhough the incidence of AKI is increased in this donor group.

P099 CLINICAL PERFORMANCE OF THE IPREDICTLIVING TOOL FOR THE PREDICTION OF POST-TRANSPLANT RECIPIENT AND LIVING DONOR OUTCOMES IN A EUROPEAN COHORT

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Background: A living donor kidney transplant (LDKT) is the preferred treatment for ESRD. The application of statistical models that could predict graft and patient survival following LDKT is attractive and could guide informed consent. A prediction tool based on clinical and demographic data available pre-KT was developed in a Norwegian cohort with three different models to predict a) graft loss up to 10 years after KT (C statistic of 0,66), b) recipient (R) death within 10 years (C statistic of 0,77), c) donor (D) candidate's risk of death within 20 years after donation (C statistic of 0,81). No external validations are yet available.
Methods: We evaluated the predictive performance of the iPREDICTLIVING tool in our cohort of LKDT, submitted to KT from 1998 to 2019. The discriminative and calibration performance of the models were evaluated considering the Harrel C-statistic and time-dependent ROC analysis and the calibration slope. The outcomes of interest were censored graft failure (CGF), the R and D death.
Results: A total of 352 pairs were included in the study (Tab1). Observed censored graft (CG) loss and R death were, respectively, 2 (CI 1-5)% and 0.3 (0-2.2)% at 5 years and 14 (10-20)% and 4 (2-8)% at 10 years. The predicted CGF at 10 years was 12.3% (IQR 8.7-18.1), and R death at 10 Y was 6.8 % (IQR 3.5-13.9). Observed D death at 10 and 20 years was 3 (1-7) and 4 (2-9)%. The predicted D death was 0.2 (0.1-0.5) % at 10 years and 1.4 (0.6-3.1) % at 20 years. The model for CG loss showed the worse discriminative performance with Harrell C of 0.663, and a time-dependent AUC of 0.566, with a slope of 1.004. For R death, at 10 years, the model had a Harrell C of 0.776, and AUC 0.773, slope 0.994. The models for D death were reasonably discriminative, although with a poor calibration, particularly for 20 years death with a Harrell C of 0.711, and AUC of 0.694 with a slope 0.981. (fig1).
Conclusions: These tools have moderate discriminative and calibration performance in our population, especially for the CGF model, which also had worse discrimination in the original model. This may represent the unneglectable effect of recipient factors on graft outcomes. Albeit that, the tool was successfully validated in our cohort. It can improve the informed decision-making process at the living donor consultation, joining clinical and other relevant information.
Table 1.

Characterization of the study population	Total N=352
Donor	
Age, mean±SD	46.8±10.7
Age>50, n (%)	143 (41)
Female R, n (%)	244 (69)
Total cholesterol, median (IQR)	194 (170-218)
Smoking habits n (%)	56 (16)
Serum creatinine, median (IQR)	0.72 (0.64-0.88)
eGFR, mean±SD	100.5±14.8
Donor death, n (%)	6 (2)
Years of follow-up (donor), median (IQR) [Min-Max]	7.1 (4.2-11.8) [0.3-30.9]
Recipient	
Age, mean±SD	40.4±13.6
Female R, n (%)	117 (33)
Years on dialysis, median (IQR)	1.2 (0.3-2.6)
Vintage, n (%)	
Preemptive	69 (20)
HD	203 (58)
PD	80 (23)
Cardiovascular D, n (%)	26 (7)
Cerebrovascular D, n (%)	5 (1)
Peripheral vascular D, n (%)	3 (1)
CKD etiology, n (%)	
Diabetes	9 (3)
GN	163 (46)
Vascular	8 (2)
Other	172 (49)
Transplant	
Transplant year	2013 (2009-2016)
MM A, mean±SD	0.90±0.66
MM B, mean±SD	1.13±0.69
MM DR, mean±SD	0.97±0.68
Years of follow-up (graft), median (IQR) [Min-Max]	7.5 (4.9-11.4) [2.1-22.3]
Years of follow-up (recipient), median (IQR) [Min-Max]	8.1 (5.1-12.7) [2.1-22.3]
Post-transplant outcomes	
Overall graft failure, n (%)	55 (16)
Censored graft failure, n (%)	44 (13)
Recipient death, n (%)**Not censored at graft failure	17 (5)

Figure 1
Measures of performance of iPREDICTLIVING tool

	Discrimination		Calibration	Time-dependent ROC		
iPREDICTLIVING tool	AUC Harrell C	Explained variation %	Slope	AUC	Optimal cutoff (youden)	Sensitivity (%) Specificity (%)
Model a) Predicted censored failure graft 10-years (%)	0.663	8.6	1.004	*0.566*	18.6	41 79
Model b) Predicted failure recipient 10-years (%)	0.776	16.7	0.994	0.773	8.3	94 62
Model c) Predicted failure donor 10-years (%)	0.697	25.1	*0.984*	0.636	0.1	100 30
Model c) Predicted failure donor 20-years (%)	*0.711*	22.9	0.981	*0.694*	3.1	*64* *77*

P100 'WALKING IS FUN BUT WALKING TOGETHER IS EVEN MORE FUN': AN EVALUATION OF THE WALK&TALK PROGRAM IN THE NETHERLANDS

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Background: In 2019, the first Walk&Talk group was established in the Netherlands. Walk&Talk is a physical intervention for and organized by transplant recipients (TRs). The aim of Walk&Talk is to promote physical activity and peer support among TRs and their significant others. Upon request, transplant professionals can join. Walk&Talk is financially supported by Chiesi Pharmaceuticals. The aim of this study was to evaluate the development of the Walk&Talk program, the satisfaction of Walk&Talk participants, and its effect on wellbeing.
Methods: A mixed-methods study was performed among Walk&Talk participants using a brief survey (n=38) after each walk and semi-structured interviews with ten participants (summer 2022). Data were analysed using descriptive statistics and content analysis.
Results: Seven Walk&Talk groups have been established since the start of the program. Each group organizes a monthly walk of about one hour. Although most groups consist of a total of 20 participants, five to ten participants are present at each Walk&Talk. Some TRs were joined by a significant other, most often their partner. Coordinators (n=4) were motivated to take this role because they wanted to promote physical activity among TRs. Participants (n=6) mainly wanted to get in touch with other TRs and/or their partners. Overall, participants were satisfied with the frequency, duration, and intensity of the walk. Although transplant professionals did not join the walks frequently, participants appreciated their presence when they did as this setting made them feel more comfortable discussing personal, transplant-related problems. Regarding the effect of Walk&Talk on wellbeing, participants indicated that the program helped them to get in touch with other TRs and their significant others. By talking to their peers, they felt heard and experienced a strong feeling of mutual understanding. This helped them process the transplant experience, which consequently made them feel stronger mentally. As most participants were already physically active, only a few participants indicated that it improved their physical fitness.
Conclusions: Walk&Talk is an easy-to-start physical intervention for TRs and their significant others that enhances peer support, which may have a positive effect on their psychosocial wellbeing.

P101 BROADENING CRITERIA FOR DONOR LIVERS: SUCCESSFUL LIVER TRANSPLANTATION OF TWO DONOR LIVERS WITH PORTAL VENOUS GAS

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Background: Maximising the utilisation of the deceased donor organ resource for liver transplantation (LT) is critical. Portal pyaemia, evidenced by the presence of portal venous gas (PVG), is typically associated with intestinal ischaemia and is generally a harbinger of poor outcome. Donor PVG is traditionally a contraindication to transplantation.
Methods: We present two cases of successful LT utilizing donor livers with pre-transplantation findings of PVG.
Results: Both cases were brainstem death donors having experienced a preceding cardiac arrest. CT scans demonstrated gastric ischaemia and PVG. Donor 2 had evidence of ischaemic hepatitis that improved over time. Neither donor showed signs of uncontrolled infection at the time of organ offer. At organ retrieval there was no evidence of ischaemia on evaluation the liver and entire gastrointestinal tract. The donors had routine broad spectrum antibiotics prior to donation. The retrieval was uncomplicated with blood washed from the organs with UW solution, including back table PV flush as routine. Recipient 1 was a 42-year-old woman with autoimmune hepatitis, and recipient 2 a 54-year-old woman with non-alcoholic steatohepatitis. Both recipients recovered well post-operatively with no infective complications. Recipient 1 was found to have a cystic duct stump leak, which was treated with good effect with an ERCP and stent. At 90-day follow-up, both were clinically well with additional no complications.
Conclusions: Our patients are the first reported cases of successful LT using donors with PVG. With careful evaluation, donors with PVG can be used for LT and that this can prevent underutilisation of the donor resource.

P102 IMPACT OF HEMOADSORPTION ON PHARMACOKINETICS OF IMMUNOSUPPRESSIVE DRUGS IN A SHEEP MODEL

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Background: Potential removal of immunosuppressant drugs (ID) during extracorporeal hemoadsorption in organ transplantation patients may have important clinical implications. The current study aimed to investigate the impact of extracorporeal hemoadsorption on the pharmacokinetics (PK) of ID in a sheep model.
Methods: Healthy sheep were administered seven different ID (tacrolimus (TAC), ciclosporin A (CYA), mycophenolate mofetil (MMF), everolimus (EVER), basiliximab (BAS), methylprednisolone (MP) and prednisolone (PRE) in clinically relevant doses and combinations. Animals were treated either with CytoSorb® hemoadsorption (intervention group, n=5), or a sham extracorporeal circuit (control group, n=3). Blood samples for PK measurements were collected over the treatment period of six hours in both groups. In the intervention group samples were collected pre (inlet) and post (outlet) adsorber. Additionally, for TAC, CYA, EVER, MMF and MP a population pharmacokinetic analysis (NONMEM® 7.5) was performed to investigate the adsorption characteristics.
Results: For PRE and BAS negligible clearance was observed in pre- versus post adsorber measurements. For all other substances a saturable adsorption submodel with linear decrease of the adsorption effect over the adsorbed amount best described the measured data. Calculated maximum absolute adsorbed amounts (95 % confidence interval) for TAC, CYA, MMF, EVER and MP were 0.040 (0.028 - 0.053), 1.15 (0.39 – 1.91), 4.17 (2.00 – 6.35), 0.0163 (0.007 – 0.026), 53.4 mg (20.9 – 85.9), respectively. This equals an adsorption of less than 5% of the daily administered dosages for all tested substances.
Conclusions: In this large animal model, CytoSorb® hemoadsorption had very limited effect on the clearance of ID. These findings provide reassuring information for the safe use of the device in patients receiving ID and may be further complemented by therapeutic drug monitoring according to clinical judgment.

P103 "YOU CAN LEARN FROM EACH OTHER... AND GROW": EXPERIENCES OF ADOLESCENT THORACIC TRANSPLANT RECIPIENTS PARTICIPATING IN THE IPEER-2PEER MENTORSHIP PROGRAM

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Background: Adolescent thoracic transplant (Tx) recipients require life-long medical management and are at increased risk of psychological distress, social isolation and impaired social and cognitive functioning compared to healthy peers. This is concerning as adolescent recipients are undergoing critical developments in their identity and independence as they prepare to transition to adult care. iPeer2Peer (iP2P) is an established online support mentorship program enabling trained young adult mentors to provide modelling and reinforcement to adolescent mentees with the same chronic illness. This study assessed the experiences and perspectives of adolescent thoracic Tx mentees participating in the program.
Methods: The iP2P program in thoracic Tx was piloted at two Canadian pediatric Tx centers. Adolescent mentees (12-17 years old) who received a heart or lung Tx were matched one-to-one with trained mentors (18-25 years old) who were successfully managing their Tx. Mentee-mentor pairs connected virtually over 15 weeks through video calls and text messaging. A qualitative descriptive approach was used and individual interviews were conducted with mentees following the iP2P program. Interviews were audio recorded, transcribed verbatim and subject to thematic and content analysis.
Results: Mentee participants included 13 heart and 2 lung Tx recipients (median age: 15 years old) with diverse gender and ethnic backgrounds. Three themes emerged: (1) Seeking a sense of normalcy in personal Tx journey, (2) Enabling meaning-making through reciprocal story sharing, and (3) Nurturing confidence and disease self-management skills. Mentees reported high satisfaction and engagement with the iP2P program, and all would recommend iP2P to other adolescent thoracic Tx recipients. *"It definitely helped me. I feel like if [other Tx recipients] had any troubles, it would definitely help them as well."*
Conclusions: The iP2P program is a promising intervention to improve quality of life for adolescent thoracic Tx recipients. Next steps involve examining the implementation effectiveness outcomes of the iP2P program and interviewing mentors to capture their perspectives. Findings will inform a future multi-centre randomized controlled trial evaluating the iP2P program across solid organ Tx clinical populations.

P104 IMPROVEMENT GAPS TO DEAL WITH THE SHORTAGE OF LUNGS FOR TRANSPLANTATION FROM A MIDDLE INCOME COUNTRY'S PERSPECTIVE

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Background: In Argentina 78% of the lung waiting list have been waiting longer than 1 year. During 202, only 5.9% of our actual donors were lung donors. Regardless of donation activity in Argentina, we have a clear problem on achieving the lung donation rates expected.
Methods: A cross-sectional study was performed using digital self-report surveys. Critical care specialists and transplant coordinators from different regions in Argentina were surveyed. The Surveys included questions directed to obtain information regarding donor management, selection criteria and resource availability that demonstrated an impact on increasing lung procurement. The objectives of the study were 1) To identify the potential causes for the low lung procurement rate in Argentina. 2) To develop strategies to the actual problems in the donor management focused on lung retrieval.
Results: From the total surveyed 23.7% do not use advanced haemodynamic monitoring. When using CVP to guide decisions only 35.8% consider maintaining a CVP lower than 10 mmHG during the maintenance. In donors with severe deterioration of the ejection fraction only 23.2% would use an advanced monitoring of the haemodynamic status to guide their fluids management. 27.8% of them would routinely use steroids in all their donors for improving lung function. 80.4% of the surveyed population consider they are using protective ventilation, but only 4.10% of them use it adequately. Recruitment manoeuvres were routinely used by only 3.1% of the surveyed. In a multivariate analysis on the variables analysed to study the expanded selection criteria (Age > 55 years, smoking habit > 20 paq/year, positive upper airway cultures, unspecific x-ray infiltrates and more than 72 hours of mechanical ventilation), 92.8% of the surveyed population would discard a patient with 1 of these expanded selection criteria without considering offering the lungs for donation.
Conclusions: The main opportunities for improvement seem to be: 1) Training the physicians involved in the donor's management in the management of potential lung donors seems to be a way of increasing the lung donor rates. 2) The donor selection criteria used should be reviewed together with the transplant teams in order to achieve an increase in the adherence to the expanded selection criteria.

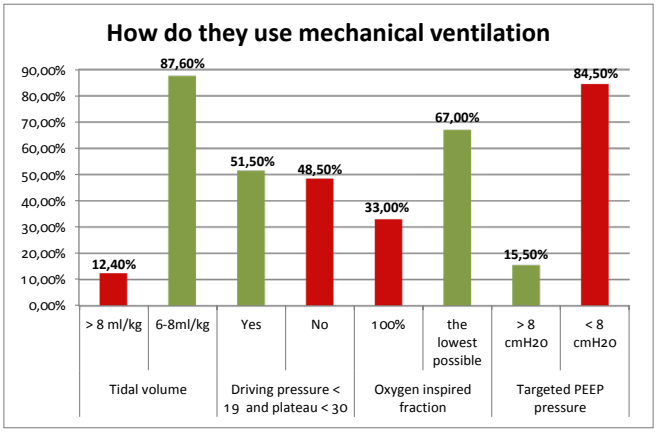

Table 1: Efficiency in considering expanded selection criteria

Amount of expanded criteria used	Frequency	Percentage of total responders	Accumulated percentage of total responders
0	2	2.1%	2.1%
1	2	2.1%	4.1%
2	16	16.5%	20.6%
3	38	39.5%	59.8%
4	32	33%	92.8%
5	7	7.2%	100%
Total	97	100%	

P105 "WE'VE ALL GONE THROUGH THE SAME JOURNEY": EFFECTIVENESS OF A MINDFULNESS-BASED RETREAT FOR MOTHERS OF PEDIATRIC HEART TRANSPLANT RECIPIENTS

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Background: Mothers of pediatric heart transplant (HTx) recipients are at high risk for psychosocial concerns and lower quality of life (QoL), which may impact familial, social and health outcomes. Mindfulness is proposed as an evidence-based intervention to support maternal coping, distress tolerance and QoL. This study investigated the implementation and preliminary effectiveness of a mindfulness-based retreat (MBR) for mothers of pediatric HTx recipients.
Methods: A two-day MBR was piloted with mothers of pediatric HTx recipients from a Canadian pediatric HTx center. Mindfulness-based practices were led by two trained facilitators and included formal meditation, deep relaxation and circle sharing. A convergent parallel mixed methods design was used for evaluation. Five standardized questionnaires assessing maternal coping, distress tolerance, perceived social support, QoL and mindfulness were completed 24 hours before the MBR (T1), immediately after the MBR (T2) and three months after the MBR (T3). Qualitative interviews exploring participants' experiences were conducted at T2 and T3. Quantitative and qualitative data were analyzed independently and then amalgamated to evaluate implementation and effectiveness outcomes.
Results: Sixteen mothers participated in the MBR held at a Canadian retreat centre. The MBR demonstrated high feasibility, fidelity and adoption, and participants reported high engagement and satisfaction with the intervention. Significant improvements were seen at T3 in participants' ability to be mindful in daily life, coping through maintaining family integration, and perceived social support from family members. Qualitative analysis illuminated three themes: (1) Respite – the significance of being immersed in a retreat environment, (2) Reflections – the value of learning mindfulness-based skills to build coping capacity, and (3) Relations – the importance of connecting and sharing stories with other mothers.

Conclusions: Results support the MBR as a feasible and effective intervention that improves maternal coping, social support and QoL, contributing to family-centred care in pediatric HTx. Findings inform future studies exploring the sustainability and transferability of the MBR for caregivers and family members affected by pediatric chronic illnesses.

P107 ADIPONECTIN / LEPTIN RATIO AS AN INDEX TO DETERMINE METABOLIC RISK IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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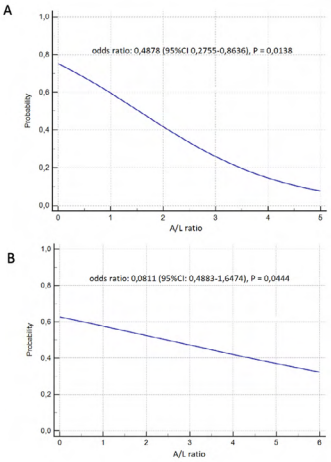
Background: It has been confirmed that adiponectin / leptin (A/L) ratio correlates better with cardiometabolic risk factors than hormone levels alone. The aim of our study was to determine the risk of developing post-transplant diabetes mellitus (PTDM) and other metabolic conditions depending on the A/L ratio after kidney transplantation (KT).
Methods: In the prospective analysis, studied sample of 104 patients was divided into three groups: 1. control group, 2. patients who developed a pre-diabetic condition after KT (impaired glucose tolerance, fasting hyperglycemia) and 3. patients who developed de novo PTDM. Pre-transplantation, at 3, 6 and 12 months after KT, we recorded basic characteristics of donor and recipient. We also monitored levels of adipocytokines and calculated A/L ratio.
Results: During observed period, we recorded significant increase in A/L ratio in control group (P=0.0013), on the contrary, a significant decrease in PTDM group (P=0.0003). Comparing the individual subgroups divided according to the values of the A/L ratio in 1 year after KT, we found that patients with an A/L ratio < 0.5 compared to those with a value > 1 were significantly longer in the dialysis program, had a higher body mass index, waist circumference, poorer graft function, higher proportion of prediabetes and PTDM in 1 year after KT. Using Cox regression Hazard model, we identified age at time of KT (HR 2.8226, P=0.0225), triglycerides at 1 year (HR 3.5735, P=0.0174) and A/L ratio < 0.5 as independent risk factors for prediabetes and PTDM 1-year post-transplant (HR 3.1724, P=0.0114).
Conclusions: This is the first study to evaluate the relationship between A/L ratio and the risk of PTDM and associated metabolic conditions after KT. We found out that A/L ratio < 0.5 is an independent risk factor for prediabetes and PTDM 1-year post-transplant.

Table 1. Cox regression Hazard model

end point: PTDM + prediabetes 1Y	Hazard ratio	95%CI	P value
men (%)	1,5297	0,6782-3,4502	0,3057
Age at the time of KT ≥ 50 years	**2,8226**	**1,1579-6,8804**	**0,0225**
Dialysis duration ≥ 24 months	1,4736	0,7008-3,0988	0,3066
BMI base line ≥ 30 kg/m²	1,3390	0,5315-3,3729	0,5358
BMI 1Y ≥ 30 kg/m²	0,9215	0,3288-2,5829	0,8765
Waist circumference 1Y (men > 94 cm, women > 80 cm)	1,2019	0,5328-2,7109	0,6577
C-peptide 1Y > 5,19 µg/l	1,2446	0,4905-3,1577	0,6451
IRI 1Y > 23 mU/l	0,8970	0,3413-2,3574	0,8255
cholesterol 1Y > 5,17 mmol/l	1,5615	0,6311-3,8633	0,9297
LDL 1Y > 3,88 mmol/l	0,8821	0,3000-2,5931	0,8196
HDL 1Y in men < 1.03, in women < 1.29 mmol/l	1,1066	0,4696-2,6077	0,8169
triglycerides 1Y > 1,7 mmol/l	**3,5735**	**1,2504-10,2128**	**0,0174**
A/L ratio < 0,5 base line	0,7633	0,2663-2,1880	0,6152
A/L ratio 0,5-1 base line	1,5126	0,5580-4,1000	0,4160
A/L ratio > 1 base line	0,4704	0,1776-1,2454	0,1290
A/L ratio < 0,5 1Y	**3,1724**	**1,2968-7,7610**	**0,0114**
A/L ratio 0,5-1 1Y	2,1176	0,9139-4,9071	0,0801
A/L ratio > 1 1Y	0,5488	0,1794-1,6781	0,2927
vitamin D 1Y < 30 µg/l	0,7691	0,3794-1,5591	0,4666
TAC value 1Y > 6 ng/ml	0,8068	0,3968-1,6404	0,5532

A/L – adiponectin / leptin, KT – kidney transplantation, BMI – body mass index, Y – year, M – month, IRI – immunoreactive insulin, LDL – low-density lipoprotein, HDL – high-density lipoprotein, TAC – tacrolimus, PTDM – post-transplant diabetes mellitus

Figure 1. The risk of developing prediabetes and PTDM depending on the A/L ratio A: baseline, B: 1 year after KT



P108 BLUEPRINTING EXTENDED REALITY AND TANGIBLE RESOURCES FOR SURGICAL EDUCATION; EXPERIENCES AND POTENTIALITIES FROM THE ENTICE PROJECT

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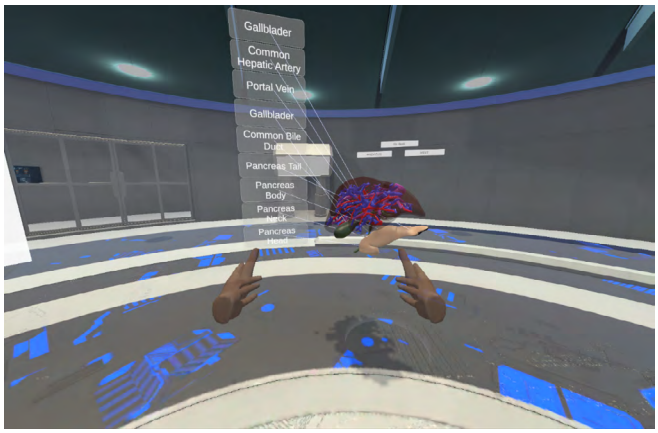
Background: Surgical training is an active learning process. Cognitive apprenticeships and team consultations prepare surgeons for operation. Virtual, augmented and mixed reality (VR/AR/MR – collectively XR) have found use in surgical training due to their active nature. Also, 3D printing has also been added to the arsenal of surgical training.
A core challenge in immersive media for healthcare training is the divide between the subject and the medium. Evidence demonstrate that XR resources may inhibit learning by distracting the learner, focusing on visuals instead of education. The goal of the Evaluating Novel Tangible & Intangible Co-creative Experiential (ENTICE) medical education project is to provide a platform of immersive XR technology where the educational goal maintains primacy.
Methods: Co-creative workshops with surgical anatomy experts and technologists developed the resource material. Strict adherence to AGILE methodologies developed 3 highly relevant XR and 3D printed resources of hepatic and surgical anatomy supporting specific learning objectives. A bespoke evaluation plan created the toolset for estimating educational efficacy and learner acceptance of the immersive modality for surgical anatomy education.
Results: Several insights have been recognized from the project's activities on design and implementation of immersive surgical resources. A) Participatory knowledge sharing, like cognitive apprenticeships, facilitates direct and tacit knowledge transfer. B) Predetermined educational content will always facilitate better training even with reduced impressiveness. The ability to pick-up an anatomical structure and manipulate it and sequencing of 3D models according to the lesson plan impact more than graphical fidelity. Evaluation of the platform by attending, residents and medical students was overall positive, based on interview evaluation.
Conclusions: The presented work blueprints a cohesive participatory process for XR and 3D print resource development. We aim to use and evolve this blueprint, creating a versatile portfolio of immersive XR and tangible resources, which will be helpful both in terms of educations, as well as surgical planning.

Fig. 1: A surgical education resource. The user manipulates objects in VR, to demonstrate important features.



P109 ADIPONECTIN / LEPTIN RATIO AS A PREDICTOR OF ACUTE REJECTION IN EARLY POST-TRANSPLANT PERIOD IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Background: Adipokines are largely involved in the regulation of immune system activity. While leptin is the main pro-inflammatory marker of adipose tissue, adiponectin is characterized by anti-inflammatory effects. The aim of our study was to determine the risk of acute graft rejection in protocol biopsy depending on the adiponectin / leptin (A/L) ratio in patients after kidney transplantation (KT).
Methods: 104 patients were included in the prospective analysis, in whom the levels of adipokines were examined pre-transplant, in the 3rd month after KT and the A/L ratio was calculated. In the 3rd month after KT, all patients underwent protocol biopsy of the graft and examination of donor-specific antibodies (DSA) using the Luminex method.
Results: After adjusting for differences in the basic characteristics of the donor and recipient, we identified a subgroup with A/L ratio < 0.5 pre-transplant [HR 1.6126, (P = 0.0133)] and 3 months after KT [HR 1.3150, (P = 0.0172)] as independent risk factor for acute graft rejection. In the subsequent specification of the rejection episode, we identified the risk ratio A/L < 0.5 before KT [HR 2.2353, (P = 0.0357)] and 3 months after KT [HR 3.0954, (P = 0.0237)] as independent risk factor for the development of antibody-mediated rejection with DSA positivity.
Conclusions: This is the first study to investigate the relationship between A/L ratio and immunological risk in terms of the development of rejection changes in patients after KT. In our study, we found that A/L ratio < 0.5 is an independent risk factor for the development of antibody-mediated rejection and de novo DSA production in the third month after KT.

Table 1. Cox proportional hazard model, end point: acute rejection in protocol graft biopsy

Rejection (ACR + AMR)	HR	95% CI	P
Hyper IL-6 base line	0.1795	0.0187-1.7247	0.1368
Hypo IL-10 base line	1.6744	0.2095-13.3851	0.6269
Adiponectin/Leptin ratio base line < 0,5	1.6126	1.3530-1.9798	**0.0133**
Adiponectin/Leptin ratio base line 0.5-1	1.3893	0.3730-2.5743	0.6240
Adiponectin/Leptin ratio base line > 1	1.1250	0.5455-2.3200	0.7499
Hyper IL-6 3M	0.2317	0.0224-2.3953	0.2198
Hypo IL-10 3M	1.7000	0.4252-6.7972	0.4530
Adiponectin/Leptin ratio 3M < 0.5	1.3150	1.0169-1.7094	**0.0172**
Adiponectin/Leptin ratio 3M > 1	1.3969	0.3751-5.2016	0.6183

ACR – acute cellular rejection; AMR – antibody-mediated rejection; IL – interleukin; M – month

* Hyper IL-6: IL-6 value > 7.5 pg/ml; Hypo IL-10: IL-10 value < 10 pg/ml

Table 2. Cox proportional hazard model, end point: antibody-mediated rejection in protocol graft biopsy

AMR	HR	95% CI	P
Hyper IL-6 base line	0.5386	0.0337 to 8.6109	0.6617
Hypo IL-10 base line	6.7241	4.8469-8.3160	0.9510
Adiponectin/Leptin ratio base line < 0.5	2.2353	1.4094-3.2031	**0.0357**
Adiponectin/Leptin ratio base line 0.5-1	0.8710	0.1593-4.7404	0.8689
Adiponectin/Leptin ratio base line > 1	0.9027	0.7939-1.6399	0.8570
Hyper IL-6 3M	0.4617	0.0289 to 7.3812	0.5847
Hypo IL-10 3M	0.2160	0.0252 to 1.8489	0.1618
Adiponectin/Leptin ratio 3M < 0.5	3.0954	1.9346 to 6.8478	**0.0237**
Adiponectin/Leptin ratio 3M 0.5-1	0.2724	0.0672-1.9113	0.9584

AMR – antibody-mediated rejection; IL – interleukin; M – month

* Hyper IL-6: IL-6 value > 7.5 pg/ml; Hypo IL-10: IL-10 value < 10 pg/ml

P110 ANTICOAGULATION DECREASE THE VENOUS THROMBOSIS IN KIDNEY TRANSPLANTATION FROM UNCONTROLLED DONATION AFTER CARDIAC ARREST WITH HIGH RESISTANCE INDEX

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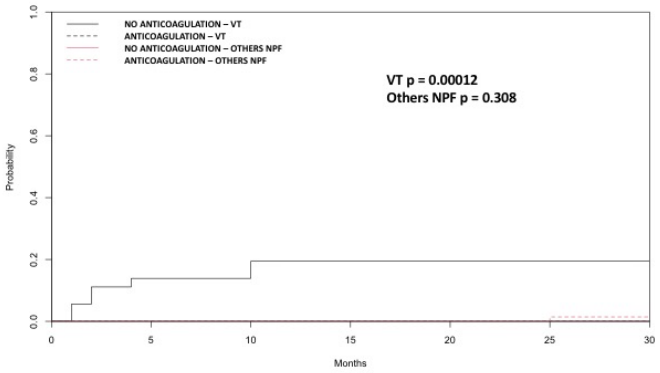
Background: Kidney transplantations (KT) from uncontrolled donation after cardiac death (uDCD) achieve very good outcomes to short and long follow-up, but the incidence of primary non function and venous thrombosis (VT) is very high. The resistance index (RI) after kidney transplantation increase in the VT cases and in other kidney diseases.
Methods: Unicentric retrospective cohorts study that included all KT from uDCD with RI ≥0.8 measured by ecodoppler in the first 72 hours post-transplantation. We compared one group who never received anticoagulation (Group I) and a second one who received prophylactic anticoagulation (Group II). The anticoagulation was performed with sodic heparin to achieve aPTT 1.5-2 time normal range and/or low molecular weight heparin adjusted to patient's weight and renal function. Aim: To describe the effect of prophylactic anticoagulation in KT from uDCD with RI 0.8 to avoid VT and their secondary's effect.
Results: We included 107 KT from uDCD with RI≥0.8, 36 belong to Group I and 71 belong to Group II. In Group I the donors were younger (39 ± 12 vs 46 ± 8; p=0.003) and there were more men donors (97.2% vs 81.7%; p=0.032). The prevalence of VT was higher in Group I (19.4% vs 0%; p<0.001). Patients in Group II needs more red blood transfusions (19.4% vs 39.4%; p=0.05) and had more macroscopic haematuria (5.6% vs 21.1%; p=0.049). The risk competitive analysis shown a higher probability to develop a VT in non-anticoagulation group (p=0.00012) than anticoagulation group or other causes of primary non function (Graphic).
Conclusions: The prophylactic anticoagulation treatment in KT from uDCD with RI≥0.8 decrease the VT incidence and it is safe also donor as recipient.



P111 A PERSISTENT LEFT SUPERIOR VENA CAVA IN A PATIENT WITH RIGHT SUPERIOR VENA CAVA THROMBOSIS UNDERGOING EMERGENCY LT

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Background: Persistent left superior vena cava (PLSVC) is the most common congenital thoracic venous anomaly. It is usually found incidentally on examination or during invasive procedures. In most cases, the blood flows back to the right atrium through the coronary sinus without hemodynamic abnormalities and it is usually asymptomatic. There is some controversy regarding the clinical use of PLSVC. In a few cases, a PLSVC has been used for hemodialysis or large bore intravenous access.
Case report: A 62-year-old woman with a previous hepatectomy for hepatocellular carcinoma and liver cirrhosis developed hepatic failure. Owing to her worsening condition, she needed liver transplantation (LT). However, a superior vena cava thrombus was found between the right atrium and proximal superior vena cava on preoperative transesophageal echocardiography. Usually, right-sided central venous catheterization is performed for LT preparation, but the embolic risk was very high in our patient. Fortunately, she had already been diagnosed with PLSVC. Therefore, we decided to perform fluoroscopy-guided catheterization through the PLSVC. For the safe use of a PLSVC catheter during surgery, the rapid infusion system pressure, coronary sinus inflow pressure, and intraoperative transesophageal echocardiography were monitored. The patient successfully underwent LT.
Conclusions: Based on a literature review and this case, PLSVC can be used clinically when accompanied by a detailed history, preoperative imaging examination, and close intraoperative monitoring. We suggest that a PLSVC is a feasible alternative to central venous access for LT.

P112 MULTIPLE ARTERY ANASTOMOSIS IN KIDNEY TRANSPLANTATION ; INTERNAL ILIAC ARTERY INTERPOSITION GRAFT

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Background: Anastomosis of multiple renal arteries in kidney transplantation is technically demanding. Previously this condition was considered a relative contraindication to use of the donor, due to an increased risk of vascular and urologic complications.
Methods: Between August 1990 and December 2022, we have performed 736 renal transplants, among which 116 patients(15.8%) of the multiple donor arteries were encountered and total 126 cases of procedure was done. We reviewed these cases for the type of vascular reconstruction and outcome of 16 interposition graft cases using branched internal iliac artery.
Results: The type of reconstruction were illustrated as follows ; ligation of an upper polar artery in 38 cases, double barrel anastomosis in 42 cases, end to side anastomosis between a polar artery and main renal artery in 14 cases, separate anastomosis of two renal arteries to the branch of the internal iliac artery in 1 case, use of the inferior epigastric artery of the recipient for end to end anastomosis to lower polar artery in 15 cases, interposition graft using branched internal iliac artery in 16 cases. We reviewed the 16 cases of the internal iliac artery interposition. Anastomosis between donor renal artery and recipient's interposed internal iliac artery was done at bench extracorporeal technique. By use of this technique, warm ischemic time was not prolonged and postoperative course was good without vascular and urologic complications
Conclusions: Our method enables to select an appropriate recipient's interposed arterial branch to be anastomosed that is compatible with donor's multiple renal artery and is easy to perform. Anastomotic arterial pseudoaneurysm formation or rupture is thought to be possibly low compared with that of the double barrel anastomosis. And multiple arterial anastomosis are conducted in cold extracorporeal environment and a simple end to end arterial anastomosis is done in recipient's body. This technique would reduced warm ischemic time, therefore renal damage could be diminished

P113 USE OF NATIVE URETER (NU) IN RE-INTERVENTIONS AFTER KIDNEY TRANSPLANTATION (KTX)

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Background: Early and late term urinary obstruction after KTX is reported to be up to 2-10%. When non-invasive methods fail to re-establish the continuity of urine flow, utilization of NU as a conduit is an effective option when the graft ureter quality is severely disturbed.
Methods: Following local Ethical Committee approval, patients who experienced urinary obstruction after KTX from either cadaveric or living donors were retrospectively analysed. All patients received induction immunosuppression followed by maintenance suppression. In case of suspected urinary obstruction, ultrasound exam, DMSA scan, CT scan or MR urography were performed. Depending on the obstruction level, endoscopic or percutaneous ureteral catheterization was first attempted. If those were unsuccessful, surgical exploration was performed and in case that a necrotic or short, thickened-scarred, bad quality ureter was found, the NU was dissected and cut at the level of renal graft ureteropelvic junction and its proximal part was ligated, if the native kidney urine production is negligible. Thereafter an end to end anastomosis was performed between the pelvis and the distal side of the NU over a double J catheter.
Results: A total of 3 patients were treated using NU. One patient (63 yr, male) developed early urinary obstruction on the 13th day after living donor KTX. Upon noticing a "pooling sign" at the hilum level in renal DMSA scan, emergency surgery revealed a necrotic ureter which was resected and the NU was then used to re-establish the continuity. The remaining 2 patients (40 yr, male and 60 yr, female) had cadaveric kidney transplants and both had ureteroneocystostomy site leak repair surgeries at 15th and 20th day after transplant retrospectively with full recovery. However, they developed recurrent strictures 4 months and 1 year after transplant respectively and those were treated using elective interposition of NU. All 3 patients had no urine output from their own native kidneys. All recovered uneventfully. At the time of this reporting, patients were 9 mo, 4 yr, and 3 yr after their NU surgery, none of them demonstrated any problem and their graft kidneys functioned well.
Conclusions: NU interposition can be a life-saver option to re-establish normal urine flow in case of graft ureteral obstructions.

P114 INTRAOPERATIVE SOMATIC TISSUE OXYGEN SATURATION FOR DETECTING POSTOPERATIVE EARLY KIDNEY DYSFUNCTION PATIENTS UNDERGOING LDLT

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Background: Somatic tissue oxygen saturation (SstO2) is associated with systemic hypoperfusion. Kidney dysfunction may lead to increased mortality and morbidity in patients who undergo living donor liver transplantation (LDLT). We investigated the clinical utility of SstO2 during LDLT for identifying postoperative kidney dysfunction.
Methods: Data from 304 adults undergoing elective LDLT between January 2015 and February 2020 at Seoul St. Mary's Hospital were retrospectively collected. Thirty-six patients were excluded based on the exclusion criteria. In total, 268 adults were analyzed, and 200 patients were 1:1 propensity score (PS)-matched.
Results: Patients with early kidney dysfunction had significantly lower intraoperative SstO2 values than those with normal kidney function. Low SstO2 (< 66%) 1 h after graft reperfusion was more highly predictive of early kidney dysfunction than the values measured in other intraoperative phases. A decline in the SstO2 was also related to kidney dysfunction.
Conclusions: Kidney dysfunction after LDLT is associated with patient morbidity and mortality. Our results may assist in the detection of early kidney dysfunction by providing a basis for analyzing SstO2 in patients undergoing LDLT. A low SstO2 (< 66%), particularly 1 h after graft reperfusion, was significantly associated with early kidney dysfunction after surgery. SstO2 monitoring may facilitate the identification of early kidney dysfunction and enable early management of patients.

P115 ORGAN DONATION: PROMOTING INTER-CULTURAL AND INTER-FAITH DIALOGUE

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Background: Trust and credibility of the society in donation is a key factor for Spanish model success. In 2019 a "Donation and religions" Project was conceived as a multidisciplinary approach to discuss donation and transplantation concepts with religious leaders from Catalonia, with the aim to improve knowledge about religious or cultural aspects that could encourage dialogue and reduce refusal for donation.
Methods: The project developed 7 activities: 2 open conferences (inauguration and conclusions) and 5 closed workshops. Moderated by Transplant Coordinators (TC) of Catalan hospitals and experts in religious diversity, each workshop focus in a particular confession: Catholicism, non-Catholic Christian, Islam, Judaism and Oriental religions (Hinduism, Sikhism, others). Finally, 60 religious or cultural leaders, 5 Transplant Patients Associations, 11 TC and 5 religious experts participated.
Results: Workshops confirmed that none of the major religions are against organ and tissue donation and reinforced the idea that information and knowledge about donation and its value are basic for a positive donation attitude. However, each religion has some particularities that TC should know before a donor family interview. For Catholics, donation is widely accepted and reinforced by the last three Popes declarations. However, for some Buddhist, aspects related with death (*bardo* state) could difficult donation, or for Hinduism, is still difficult to recognize brain death as the death of the person. To improve society knowledge and facilitate community dialogue, 6 leaflets explaining organ donation and religions and a TC Tool Guide for family approach was developed, according to specific cultural or religious beliefs. In 2022, donation rate in Catalonia increased until 46 pmp donors and 18% of families refuse donation (2% of negatives due to religious reasons, compared with 2-8% during previous years).
Conclusions: Until now very few common donation dialogues have been promoted between TC and religious leaders. The Project facilitate an inclusive multidisciplinary forum for all religions creating a shared space to exchange knowledge and facilitate productive dialogue. The elaboration of informative leaflets and TC guides will facilitate donation dialogues and awareness in our society.

P117 THE USE OF HISTOPATHOLOGICAL FEATURES AS ENDPOINTS IN ACUTE T CELL-MEDIATED REJECTION (TCMR) RESPONSE IN RENAL ALLOGRAFTS

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Background: Graft histology early after treatment is a critical endpoint for the therapeutic success of rejection therapy and is crucial in correlating long-term graft survival. Thus, we aimed to find the best time to assess for complete histological reversal of rejection.
Methods: 105 patients with acute TCMR were included in the study. A total of 562 follow-up biopsies were re-examined. All patients were treated with corticosteroids, and lymphocyte-depleting agents (LDA) were used in steroid-resistant AR patients.
Results: Of 105 recipients, 12 had borderline, 27 had grade 1A, 23 had grade 1B, 29 had grade 2A, and 14 had grade 2B acute TCMR. The steroid treatment was successful in 43 (41%) patients. Totally 62 cases did not respond to steroids. Of 62 steroid-resistant cases, 20 received OKT3, and 42 received ATG. The highest steroid response was noted in the borderline and grade 1A groups, with 91% and 55% rates, respectively. Only 26% of grade 1B and 34% of grade 2A patients have shown steroid response, while only 7% of grade 2B cases respond. The mean time between the index and the follow-up biopsy with the histological response after steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients. It was 1,68 months for grade 2A and 3 months for grade 2B patients. Only 63% of cases with steroid-resistant TCMR showed a response to LDAs at 3,58 months. While all individual Banff scores affected the steroid response, only glomerular and vascular scores affected the response in the lymphocyte-depleting treatment groups. Banff scores less than 5 are most likely reversible and responsive to steroids and LDAs. A sum score greater than 6 is associated with increased steroid resistance. Only Glomerular and vascular scores showed a significant association with serum creatinine levels. Banff scores significantly influence 10-year allograft survival and IFTA development in the first 36 months after transplantation.
Conclusions: We determined that the histological response after steroid treatment was one month. Additionally, steroid-resistant TCMRs under lymphocyte-depleting treatment went to histological resolution at 3.5 months after index biopsy. Thus we can suggest that the most appropriate time for the biopsy for histological reversal of AR after treatment is between 1 to 4 months.

P118 RENAL ALLOGRAFT BIOPSY FINDINGS IN PATIENTS WITH COVID-19

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Background: Although the respiratory system is the primary target of COVID-19, several studies have reported frequent renal involvement, and the clinic ranges from mild to moderate proteinuria to advanced acute kidney injury (AKI). However, there is little data about the histopathological features of renal allograft biopsies.
Methods: Biopsies of 17 Kidney transplant recipients (KTRs) with COVID-19 were evaluated. Clinical features, pathologic findings, and outcomes of each recipient were assessed, and the incidence of AKI and glomerular diseases were documented.
Results: A total of 17 KTRs had SARS-CoV-2 infection. Six of 17 KTRs (35.3%) developed AKI, and 83,3% required hemodialysis (HD). KTRs with AKI was associated with the severity of COVID-19, defined by the presence of pneumonia (P=0,02), hospitalization (P=0,002), and the need for HD (P=0,005). Thirteen KTRs (76,5%) showed a significant difference between proteinuria a month before and after COVID-19. Allograft biopsies that most patients (82.4%) showed varying degrees of acute tubular necrosis features, and 10 KTRs (58,8%) showed viral inclusion-like changes in the nucleus of tubular cells. Almost all KTRs (88,2%) developed T-cell mediated and/or antibody-mediated rejection at a mean time of 3,36±0,6 months after COVID-19. In addition, 5 KTRs had collapsing-FSGS, 3 had non-collapsing FSGS, 2 had FSGS recurrence, 3 had acute TIN, one had crescentic GN with IgA nephropathy, and another had MPGN at a mean time of 4,3±1,1 months after COVID-19. A total of 8 KTRs lost their graft at a mean time of 8,2±2 months after COVID-19. The development of proteinuria and hospitalization of the recipient after COVID-19 showed a significant association with graft loss (P<0.05).
Conclusions: Glomerular pathology with proteinuria with or without AKI is a leading presentation of COVID-19. It should be noted that severe proteinuric kidney disease without severe respiratory or systemic symptoms may develop in COVID-19. The T-cell and antibody-mediated rejection episodes were also found to be the most common in renal allografts with COVID-19 infection. These findings suggest that COVID-19 may cause various effects on the renal allograft. Nevertheless, it should not be forgotten that glomerulopathies may also occur coincidentally with COVID-19 infection.

P120 PSYCHOSOCIAL ASSESSMENT AMONG DECEASED DONOR KIDNEY TRANSPLANTATION CANDIDATES IN SOUTH KOREA

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Background: Psychosocial assessment of candidates is an integral component of transplantation evaluation, especially because transplantation is a highly complex procedure that requires frequent pre- and post-transplant medical care and systematic management of the patient. Standardized screening tools and evaluation criteria are essential for successful DDKT candidate management in the clinical setting. Assessment of DDKT candidates' psychosocial status using specific, standardized tools and screening of their psychosocial vulnerability in the pretransplant period is of particular importance to allow transplantation teams to identify predictors of psychosocial risk.
Methods: The purpose of this study was to assess the psychosocial status levels of candidates for DDKT in Korea. The convenience sample consisted of 157 DDKT candidates enrolled at an organ transplantation center in a city in Korea. Under the inclusion criteria, study participants had to be 19 years of age or older, able to respond to the questionnaire, and registered as a candidate in KONOS. From March 1 to December 31, 2017, data were collected. To assess participants' psychosocial status, PACT developed by Olbrisch et al. (1989) was used.
Results: When the AUC as a measure of predictive power was compared between the 3cutoff and 2, the AUC of the 3cutoff was higher (AUC=.797; 95% CI=.725-.869) than that of the cutoff point of 2 (AUC=.775; 95% CI=.692-.859). The mean score of the PACT final rating was 2.10±1.06. Among the PACT subscales, participants' social support was rated the highest (3.59±1.36), whereas the understanding of the transplantation process and follow-up was rated the lowest (2.37±1.27).
Conclusions: The result shows that the Korean DDKT candidates were somewhat vulnerable in terms of their psychosocial status. The development of effective strategies for management of candidates is crucial for improving their psychosocial status and post-transplantation outcomes. Continuous education is needed to enhance candidates' understanding of the transplantation process.

P121 DONOR, RECIPIENT AND SURGEON SEX AND SEX-CONCORDANCE AND THEIR IMPACT ON LIVER TRANSPLANT OUTCOME

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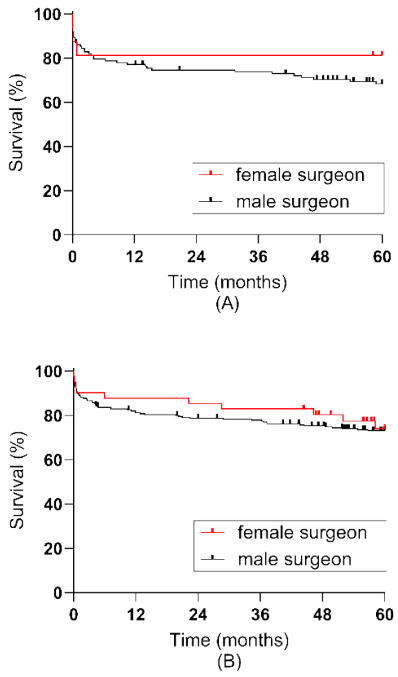
Background: Patient sex is associated with differential outcome of many procedures although the exact mechanisms remain unknown. Recently, worse outcome for female patients treated by male surgeons following common surgical procedures was reported. Especially in transplant surgery, surgeon-patient sex-concordance is rarely present for female patients and outcome may be negatively affected.
Methods: We performed a single-center retrospective cohort study, including all adult patients undergoing first-time deceased-donor liver transplantation between 2013 and 2018 at our transplant center. Recipient, donor, and surgeon sex were evaluated and short- and long-term outcome was analyzed with regards to sex and sex-concordance of patients, donors, and surgeons.
Results: We included 425 recipients in our study; 50.1% of organ donors, 32.7% of recipients, and 13.9% of surgeons were female. Recipient-donor sex concordance was present in 82.7% of female recipients and in 65.7% of male recipients (p=0.0002). Recipient-surgeon sex concordance was present in 11.5% of female recipients and in 85.0% of male recipients (p<0.0001). Donor risk index (DRI) of female donors was significantly higher (1.908 [0.9730-2.678] vs.1.672 [0.9730-2.855], p<0.0001), and female recipients received organs with significantly increased DRIs (1.837 [1.040-2.855] vs. 1.746 [0.9730-2.678], p=0.0272). Five-year patient survival was comparable between female and male recipients (70.0% vs. 73.3%, p=0.3978). Recipient-donor sex concordance did not significantly affect survival of female or male recipients. Five-year patient survival of female recipients treated by female surgeons was improved; however, this did not reach statistical significance (81.3% vs. 68.4%, p=0.3621).
Conclusions: Female recipients and female surgeons are underrepresented in liver transplant surgery. Societal factors influencing outcome of female patients suffering from end-stage organ failure need to be further examined and acted upon to possibly improve the outcome of female liver transplant recipients.

Figure 1. Five-year patient survival with regards to surgeon sex: (A) female recipients (p=0.3621), (B) male recipients (p=0.7238).



P122 SUBNORMOTHERMIC EX VIVO MACHINE PERFUSION FOR THE PRESERVATION OF DCD PORCINE KIDNEY GRAFTS

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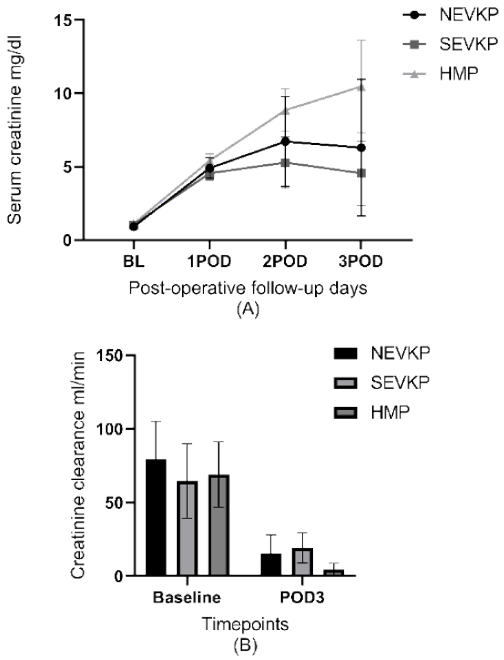
Background: To enhance the usage of marginal kidney grafts, ex-vivo machine perfusion represents a solid alternative to static cold storage (SCS) and hypothermic machine perfusion (HMP) has already been integrated in the clinic. The ideal ex-vivo machine perfusion approach and the optimal temperature for perfusion remain controversial. In the current study, we assessed the advantages of normothermic ex-vivo kidney perfusion (NEVKP) and subnormothermic perfusion (SEVKP) in a porcine kidney autotransplantation model.
Methods: All pig kidneys were exposed to 60 min of warm ischemia followed by 7.5 hrs of either HMP (4°C), SEVKP (22°C) or NEVKP (37°C) (n=5 in each group). After contralateral nephrectomy, grafts were autotransplanted and animals were followed for 3 days. Ex-vivo perfusion parameters and kidney function were compared between groups.
Results: All animals survived the follow-up period. Grafts preserved by NEVKP showed comparable postoperative function to those preserved by SEVKP. In the HMP group, daily values were higher than in the other two groups. In the HMP vs SEVKP group, there was a significant difference in daily SrCrea on all postoperative days (POD; POD1 - 5.4±0.5 mg/dl vs 4.6±0.5 mg/dl, POD2 - 8.9±1.5 mg/dl vs 5.3±1.8 mg/dl, POD3 - 10.5±3 mg/dl vs 4.6±2.2 mg/dl). On POD3, creatinine clearance was increased in the NEVKP and SEVKP groups (NEVKP vs SEVKP vs HMP: 15.4±12.5 mL/min vs 19.2±10 mL/min vs 4.4±7.7 mL/min). Oxygen consumption was reduced during SEVKP (NEVKP vs SEVKP: 805±103 ml/min/g vs 248±71 ml/min/g). Urinary NGAL, a marker of kidney injury, was significantly lower on POD3 in the NEVKP and SEVKP groups compared to the HMP group (1.5±0.9 vs 1.8±0.9 vs 5.4±1.5). Serum NGAL was lower in the NEVKP and SEVKP groups compared to the HMP group after transplant.
Conclusions: Despite reduced metabolic activity during SEVKP, grafts preserved with SEVKP vs NEVKP demonstrated comparable function directly after transplantation. Both groups showed improved kidney function and less kidney injury compared to graphs preserved with HMP. Further studies are warranted to explore which technology represents a better platform to assess and repair expanded criteria kidney grafts.

Figure 1: (A) Serum creatinine during the 3 days follow-up. (B) Creatinine clearance at baseline and postoperative day 3.



P123 PATIENT EXPERIENCE IN TRANSPLANTATION- A QUALITATIVE ANALYSIS USING FINDINGS OF THE ORGAN UTILISATION GROUP REPORT

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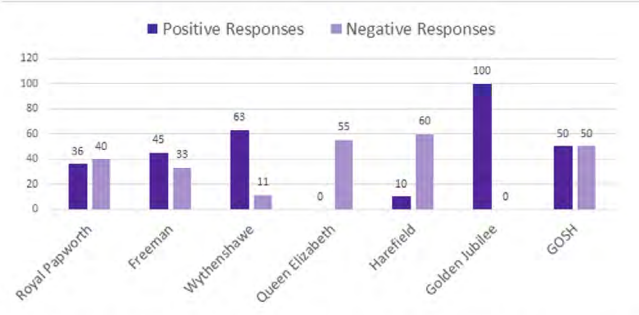
Background: The Organ Utilisation Group (OUG) was established by the Department of Health and Social Care in England, to identify ways to improve organ utilisation. The OUG placed patients at the heart of their work.
Methods: Patient representation included two full OUG membership positions, Co-Chair of the Stakeholder forum and significant presence in that group. Online surveys and calls for evidence were issued to seek views from patients who were pre- or post- transplant, and their families and carers, and capture those “less heard voices” and their experiences of transplant services. They were asked to anonymously rate different aspects of their care using a star rating. Additionally, four focus groups were held looking in depth at feedback from lung, liver and kidney patients and their families.
Results: The survey had 258 respondents, 193 of whom had received a transplant, and 26 were on the waiting list. The focus groups comprised 27 patients, from Asian, black and white delegates of both sexes, but majority female. Patients, especially those “less heard voices”, were reluctant to participate due to concerns it may affect their care. As demonstrated in table 1, there were high levels of satisfaction amongst patients across the care pathway. The greatest area of concern was the disjointed care as patients move between service providers. Focus groups were used to identify particular areas for improvement. Feedback highlighted these as: disparities in level of care offered between centres and patients; lack of psychological care for patients and their families pre- and post-transplant, leading to a strong adverse impact on their experience, wellbeing and relationships; lack of clear, consistent advice and communication. Some patients felt they had to fight to get the care they needed, even whilst seriously ill. Post-transplant support was reported as lacking for those in need of ongoing care for their specialist condition. Figure 1 shows inequitable psychological provision across cardiothoracic transplant services.
Conclusions: Access to transplant services and patient experience is inequitable across the country. This is exacerbated by gender, ethnicity and socio-economic factors.

Fig. 1 Percentage patients reporting sufficient psychological care by centre (cardiothoracic transplant)



NHSBT Cardiothoracic Patient Group Report 'Psychology Support for Cardiothoracic Patients'

Table 1. Organ Utilisation Group Patient Survey

Question asked	Star rating (1-5)				
	1	2	3	4	5
Referral for listing	9	2	19	46	181
Assessment for transplant/ living donation	2	4	14	46	184
The care you received from your transplant centre whilst on the waiting list/ as a potential living donor	4	4	19	46	175
The care you received from your local hospital or specialist whilst on the waiting list/ as a potential living donor	8	10	26	35	147
Your hospital stay before, during and immediately after transplantation/ living donation	2	1	15	49	167
Your follow up care within a year of transplant/ living donation	0	12	11	26	181
Experience of moving between different parts of the healthcare system or when speaking to different healthcare professionals involved in your care	15	28	50	60	98

Organ Utilisation Group report, Patient Feedback Survey

P124 OUTCOME OF 40 LIVING DONOR LIVER TRANSPLANTATIONS IN A NEWLY ESTABLISHED ADULT LIVING DONOR LIVER TRANSPLANT PROGRAM IN THE NETHERLANDS

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Background: Liver transplantation is the only cure for end stage liver disease. Expanding indications, with a stable supply of deceased donor grafts has led to organ shortage. Even the increasing acceptance of marginal grafts did not solve this problem. Wait list mortality reported by Eurotransplant remains at 18%, not including delisted recipients. Living donor liver transplant (LDLT) is a solution to overcome organ shortage. The development of LDLT led to superior outcomes compared to deceased grafts. In 2019 we started an adult LDLT program, here we present our outcomes.
Methods: We prospectively reviewed recipients who underwent LDLT between January 2019 and December 2022. Demographics, etiology, graft characteristics, and operative variables were assessed. Outcome was evaluated on the basis of morbidity and mortality. All complications of ≥ 3 on the Clavien-Dindo grading system were included as morbidity.
Results: Forty LDLT have been performed. Most donors were related to their recipients, 36 (94%) of donors donated their right liver lobes; 2 left lobe donations and 2 domino LDLT also took place. The median hospital stay was 6 days. There has been no significant donor morbidity, and no donor mortality. The MELD score for LDLT recipients varied between 6 – 22. Twenty six (65%) LDLT recipients had roux-en-Y biliary reconstructions. Eight (20%) biliary complications were reported in LDLT recipients, all were successfully managed with minimally invasive techniques, no revision of a biliary anastomosis was required. One LDLT recipient required re transplantation 16 months post LDLT after developing a hepatic artery thrombosis 1 week post-transplant. The other 39 LDLT recipients have good graft function, there has been no recipient mortality.
Conclusions: With meticulous preparation, appropriate case selection and continuous training of team members by experienced staff a newly established LDLT program can achieve good outcomes.

P126 POST REPERFUSION SYNDROME IN PEDIATRIC LIVER TRANSPLANTATION: EXPERIENCE OF A CENTER (LYON)

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Background: The post reperfusion syndrome (PRS) is well known in adults liver transplantation, although there are few data for pediatrics. The aim of our study was to evaluate the incidence, and the associated factors in a pediatric population.
Methods: We conducted a retrospective study including over 10 years all transplanted patients (2011- 2021) in our pediatric liver transplant center. The parents gave their written consent. The procedures were performed with preservation of the recipient’s vena cava and vascular exclusion of the liver. Reperfusion of the graft was done through the portal vein. We retain as the definition of PRS: drop in MAP ≥ 30% of at least 1 minute during the 5 minutes following graft reperfusion, without changing the dose of Norepinephine infusion. We studied the following factors: Recipient’s age and weight, type of graft (DV vs. DD), whole vs. split, donor age, cold and warm ischemia, dose of Norepinephrine infused in the donor ionized calcium T30 (Ca++ 30minutes after reperfusion), preoperative and T30 haemoglobin, weight graft ratio (WGR) and massive transfusion (>40ml/kg during the procedure).
Results: We analyzed the data of 145 patients, middle age 6.3 years [0.5-16], middle weight 23kg (58 %< 20kg). They received respectively: 64 whole and 81 partial livers. Incidence of PRS observed was 19%. PRS is not associated with massive transfusion occurrence. Donor infusion of Norepinephrine >1µg/kg/min before the graft removal, and the WGR are significantly associated with the occurrence of PRS (p<0.001). The weight of the recipient is not significantly associated with the occurrence of PRS (p=0.071), perhaps taking into account an insufficient number. Age of the donor, type of graft, warm and cold ischemia time, preoperative and T30 haemoglobin, Ca++are not significantly associated with PRS. In multivariable logistic regression, donor’s administration of norepinephrine was significantly associated with the occurrence of PRS p<0.003, OR 7.7 [2.0-29.6], as well as WGR p<0.002, OR 1.7 [1.2-2.4].
Conclusions: Reperfusion syndrome has a prevalence of around 20% in pediatric liver transplantation. The dose of Norepinephrine infused in the donor and the weight graft ratio increase the PRS occurence. The risk of having a PRS is 7 times greater when the donor received NOR>1µg/kg/min.

P127 RENAL FUNCTIONAL RESERVE, RADIOISOTOPIC GFR AND URINARY INJURY BIOMARKERS: THE NEXT STEPS FOR A SAFER EVALUATION AND FOLLOW-UP OF LIVING KIDNEY DONORS

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Background: After nephrectomy, living kidney donors (KD) develop an episode of Acute Kidney Injury (AKI). Renal Functional Reserve (RFR), defined as the capacity to increase glomerular filtration rate (GFR), plays a key role in functional recovery. The aim of this study was the dynamic evaluation of RFR, radiosotopic GFR (rGFR) and urinary injury biomarkers before donation, in the immediate postoperative period and 1 year after to investigate their predictive performance.
Methods: 112 KD were evaluated at different time points sCr, rGFR and sequential scintigraphy with 99mTc-MAG to determine left vs. right renal function and the urinary biomarkers NGAL, Nephrocheck (IGFBP7/TIMP2) and extracellular vesicles expressing the stem cell marker CD133 (CD133+uEVs) detected by flow cytometry.
Results: At study admission, mean sCr was 0.7 mg/dL, rGFR 98 mL/min, at scintigraphy the mean % of right kidney function was 47. After all left nephrectomies, renal function worsened (AKI episodes) with mean sCr values of 1.2 mg/dL. After 7 days, renal recovery was observed in all KD. After 1 year, rGFR was measured and compared with the split rGFR of the right kidney before donation with a mean compensatory increase of 18 mL/min and in % 35. Pre-donation RFR was 21.5 mL/min. Multivariate linear regression confirmed that KD age and basal rGFR represented 2 independent factors able to predict renal function 1 year after. ROC curve evidenced a value of 45 ml/min to predict rGFR higher than the median after 1 year (sensibility: 73.53%; specificity: 59.38%). There was no correlation between pre-donation RFR and post-donation AKI, whereas a strong linear correlation between RFR and the compensatory GFR increase after 1 year was observed (r=0.66). Of note, after 1 year KD still maintained a percentage of RFR (16.5 mL/min). Injury biomarkers were all negative 7 days and 1 year after: moreover, the percentage of CD133+uEVs was significantly increased 7 days after nephrectomy (24% vs. 4.5%), suggesting a regenerative potential of the remnant kidney.
Conclusions: The dynamic evaluation of renal function after nephrectomy represents the next steps for a safer follow-up of KD. Even though a longer observational period is needed, RFR, rGFR and urinary injury biomarkers may allow a better clinical management even in “medically complex” ones.

P128 “THIS FAMILY AND THE GAMES ARE MY WORLD”: CONCEPTUALISING THE BRITISH AND EUROPEAN TRANSPLANT GAMES AS THERAPEUTIC LANDSCAPES

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Background: The first Transplant Games took place in 1978 in Portsmouth, England. Since then, numerous Olympic-style sporting ‘Games’ have been established, each with the aim of increasing public awareness of organ donation, demonstrating the benefits of transplantation, and encouraging patient fitness. Despite this, research exploring the psycho-social and health impacts of the Games is limited. Drawing upon the tradition of health geography, I argue that the Games are a therapeutic landscape – an environment that contributes to improved health and wellbeing – for organ recipients.
Methods: Semi-structured interviews were conducted with 37 participants at the 2022 British Transplant Games and the 2022 European Transplant and Dialysis Games, alongside ethnographic observation. Participants were asked a range of open-ended questions, which broadly focused on their feelings towards sport and fitness, their health, and self-management. Notes were taken during and after each interview, and the data qualitatively coded using the software NVivo.
Results: Findings demonstrate that the Games are a therapeutic landscape for participants in three key ways. Firstly, the Games provide a *landscape of belonging*, where individuals can form familial bonds, receive peer-peer support, and be part of a community tied together by the shared experience of transplantation. Secondly, they function as a *landscape of hope*, with participants reporting that the Games allowed them to help others by showing them (through excelling in sport) that they can still lead a healthy, normal life. Finally, the Games operate as a *landscape of motivation*: in working towards sport and fitness-based goals, the Games improved both the physical and mental health of participants.
Conclusions: The experience of receiving an organ transplant is complex, with individuals moving through spaces of illness, surgery, recovery and beyond. The Transplant Games show how these embodied experiences converge, resulting in a therapeutic landscape with wide-ranging health benefits. Understanding these benefits and the peer-peer support the Games foster may encourage hospitals to promote the Games, in turn making transplantees more visible in society, improving health outcomes for organ recipients, and ultimately leading to increased donation rates.

P129 EVALUATING OF THE BLOOD PRESSURE PROFILE AFTER KIDNEY TRANSPLANTATION

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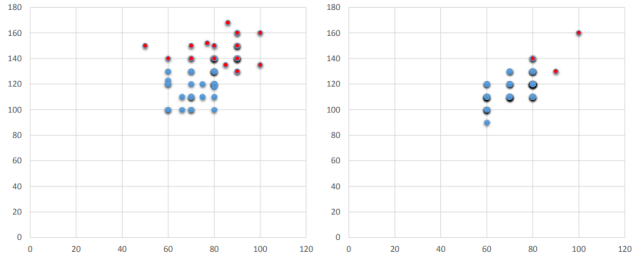
Background: hypertension in dialysis as in rénal transplantation is a major factor of morbidity and mortality, so what would be the benefit of a rénal transplantation on the blood pressure profile of our patients?
Methods: We carried out a monocentric retrospective study concerning 63 patients transplanted between 2018 and 2020 in our center from related and ABO compatible living donors. The objective is to compare the blood pressure profile in Hemodialysis and after kidney transplantation with a follow-up ranging from 1 to 3 years post transplant and this by the use of ambulatory Blood pressure measurement (ABPM).
Results: 63 patients were the subject of this study (31% women - 69% men) Sex ratio at 2.22. An average age of 37 years, the initial nephropathy was indeterminate in 59% of cases with an average duration on dialysis of 4 years before transplantation. the proportion of hypertensive patients went from 76% on dialysis to 57% after transplantation (nocturnal hypertension in 46% of cases) with a decrease in the average number of antihypertensives from 2.14 to 1.36. The non-dipper profile was found in 93% of cases after kidney transplantation. The results of our series are in line with the general trend of the studies made, concerning the évolution of the blood pressure profile of transplanted patients with a marked improvement in the latter, and better blood pressure control of patients with hypertension after kidney transplantation. We can cite the studies carried out by Haydar and al in 2004 in England and Kayrak and al in 2015 in Turkey. Moreover, persistent hypertension in renal transplantation was partly related to the treatment with vasoconstrictor anti-calcineurin, the improvement in the quality of life and the occurrence of a metabolic syndrome and the persistent activation of the renin-angiotensin system by the native kidneys.
Conclusions: Kidney transplantation significantly improves the blood pressure control of our patients and the ABPM remains a valuable tool for monitoring them.

Fig 01: Systolic BP / Diastolic BP before and after Kidney Transplantation



P130 FAMILY-CENTRED APPROACH FOR ORGAN DONATION AUTHORISATION: A GROUNDED THEORY STUDY

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Background: Approaching families to discuss deceased organ donation authorisation is one of the central stages of the organ donation process. Current evidence is fragmented and how it occurs in practice has been limited explored.
Methods: Grounded theory study. Seventy-one participants, including healthcare professionals (n=51) and bereaved families (n=20) were recruited across two large public hospitals in Chile. Data included documents (n=80), interviews (n=27) and focus groups (n=14) collected and analysed following Charmaz’ constructivist grounded theory approach (Charmaz, 2014).
Results: The theory of *Reading the family* explains how organ donor coordinators approach families and negotiate organ donation authorisation. The delicate and sophisticated skill of reading the family’s emotions involves responding to each family’s experience when negotiating authorisation and constitutes an ethical family-centred practice. Furthermore, *Reading the family* requires coordinators to manage their own and families’ emotions in the context of death and loss for bereaved families. The findings highlight how organ donor coordinators care for families and protect them from institutional pressures such as donation rates quotas, time constraints, and limited resources. Still, it also exposes the challenges of recruiting, training, and retaining organ donor coordinators.
Conclusions: A family-centred approach acknowledges the ethical complexities of caring for and supporting bereaved families beyond organ donation decision-making in a person-centred care manner. The findings, due to their intersectionality, inform clinicians, educators and policymakers and suggest a model that can guide practice and training for coordinators and the multidisciplinary team to promote person-centred care.

P131 POLYCYSTIC DISEASE: A CUMBERSOME INDICATION FOR TRANSPLANTATION

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Background: polycystic liver disease (PCLD), usually associated with polycystic kidney disease (PCLKD), is a benign condition that leads to abdominal fullness and portal hypertension. Liver transplantation (LT) or simultaneous liver-kidney transplantation (SLKT) remains the curative treatment for severe polycystic disease. We aimed at describing pre- and post-transplant characteristics of patients (pts) who underwent LT/SLKT for PCLD/PCLKD.
Methods: Pts who underwent LT/SLKT for PCLD/PCLKD in our Center from 01/01/2010 to 30/09/2022 were enrolled. Follow up was closed on 31/12/2022.
Results: Among 1754 LT, 63 LT for PCLD (3.6%) have been carried out, of which 45 (71%) SLKT. 48 (76.2%) female; median age 52 years [48-56]; BMI 24 kg/m^2 [23-26]. GFR was 11 mL/min [7-17] in pts who received SLKT (29/45 on pre-LT dialysis). 58 (92%) pts underwent LT for abdominal fullness with sarcopenia (median liver weight 3950g [2450-6750]; largest cyst size of 7 cm [5-9]); 19 (30%) had refractory ascites. 9 pts (2%) had pre-transplant cyst interventions. Of note, 10 pts (16%) were known to be pre-LT colonized by multidrug-resistant (MDR) bacteria. Median liver cold ischemia time was 447 min [369-504]. The Piggy-back technique was possible in 18/63 (29%) and 9 pts (14%) underwent temporary porto-cava shunt while only 6 pts (10%) received venous-venous bypass. Among 48 pts listed for SLKT, 7 (15%) underwent a delayed kidney transplantation (KT) and 3 (6%) were then listed for sequential KT due to the complexity of LT-surgery. Forty-one pts (65%) were extubated within 48h and the median ICU stay was 5 days [3-9]. Two pts had primary non-function and underwent re-LT after 3 days while only 1 pt had hepatic artery-thrombosis solved surgically. 28 pts (44%) underwent early post-transplant surgical revisions. After 4 years [2-8] of follow-up: 59 (94%) were alive: 3 pts died for sepsis 3 weeks after transplant and 1 pt died for HHV8-induced hemophagocytic syndrome 3 years after SLKT.
Conclusions: PCLD/PCLKD is an insidious benign disease for which transplantation is the ultimate solution, despite surgical complexity. In our cohort 16% of pts were colonized by MDR bacteria and post-LT early surgical revisions were needed in 44% of cases. Nevertheless, the expertise of a high-volume transplant Centre allowed to achieve a 3-year survival rate of 94%.

P132 ANALYSIS OF COVID19 CASES WITH RENAL TRANSPLANTATION (KTX): PREDICTIVE FACTIORS OF SEVERE DISEASE

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Background: Covid19 virus related mortality is known to be higher among pts with KTX, because pts with KTX are not only immunosuppressed but they also have higher incidence of known risk factors, such as advanced age, hypertension, other cardiovascular diseases and diabetes. Severe disease in immunocompromised individuals may reflect the inability to mount an effective immune response, even after vaccination. The spectrum of Covid19 disease ranges from asymptomatic infection to pneumonia, cytokine storm, and death. Analysing pre-disease laboratory parameters is aimed defining possible predictive factors of severe disease.
Material and Methods: After Local Ethical Committee approval, the data of KTX patients that are followed up by our center between 2020 and 2022 were retrospectively collected. All pts had either cadaveric or living related donor KTX and all received induction immunosuppression followed by standard maintenance immunosuppression. Covid19 test was done by polimerase chain reaction. Laboratory tests that were done before Covid19 infection were analysed and parameters that are well known to be affected by acute disease, such as acute phase reactants, CRP, procalcitonin, ferritin, d-dimer were excluded. Data is presented as mean (stdev) for continuous variables and as frequencies for discrete values. Statistics were performed using parametric tests and $p<0.05$ was considered significant.
Results: A total of 43 KTX patients had documented Covid19 infection in our center since March-2020. Eleven patients required hospitalization, of whom 8 had severe disease with extensive lung involvement and 5 of these eventually succumbed into death due to lung failure. Of note, 2 dead and 3 severe pts were vaccinated. Table 1 shows significant predictive factors of mortal cases.
Conclusion: Retrospective evaluation of our KTX pts with Covid19 infection revealed significant decreased lymphocyte count and lower platelet count before the actual disease.

Table 1: Significant predictive factors for mortality

	NONE (42)	MILD (32)	HOSP (5)	DIED (6)	P (anova)
Lym(#)	1.29±0.92	1.29±0.97	1.18±0.91	0.75±065	<0.05
Lym(%)	15.2±12.6	14.6±11.6	17.6±11.5	8.9±7.1	<0.05
PLT	264±113	243±90	257±95	151±76	<0.05
PCT	0.17±0.1	0.15±0.07	0.17+0.07	0.08±0.06	<0.05

P134 INCIDENCE OF MALIGNANCIES AFTER LUNG TRANSPLANTATION AND THEIR EFFECT ON OUTCOME. A 26 YEARS' EXPERIENCE

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Background: Malignancy is a significant, life-limiting long-term complication after lung transplantation (LuTx) and the second commonest cause of death, during the first 10 years after LuTx. We aimed to investigate its incidence and effect on the long-term outcome.
Methods: This is a single center retrospective observational study. Between 1996 and 2022, n=627 lung transplantations (LuTx) were performed in our department. We used our institutional database to identify those diagnosed with malignancies after LuTx and examined the malignancies' incidence and the related mortality.
Results: A number of n=59 malignancies occurred in n=55 (8.8%) LuTx recipients. The post-LTx malignancies incidence was 9.4% (59/627). We report following rates based on their location: n=17/55 (28,8% of all recipients diagnosed with malignancies) skin, n=10/55 (16,95%) gastrointestinal, n=9/55 (15,3%) respiratory, n=5/55 (8,48%) lymphatic, n=13/55 (23,6%) other, n=5 (8,48%) multiple synchronous. During this study period, a total of n=328 deaths after LuTx was determined. N=29 (8,84% of all deaths) were malignancy induced, corresponding a total malignancy induced mortality of 4.6% (n=29/627). The majority of deaths were attributed to GI adenocarcinoma and PTLD. Malignancies' origin, primary COPD diagnosis, type and specific age-group were significantly survival-related (p values <0.05). The most affected organ was skin and showed the best prognosis. PTLD had the fastest and pancreatic the latest onset.
Conclusions: This is the first report of its kind in a large cohort of german LuTx recipients. The prevalence ranking of the three commonest malignancies was skin > colorectal > PTLD. Post-LTx malignancies was the second commonest cause of death. Further studies are needed, while post-LuTx malignant disease remains a serious impairment of long-term LuTx survival.

P135 LIVER TRANSPLANTATION AT THE KOREA UNIVERSITY : ANALYSIS OF 500 CASES AND INTRODUCING OUR UNIQUE MULTI-INSTITUTIONAL NETWORK

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Background: Liver transplantation (LT) is an established therapeutic modality for patients with end-stage liver disease. Since the first case in 1994, over 500 cases liver transplantation have been performed at the Korea University medical center which is comprised of 3 tertiary hospitals (Anam, Guro and Ansan hospital). The aim of this study was to analyze our experience of over 500 cases of liver transplantation. In addition, we report our experience of creating a multi-institutional network or team (named the "**K**orea **U**niversity **R**emedy **E**nsemble" or "**KURE**") to help prepare for, to perform and especially to improve the outcomes of liver transplantation at our medical center.
Methods: We reviewed the records of 518 adults who received LT between March 1994 and July 2022 from 3 tertiary centers. Patient outcomes were analyzed. In addition, we divided the patients into 2 groups according to the date of transplant before and during the "KURE" era, respectively. Outcomes were compared between the two groups.
Results: More patients underwent deceased donor LT than living donor LT (n=265 vs n=253). The 1-, 3-, 5-year overall survival was 90.4%, 83.1%, 81%, respectively. And there was no significant difference between deceased donor and living donor LT. Similarly in HCC patients, the 1-, 3-, 5-year disease free survival was 90.5%, 84.2%, 83.0%, respectively. However the disease free survival in patients undergoing living donor LT was significantly lower (p=0.031) probably due to the large tumor burden in these patients. Of the 518 patients, 191 were transplanted during the "KURE" era. Operative time, amount of blood transfusion, non-biliary complications (above Clavien-Dindo grade 3), acute rejection, 30- and 90 day mortality and therefore overall survival all significantly improved during the "KURE" era.
Conclusions: Survival outcomes were comparable to other major centers and significantly improved during the "KURE" era. The "KURE" network can be a model for nearby tertiary institutions to improve their transplant outcome in certain regions of Korea.

P136 COMPARISON STUDY BETWEEN FULL THICKNESS AND ANTERIOR LAMELLAR CORNEAL XENOTRANSPLANTATION FROM SAME TRANGENIC PIGS TO MONKEY

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Background: Graft survival of full thickness corneal xenotransplantation with minimal immunosuppression from genetically engineered pig is not well known. In comparison, we publish that anterior lamella corneal xenotransplantation from transgenic pig shows very good results despite minimal immunosuppression. We compare the graft survival between full thickness and anterior lamella xenotransplantation from the same genetically engineered pig.
Methods: With the use of 3 transgenic pigs, six pig-to-monkey corneal transplantation was done. Two corneas from one pig are transplanted to two monkeys with the full thickness and anterior lamella for each. Transgenic type of donor pig is GTKO+CD46 in one and GTKO+CD46+TBM in two.
Results: Graft survivals of each xenotransplantation of GTKO+CD 46 are 28 days and 28 days same. With the addition of TBM, survival differences between anterior lamella and full thickness are 98 vs. 14 days and 422+(on-going) vs. 21 days. For failed graft, many inflammatory cells exist in grafts and no inflammatory cell in recipient's stromal bed.
Conclusions: Anterior lamella has the advantage of not having surgical complication such as retro-corneal membrane or anterior synechia seen in full thickness corneal xenotransplantation. In our study, graft survival of lamellar xenotransplantation is not well comparing with previous our experiments although superior survival period to full thickness. Difference of graft survival based on the transgenic type is not definitive also. More cases and improvement of graft survival will be needed to check the possibility of full thickness corneal xenotransplantation with the use of transgenic pig and minimal immunosuppression.

P137 CONTRAST ENHANCED MAGNETIC RESONANCE ANGIOGRAPHY IN THE EARLY PERIOD AFTER RENAL TRANSPLANTATION

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Background: Our objective was to evaluate the usefulness of three-dimensional contrast enhanced MR angiography (3D CE MRA) for assessment of renal parenchyma itself, arterial inflow stenosis, and peritransplant fluid collection in the early period after renal transplantation.
Methods: Between April 2019 and July 2022, a consecutive series of 62 renal transplants was examined with 3D CE MRA 14 days after transplantation. MR angiography studies were analyzed for the volume of renal parenchyma, presence of arterial stenosis, renal infarction, and peritransplant fluid collection. The degree of renal transplant artery inflow stenosis was graded qualitatively as <50% = mild, 50-70% = moderate, >70% = severe. According to severity of arterial stenosis on MRA, the following variables were compared: demographic factor, graft survival, post-operative renal function, incidence of acute rejection (AR).
Results: Kidney volume, measured with MRA, varied from 148 to 421 (226.1±46.8 mL). It is higher than that of pre-operation CT volume (171.1±32.8) (P < 0.005). Twenty (31.3%) of the 64 patients had normal CE MRA which were no parenchymal infarction, no fluid collection and no arterial inflow stenosis. MR angiography showed parenchyma infarction (n=8, 12.5%), arterial inflow stenosis (n=17, 26.6%), lymphocele (n=22, 34.4%) and hematoma (n=3, 4.7%). Among the patients with arterial inflow stenosis, 16(25.0%) showed mild, 1 patient (1.6%) moderate, and no severe stenosis. The patient with moderate arterial stenosis on CE MRA underwent selective digital subtraction angiography (DSA); PTA with stent was performed successfully. The mean creatinine level at 1month, 6month and 1 year after transplantation were not significantly different in patients with arterial stenosis from those of others (P = 0.379, 0.359, 0.136).
Conclusions: The incidence of renal parenchyma infarction, peritransplant fluid collection and arterial flow stenosis is unexpectedly high in the early period after kidney transplantation. MR angiography and MR imaging allows rapid global assessment of renal parenchyma, renal transplant arterial system, and peritransplant fluid collection. It can also help detect or exclude many of the various causes of renal transplant dysfunction

P139 PASSENGER LYMPHOCYTE SYNDROME PRESENTED AS HEMOLYTIC ANEMIA AFTER SMALL BOWEL TRANSPLANTATION: A CASE REPORT

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Background: The passenger lymphocyte syndrome (PLS) induces hemolytic anemia after minor ABO mismatched organ transplantation. We experienced a case of PLS with hemolysis after small bowel transplantation.
Methods: A 65-year-old man underwent massive small bowel resection and right colectomy for superior mesenteric artery embolism in January 2021. Around 30cm jejunum was left and he got end jejunostomy and was completely dependent on parenteral nutrition. He received small bowel from deceased donor on June 2021. His blood type was B Rh+ and donor was O Rh+. We used simulect 20mg, anti-thymocyte globulin (ATG) 1.5mg/kg for 5 times and prednisolone 1000mg as an induction and then tacrolimus with trough level 13-15ng/ml and reduced dose of prednisolone as a maintenance. Patient was stable and transfusion was not needed during the surgery.
Results: After operation, hemoglobin level was decreased gradually from 10.4mg/dL preoperatively to 5.6mg/dL at POD#5. There wasn`t any bleeding sign on physical exam and CT angiography. A platelet count was decreased together, 60K at POD#5. We thought it might be ATG related bone marrow suppression and gave him RBCs and platelets with supportive care. The platelet count was low but sustained greater than 60K and recovered over 100K at POD#23 and last transfusion was POD#9. However, hemoglobin drop was repeated and transfusion was needed weekly till POD#27. In isoagglutinin test, anti-B IgG was detected at 1:8 titer. A haptoglogin was lower than 20mg/dL and direct antibody test was positive for IgG and C3bd. We already used rituximab at POD #13 due to de novo antibody and CD19 and 20 was completely suppressed.
Conclusions: At POD 36, there`s no edema or ulcer and normal villi was observed on endoscopy. He is stable and on a diet program to reduce parenteral nutrition. Most of PLS is self-limiting but often poor outcomes have been reported, awareness and suspicion is important.

P141 PREDICTIVE MODEL OF TRANSPLANTED KIDNEY FUNCTION USING AUTOMATED COMPUTED TOMOGRAPHY VOLUMETRY

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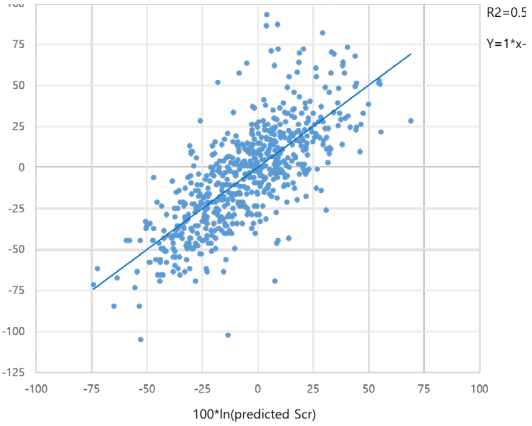
Background: Kidney function has a strong relationship with its size, especially its volume. Automated computed tomography(CT) volumetry made it easy to measure kidney and its cortical volume. This study aimed to make a predictive model of transplanted kidney function by automated CT volumetry and find other variables.
Methods: ABO compatible kidney-donate or -transplanted patients from January, 2010 to December, 2020 at Seoul National University Hospital were enrolled and those who had surgical complications were excluded. Kidney volumes were auto-segmented and measured on CT images by 'OncoStudio' (OncoSoft Inc., Seoul, South Korea). Variables were analyzed by multiple linear regression. Predictive model for ABO compatible recipients was proposed.
Results: 645 donor-recipient pairs were enrolled. ABO compatible kidney recipient's predicted serum creatinine was e^{1/100(-119.033-0.346*[Recipient Age-Donor Age]+100.746*[Recipient BSA]-0.353*[Whole Kidney Volume]. R^2 trend was 0.546.
Conclusions: Graft whole volume by automated CT volumetry, donor age, recipient age and recipient BSA were related with transplanted kidney function. Further study is needed for ABO incompatible kidney recipients and a more precise predictive model for ABO compatible kidney recipients. We expect that automated CT volumetry will help us to select the best kidney donor for recipients.



P142 LAPAROSCOPIC HAND-ASSISTED DONOR HEMINEPHRECTOMY IN LIVING DONOR WITH HORSESHOE KIDNEY (CASE PRESENTATION)

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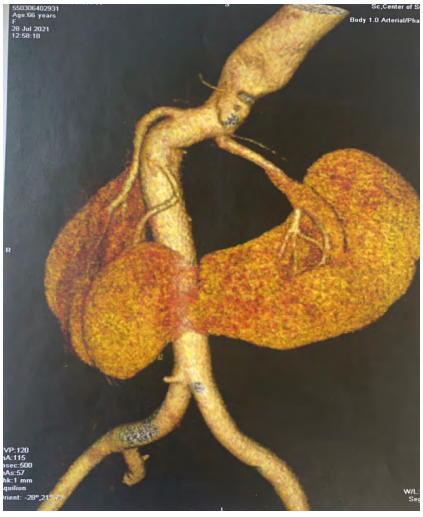
Background: Case of kidney transplantation from 65 –years old female donor with horseshoe kidney (HSK) for her 39-years old son with end-stage renal disease (ESRD), by using laparoscopic hand-assisted heminephrectomy technique.
Methods: 39-years old male with ESRD, for the last 2 years on haemodialysis, admitted to our center for kidney transplantation. Technical challenge was due to that donor had a horseshoe kidney with parenchymal isthmus, with 4 arteries on right half and 2 arteries on the left with retrocaval position of the latters (Pic.1). Recipient had concurrent arterial hypertension and otherwise there were no contraindications for transplantation during preoperative evaluation. Donor was his mother 66 –years old, with arterial hypertension 1 stage (BP max 142/90 mm/hg), during preoperative evaluation otherwise healthy. Due to the lack of others younger related donors, we inform patients about potential risks of donation and after informed consent taken we prepared patients for surgery
Results: Patient underwent laparoscopic hand-assisted donor heminephrectomy. Firstly isthmus was sewed in the middle and tied on both sides after left half of HSK was devascularized and then the isthmus was quickly transected just above the suture line, preventing bleeding from the right half. Warm ischemic time 1 was 92 seconds. Resected isthmus was sutured on back-table by interrupted suture and utilizing haemostatic sponge. Surgery was completed otherwise uneventfully. Patient was discharged postop 4 day.
Conclusions: In case of HSK it is common problem the anomaly of kidney vasculature, pelvicalyceal system, isthmus. These pitfalls are not a contraindication for organ donation anymore. There different techniques of organ procurement but in developing surgical era we must utilize minimal invasive approaches in these patients also as to affect their recovery period and return to their daily activity.

Pic. 1. HSK with aortocaval transposition, multiple arteries, parenchymal isthmus.



P143 DONOR-DERIVED MULTIDRUG-RESISTANT ORGANISMS INFECTION COMPLICATIONS IN LIVER TRANSPLANT RECIPIENTS

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Background: Due to prolonged intensive care unit stay, various medically invasive treatments or surgical interventions and history of broad-spectrum antibiotics use, donor-derived multidrug-resistant organisms (MDRO) infectious complications became a serious problem. MDRO contamination may result in overt infection or an asymptomatic, undiagnosed carrier state. With the development of MDRO complications after liver transplantation (LT), the risk of death increases by 5-9 times and one-year survival decreases to 23-30%. The aim of this study was to assess the impact of MDRO contamination of preservation fluid (PF) on the rate of post liver transplant surgical site infection (SSI) complications in country with high rate of Carbapenem-restistant flora prevalence.
Methods: In prospective single-center study 271 LT recipients were included (study period – 2019-2021). A routine study of liver graft preservation fluid during back-table was introduced. Within 24 h, if bacterial growth is detected, the MALDI-ToF analysis will be performed. If MDRO is detected, the sample is sent for a PCR-test for the presence of resistance genes. Thus, within 48 hours after organ retrieval, the presence or absence of PF contamination, the pathogen, its sensitivity and the resistance genes were detected. Primary clinical outcomes: SSI rate, SSI mortality rate.
Results: Incidence of healthcare-associated infection (HCAI) following LTx – 19% (52/271), of those, sepsis - 13% (7/52); SSI rate – 14% (37/271); SSI mortality rate – 16% (6/37). The prevalence of culture-positive preservation fluid was 22% (60/271), MDRO positive - 5% (15/271). In 10 cases (3,7%) it caused donor-derived MDRO SSI with 60% (6/10) sepsis mortality rate. Preservation fluid contamination increased the risk of SSI in 4 times (OR=6.3; p<0.001) and the presence of Carbapenem-resistant pathogen in PF caused 41-fold increase of the SSI risk of in (OR=41.2; p<0.001).
Conclusions: Contamination of the preservation fluid increases the risk of SSI after LT. The resistance profile of a pathogen affects the duration, structure, and outcome of infectious complications. Timely diagnosis and infection control measures are fundamental to preventing donor-derived MDRO infectious complications.

P144 SERUM CYSTATIN C IN RENAL TRANSPLANTATION: BEYOND GFR ESTIMATION, A PROGNOSIS MARKER?

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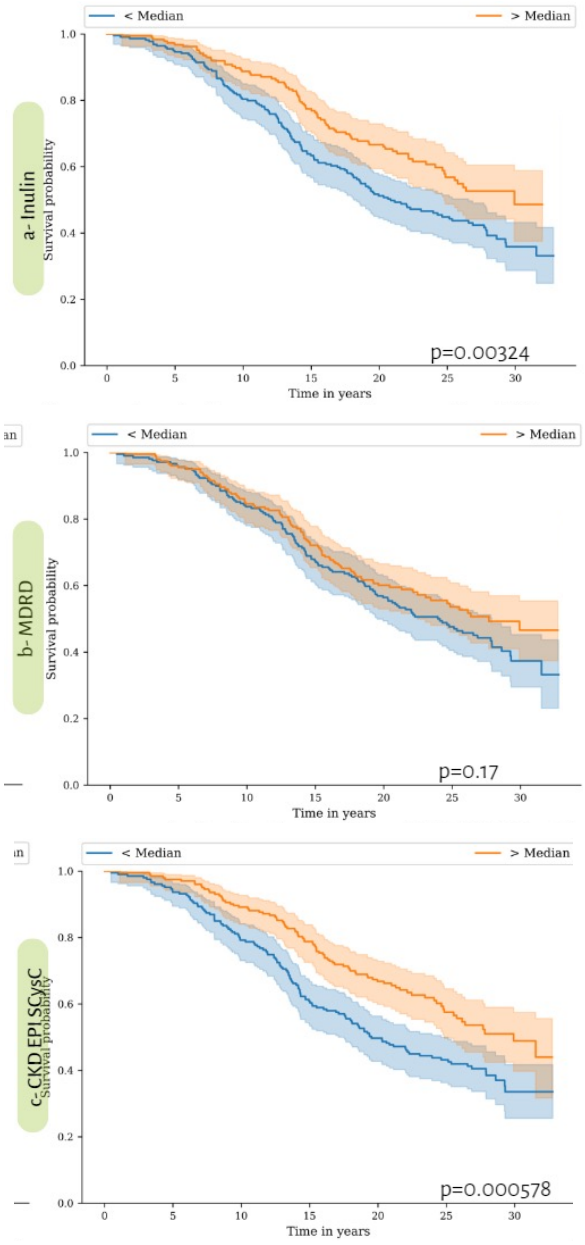
Background: In renal transplantation, death with a functioning graft remains one of the main causes of graft loss. In the general population, renal function impairment is strongly associated with cardiovascular and all-cause mortality. Whether this association holds true for kidney transplant recipients (KTR) is unclear. This uncertainty is likely to be due, in part, to the fact that glomerular filtration rate (GFR) estimation based on serum creatinine (SCr) does not always provide an accurate evaluation of the graft function in KTR. As compared to SCr, we have previously shown in a large cohort of KTR that serum cystatin C (SCysC) is a much better marker of GFR. Herein, we sought to study the ability of the 1-year-post-transplant renal function to predict all-cause mortality according to the methods used to assess GFR.
Methods: Four hundred and ten consecutive KTR for whom a measurement of GFR by inulin clearance was available at one-year post-transplant were included. SCreat and SCysC were measured with standardised methods. We studied the association between 1-year inulin clearance value, MDRD Study equation value and CKD-EPI SCysC equation value with all-cause mortality.
Results: During a median follow-up of 17 years, 212 KTR died. Mean (± SD) inulin clearance at 1-year-post transplant was 47 (±13) mL/min/1.73m2. Patients who died during the follow-up had a significant lower GFR value at one-year post-transplant as compared to patients who did not. This was true irrespective of the methods used to evaluate GFR. However, while patients' survival categorized according to MDRD study equation median value observed after one-year post transplant was not different, long-term survival was significantly improved in patients with the highest GFR values estimated by the CKD-EPI SCystC equation (which was even more discriminant than inulin clearance, fig. 1)
Conclusions: Our preliminary results suggest that cystatin C used as a GFR estimate is superior to serum creatinine to predict risk of mortality in renal transplant patients. CystC predictive value is likely to be explained by a better ability to approximate the so-called "true GFR" (given by inulin clearance) but also by other determinants not directly related to the level of renal function.

Figure 1. Survival curves according median GFR at one year post (a-insulin, b-MDRD, c-CKD-EPI SCysC)



P145 HEMOSTATIC PROTEIN PRODUCTION DURING LONG-TERM EX SITU NORMOTHERMIC MACHINE PERFUSION OF HUMAN DONOR LIVERS RESULTS IN PLASMA-LIKE PERFUSION FLUID

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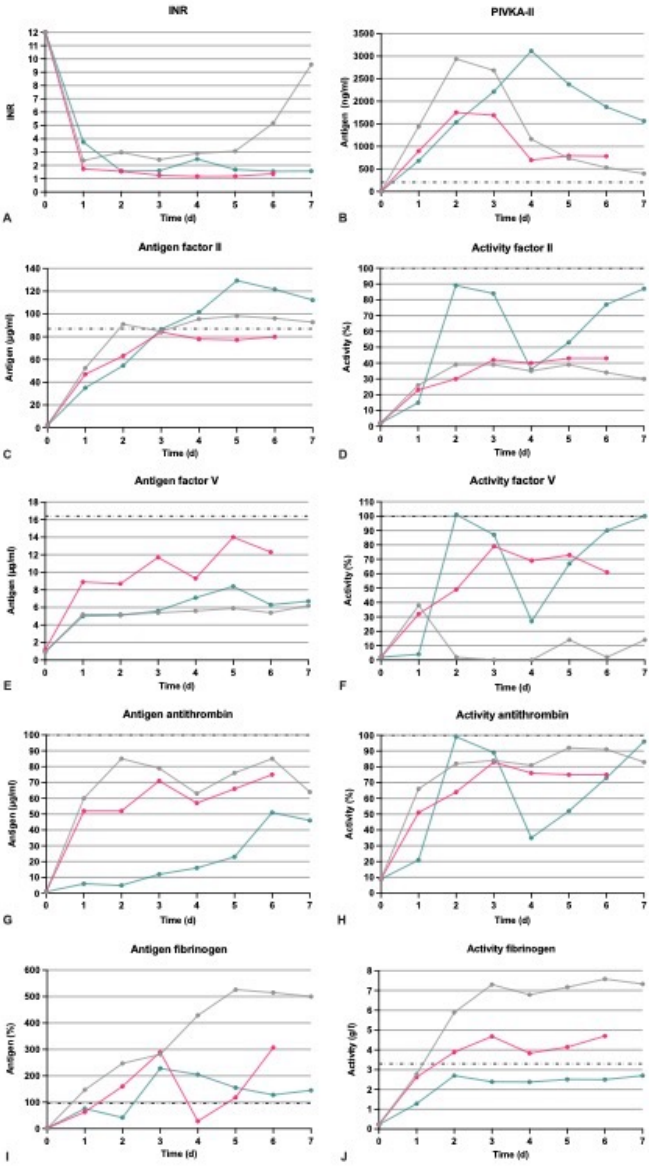
Background: Normothermic machine perfusion (NMP) is a novel method for *ex situ* preservation and/or testing of (extended) criteria donor livers prior to transplantation. During NMP, the liver is metabolically active, which enables functional assessment of the liver, including the production of hemostatic proteins. The aim of the study was to investigate the production, and activity of hemostatic proteins during long-term NMP of human livers up to 7 days.

Methods: Three discarded human donor livers underwent NMP with a perfusate based on red blood cells, albumin, colloids and parenteral nutrition, using a modified Liver Assist device (XVIVO, Groningen, Netherlands) for up to 7 days. Heparin was added to the perfusion fluid continuously. Perfusate samples were collected before the start of perfusion and daily thereafter. After *in vitro* heparin neutralization, international normalized ratios (INR) were analyzed. In addition, we measured antigen and activity levels of factor II and V, antithrombin, and fibrinogen, as well as levels of proteins induced by vitamin K absence (PIVKA-II).

Results: Perfusate INR values declined over time, which was accompanied by detection of substantial quantities of all analyzed coagulation proteins (Figure 1). Antigen and activity levels of factor V and antithrombin increased to a similar extent resulting in a specific activity comparable to pooled normal plasma (PNP). The specific activity of factor II and fibrinogen was substantially decreased compared to PNP. The lower specific activity of factor II was accompanied by elevated levels of PIVKA-II.

Conclusions: During *ex situ* NMP of human donor livers, hemostatic proteins are produced in substantial quantities, resulting in stable perfusate protein levels after a few days of perfusion, and forming a plasma like perfusate. This may indicate establishment of an equilibrium between the production and clearance of these proteins. However, this might also result in coagulation problems during perfusion, that needs to be addressed with a different anticoagulation approach.

Figure 1: Antigen and activity levels of hemostatic proteins in perfusate during normothermic machine perfusion of human livers. The dashed lines indicate values in pooled normal plasma (PNP).



P146 NO QUICK-FIX IN DETECTING SARCOPENIA IN PATIENTS ENLISTED FOR KIDNEY TRANSPLANTATION - MEASUREMENTS OF PSOAS MUSCLE

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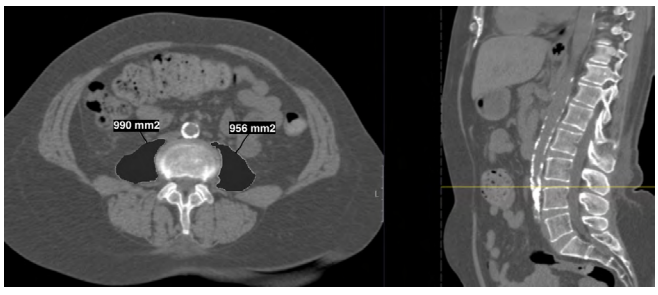
Background: Frailty is associated with inferior outcomes after kidney transplantation (KT). Age related reduction of muscle mass, sarcopenia, can serve as a marker of physical frailty. In heart-, lung- and liver transplant recipients, low psoas muscle area has been associated with increased mortality and risk of post-operative complications. Any association between pre-transplant psoas muscle area and outcomes after KT has not been described. We aimed to evaluate the association between pre-transplant psoas muscle area and postoperative complications and death in KT recipients older than 55 years.
Methods: A single center retrospective case-control study was performed. Data from 639 de novo kidney transplanted recipients > 55 years transplanted between January 1st 2011 and December 31st 2015 were evaluated. Twenty-one cases who were admitted to the intensive care unit (ICU) for more than 24 hours during the first seven days after KT were identified and compared with 42 controls without any ICU stay. The cases and controls were matched with respect to age, gender and comorbidity. Psoas area was assessed using CT scans taken as a part of the routine work-up for kidney transplantation and a psoas muscle index (PMI) was calculated as total psoas area divided by the square of the body height. Sarcopenia was defined based on our data as PMI less than the gender specific median or less than the gender specific 25 percentile.
Results: Good quality CT scans were available in 60 recipients. Results are presented in table 1. We found no statistical difference in PMI of cases and controls. There were no associations between pre-transplant PMI and post-transplant ICU admission or death.
Conclusions: Our findings indicate that a single pre-transplant measurement of psoas muscle area as an indicator of sarcopenia has limited value in the risk evaluation of KT candidates above 55 years of age.

	> 24 hr. ICU (N=21)	No ICU (N=41)	P-value
Age (years)	66,8 ± 7,5	66.8 ± 6.9	0.98
Male gender	15 (75 %)	30 (75 %)	1.00
Psoas area (cm^2)	21.99 ± 5.77	22.59 ± 6.49	0.72
PMI (cm^2/m^2)	7.3 ± 1.7	7.4 ± 1.8	0.82
Sarcopenia_median	11 (52 %)	21 (51 %)	1.00
Sarcopenia_25	6 (29 %)	9 (22 %)	0.76
Comorbidity score	5.05 ± 3.69	2.73 ± 2.58	0.02
Time between CT scan and Tx (months)	23.4 ± 4.9	18.3 ± 2.6	0.07
Living Donor	2 (10 %)	9 (23 %)	0.39
Dialysis vintage (months)	28.1 ± 22.3	19.6 ± 18.8	0.15



P147 UTILIZATION AND CLINICAL OUTCOMES OF SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION FROM OLDER PANCREAS DONORS

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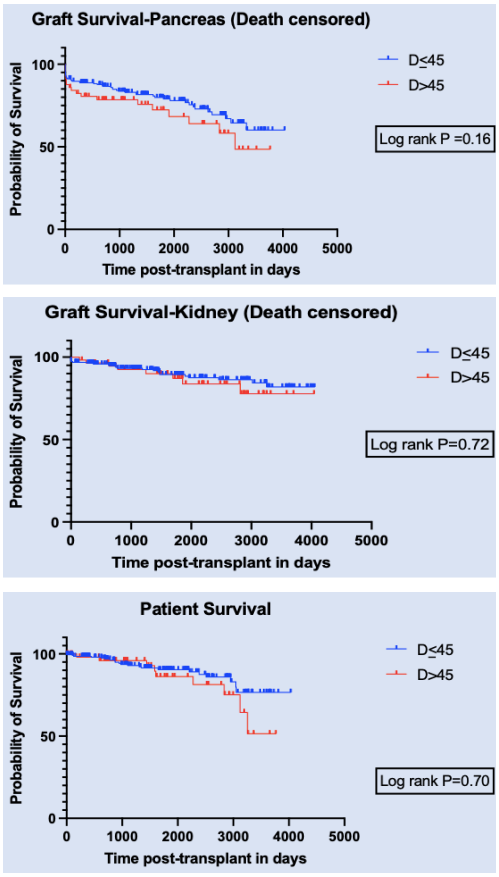
Background: Donor pancreas utilisation rates for transplantation are inferior to that of other organs. Despite the revised NHSBT donor age limit (DBD<61-years/DCD<56-years), pancreas utilization rates from donors >45-years remain low due to the perceived poor outcomes. Hence, we aimed to investigate the outcomes of simultaneous pancreas & kidney (SPK) transplants from donors >45-years & their utilisation rate in our cohort.
Methods: Our centre's data on all SPK transplants performed and named SPK offers received between 01-01-2010 to 31-12-2020 was retrospectively analysed. The primary aim was to compare the pancreas graft loss (3-month & 1-year) and long-term survival between SPK transplants done from donors aged ≤45-years (D≤45) & >45-years (D>45). The secondary aim was to compare the utilisation rates between the two groups. Appropriate univariate & multivariate analysis were performed.
Results: 276 transplants were done and the baseline characteristics as in table-1. The 3-month & 1-year pancreas graft loss were comparable between D≤45 & D>45 cohorts (8.6% vs. 14.03%, p=0.21; 10.9% vs. 19.29%, p=0.09, respectively). The overall patient survival and death-censored dual graft survival was comparable (figure-1). In a cox proportional hazards regression model, donor age>45-years was not at increased risk for pancreas graft loss (HR 1.57, CI 0.89 to 2.69, p=0.10). Among the 2574 named offers received, 55% were from D>45 group (median donor age-54-years; IQR 50-57). The offer decline rate was significantly higher in the D>45 group (96.34% vs. 83.57%, p<0.0001). 13.1% (180/1371) of the offers in the D>45 group were declined solely based on the donor's age.
Conclusions: We are the first to report utilisation and outcomes from older donors. We are likely to be more selective in accepting these donors. Survival outcomes from this under-utilised cohort are equivalent to younger donors, thereby supporting the usage of older pancreas donors to improve organ utilisation.

Table-1:

Donor/ recipient/ transplant characteristics	Donor age > 45 (n=57)	Donor age ≤45 (n=219)	P value
Median donor age (IQR)	51 (48-54)	26 (19-36)	<0.0001
Median donor BMI in Kg/sq.m (IQR)	24.5 (22.7-26.8)	22.7 (20.5-25)	<0.0001
Median donor abdomen girth in cms (IQR)	94 (83-97)	80 (74-89)	<0.0001
Proportion of non-Caucasian donors (Number)	10.52% (6/57)	7.76% (17/219)	0.50
Proportion of non-traumatic COD (Number)	96.49% (55/57)	89.04% (195/219)	0.08
Proportion of local donors (Number)	26.31% (15/57)	23.74% (52/219)	0.68
Proportion of insulin use in donors (Number)	50.87% (29/57)	35.15% (77/219)	0.03
% of heavy alcoholic (>9 U/day) donors (Number)	61.40% (35/57)	56.16% (123/219)	0.47
Median recipient age in years (IQR)	42 (36.5-49)	40 (34-48)	0.11
Median recipient BMI in kg/sq.m (IQR)	24.6 (21.8-26.6)	24.4 (22.1-27.2)	0.77
Median pre-Tx Insulin use in U/day (IQR)	40 (30-50)	40 (32-50.7)	0.29
Median duration of diabetes in years (IQR)	28 (23-36)	27 (22-32.5)	0.41
Proportion of sensitised recipients (Number)	24.56% (14/57)	30.13% (66/219)	0.40
Median waiting time in days (IQR)	528 (304.5-793.5)	458 (173-654)	0.10
Proportion of DCD Tx (Numbers)	17.54% (10/57)	38.81% (85/219)	0.002
Proportion of non-Caucasian recipients (Number)	3.50% (2/57)	5.47% (12/219)	0.54
% of recipients with non-favorable MM (Number)	93% (53/57)	97.26% (213/219)	0.12
Median CIT in mins (IQR)	690 (537-800)	653 (558-781)	0.87
Median WIT in mins (IQR)	38 (30-45)	36 (31-44)	0.74

Figure-1:



P148 DUAL INHIBITION OF THE COMPLEMENT SYSTEM AND TOLL-LIKE RECEPTORS PREVENTS SYSTEMIC AND LOCAL KIDNEY INFLAMMATION IN MICE EXPERIENCING BRAIN DEATH

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Background: Brain death (BD) induces a potentially harmful systemic inflammation, which may reduce organ quality for transplantation. The complement system (CS) and Toll-like receptors (TLRs) are key for the innate immune system both for recognition and response. The cluster of differentiation 14 (CD14) is a co-receptor for several TLRs, necessary for TLR signaling. We hypothesized that dual inhibition of CS and TLRs by complement protein 5 (C5) and CD14 inhibition will prevent innate immune-mediated inflammation during BD.
Methods: BD was induced with a fluid-filled intracranial balloon in wild-type C57/BL6 mice. Prior to BD, mice were left untreated (n=8), treated with a C5 inhibitor (n=7), a CD14 inhibitor (n=7), or both inhibitors (n=7). Sham mice did not experience BD and were left untreated (n=8). Blood and kidneys were collected three hours after BD. Inflammatory plasma cytokines were analyzed using a 23-plex immunoassay, kidney mRNA expression by qPCR.
Results: In plasma, BD significantly induced expression of interleukin-6 (IL-6), human IL-8 homolog, IL-12, monocyte chemoattractant protein (MCP-1), macrophage inflammatory protein MIP-1α, and MIP-1β compared to sham (all $p<0.01$). In kidneys, BD significantly induced IL-6, IL-8, TNF, MCP-1, P-Selectin, and VCAM-1 (all $p<0.01$). C5 and CD14 single inhibition significantly reduced BD-induced activation of all markers in plasma (all $p<0.01$) and in kidneys ($p<0.01$, except C5 inhibition for P-Selectin $p=0.06$). Dual inhibition of C5 and CD14 further reduced all plasma cytokines to levels comparable with sham animals (all $p>0.05$). In kidneys, double inhibition was comparable to single inhibition.
Conclusions: The innate immune system is crucial for inducing inflammatory reactions during BD. Inhibition of both the CS and TLRs is necessary to efficiently prevent BD-induced systemic inflammation and to reduce local kidney inflammation. CS and TLR inhibitors are clinically available and clinical studies should be performed on deceased BD donors to enhance donor organ quality.

P149 IMPACT OF COVID-19 SAFETY MEASURES ON NON-COVID-19 INFECTIONS IN SOLID ORGAN TRANSPLANT PATIENTS DURING THE PANDEMIC; A SINGLE CENTRE STUDY

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Background: Transplant patients are predisposed to a higher risk of infections due to the necessary immunosuppression they must take. During the COVID-19 pandemic, extra precautions were taken to reduce risk of transmission and avoid spread of the virus amongst the vulnerable population including immunocompromised patients. This study was undertaken to assess whether such precautions and measures had any influence on non-covid infections in transplant patients.
Methods: Data was collected retrospectively from health board clinical portal and Welsh government to cover 2 periods: pre-pandemic (March 2018- March 2020) and peri-pandemic (March 2020- March 2022). Data was collected for opportunistic infections (CMV, BKV) and notifiable diseases (Clostridium difficile, Norovirus, MRSA).
Results: There were 343 and 293 admissions for infections in the pre-covid and peri-covid cohort (median age 61 vs 53 years) respectively. Median length of stay decreased to 6 days in the pandemic compared to 9 days pre covid.
Pre-pandemic rates of infection were 22 and 1 for CMV and BKV respectively, compared to 7 CMV and nil BKV during pandemic. Clostridium difficile cases were similar between the groups (n=3). There were no cases of Norovirus and 1 case of MRSA pre and nil during the pandemic. UTI related admissions decreased by 5% during the pandemic.This decrease in the infection rates in peri-covid period compared to pre-covid were not statistically significant ($p<0.05$)
Conclusions: There was a reduction in CMV, BKV and MRSA during the pandemic amongst transplant patients. This suggests that measures designed to reduce COVID-19 infection also have the potential to reduce non-COVID infections

P150 THE QUALITY OF LIFE OF LIVING LIVER DONORS POST-DONATION: AN AMBIDIRECTIONAL COHORT STUDY

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Background: Living donor liver transplantation (LDLT) is an option for the donor liver shortage. A systematic review showed some impaired quality of life (QoL) parameters 3 months post-donation. This study compares the QoL of living liver donors (LLD) post-donation to pre-donation and to the QoL of the general Dutch population.
Methods: Donors are included from May 2004 to May 2023. Donors filled in Short Form-36 Health Survey (SF-36), and EuroQol-5 Dimension-5 Levels (EQ-5D-5L) pre-donation, and 3-, and 12- months post-donation. These 3 time points were compared with a reference (Dutch population) and with each other. Subgroup analyses were done for sex, age (<40 vs ≥40), donor hospital stay (<7 vs ≥7 days), and donor and recipient complications. For these factors and body mass index, multiple linear regression analyses were done.
Results: Forty-eight donors are included. For SF-36, mean Physical Component Score (PCS) was 91.5 pre-donation, 87.4 3 months post-donation, and 89.9 12 months post-donation. Mean Mental Component Score (MCS) was 87.6 pre-donation, 87.9 3 months post-donation, and 85.3 12 months post-donation. There were no significant differences between the 3 time points and all means were significantly higher than the reference (PCS: $P=0.004$, $P<0.001$, $P<0.001$; MCS $P=0.004$, $P<0.001$, $P=0.002$). Subgroup analyses showed a significantly 6.3 higher PCS pre-donation in older donors ($P=0.02$). Multiple linear regression showed no predictors of PCS and MCS. For EQ-5D-5L, mean Visual Analog Scale (EQ-VAS) was 82.5 pre-donation, 89.2 3 months post-donation, and 84.9 12 months post-donation. Mean composite Time Trade-Off (cTTO) was 0.97 pre-donation, 0.98 3 months post-donation, and 0.89 12 months post-donation. There were no significant differences between the 3 time points. Mean EQ-VAS 3 months post-donation ($P<0.001$) and cTTO at all 3 time points ($P=0.03$, $P<0.001$, $P=0.04$) were significantly higher than the reference. Subgroup analyses and multiple linear regression showed no significant differences or predictors.
Conclusions: QoL of LLDs 3 months after LDLT returned to their pre-donation QoL. Older donors report better physical QoL pre-donation than younger donors. QoL of LLDs is often higher compared to the general Dutch population. Our results show a faster QoL recovery than the current literature.

Table 1. SF-36 results.

	Reference	Pre-donation mean (SD) [min-max]	3 months post-donation mean (SD) [min-max]	12 months post-donation mean (SD) [min-max]	Time point differences
Physical functioning	83	99.4 (1.7) [95-100] P = 0.004*	96.5 (5.4) [80-100] P <0.0001*	93.8 (13.6) [50-100] P = 0.01*	-
Role physical	76.4	94.4 (16.7) [50-100] P = 0.15	79.2 (35.6) [0-100] P = 0.49	92 (26.7) [0-100] P = 0.003*	-
Role emotional	82.3	96.3 (11.1) [66.7-100] P = 0.008*	87 (25.9) [0-100] P = 0.008*	92.9 (26.7) [0-100] P = 0.01*	-
Energy/ fatigue	68.6	76.1 (17.6) [45-95] P = 0.24	80.3 (11.5) [55-100] P = 0.0007*	73.9 (16.7) [45-100] P = 0.25	-
Emotional well-being	76.8	82.2 (7.2) [68-92] P = 0.05	87.1 (6.4) [76-100] P <0.0001*	82.3 (14.4) [48-100] P = 0.18	-
Social functioning	84	95.8 (8.8) [75-100] P = 0.012*	97.2 (8.1) [75-100] P <0.0001*	92 (17.4) [37.5-100] P = 0.02*	-
Pain	74.9	88.1 (20.1) [37.5-100] P = 0.13	87.9 (22.2) [30-100] P = 0.02*	93.2 (11.7) [67.5-100] P = 0.0005*	-
General health	70.7	83.9 (11.4) [60-95] P = 0.02*	85.9 (13.2) [55-100] P = 0.0006*	80 (21.2) [40-100] P = 0.23	-
PCS	61	91.5 (6.9) [75-97.5] P = 0.004*	87.4 (13) [57.5-100] P = 0.0001*	89.9 (7) [39.4-100] P = 0.0006*	-
MCS	62.3	87.6 (10.1) [67.4-96.8] P = 0.004*	87.9 (8.9) [65.8-97] P <0.0001*	85.3 (5.4) [33.9-100] P = 0.002*	-

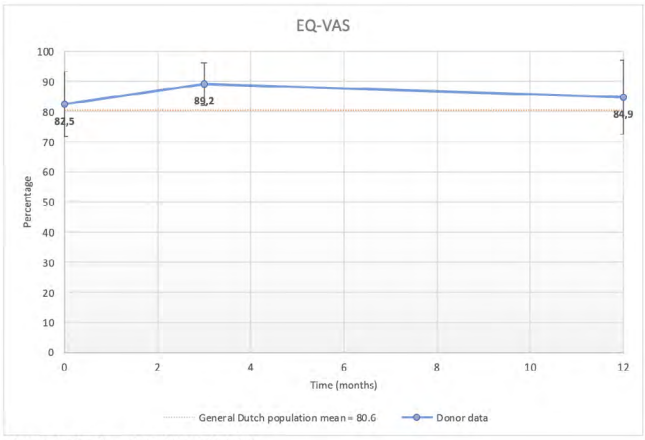

Figure 1. Scatter plot of the EQ-VAS.

P151 SUCCESSFUL KIDNEY TRANSPLANTATION WITH ARTERIAL RECONSTRUCTION FROM A DECEASED DONOR WITH MARFAN'S SYNDROME – A CASE REPORT

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Background: Despite growing awareness of recognizing potential organ donors and enhancement in transplantation procedures, the shortage of organs persists. This leads us to careful recognition of any contraindications for donation. Marfan's syndrome is a genetic disorder caused by a mutation in the extracellular matrix protein fibrilin-1 which leads to systemic dysfunction of connective tissue. Pathological manifestations of the syndrome include cardiovascular, skeletal and ocular systems. To our knowledge, transplantations from donors with Marfan's syndrome were only scarcely reported. The safety and efficacy of such organ donation remain unexplored
Methods: A 56-year-old woman with aortic dissection, with a previous diagnosis of Marfan's syndrome and arterial hypertension, was declared brain dead on the 5th day after emergency surgery. After careful recognition, she was considered a potential organ donor. Both kidneys and liver were harvested. At organ procurement It was also discovered that the right kidney has two independent arteries, which required arterial reconstruction. Subsequently, both kidneys were successfully transplanted performing an arterial anastomosis without the use of an aortic Carrel patch.
Results: Postoperatively, no major complications occurred. The recipient of the kidney with arterial reconstruction needed one course of hemodialysis. Both recipients were released from the hospital with abundant diuresis and decreasing serum creatinine level. In one year follow-up, patients remain stable with normal kidney function. Ultrasound examination of grafts shows no sign of arterial dysfunction.
Conclusions: Although transplantations of organs from donors with Marfan's syndrome might face technical difficulties and challenges, it seems they are both safe and efficient. Still little is known about the influence of genetic defect underlying Marfan's syndrome on renal function. Because of the high prevalence of vascular manifestations of Marfan's syndrome, the main concern remains about possible artery-related complications. Long-term follow-up will reveal more knowledge about the outcomes of such transplantations. In conclusion, Marfan's syndrome should not be considered a contraindication for organ donation.

P153 DIVERSITY OF CIRCULATING B CELL SUBSETS INRENAL TRANSPLANT RECIPIENTS EARLY POST-TRANSPLANT

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Background: B lymphocytes are actively involved in kidney transplantation. We aimed to assess frequency alterations of circulating B cell subsets 6 months posttransplant compared to pretransplant time point and associate them with stratification to donor type.
Methods: 39 kidney transplant recipients with good kidney function, eGFR>55ml/min/1.73m2, 8/39(21%) living donor, 21/39(79%) deceased donor, age 55(20–60) years, 8/39(21%) female, was the study group. The frequencies of 12 B cell subsets were determined by multiparameter flow cytometry pretransplant (T0) and 6 months posttransplant (T6).
Results: Analysis of B subset frequency from T0 to T6 revealed a statistically significant reduction in naïve (CD19+IgD+CD27-) p=0.003, transitional Bregs(CD19+CD24++CD38++) p=0.001, plasmablasts(CD19+IgD+/-CD27+CD38+) p=0.004 accompanied by a significant increase in the memory population (switched+nonswitched) p=0.037. Spearman's correlation coefficient with Bonferroni correction for 13 subsets frequencies (12 subsets and total B cells) at T0 and T6, gave negative correlation between naive and total memory p<0.001, switch memory cells p<0.001 and nonswitch memory p<0.001 and a positive correlation between total memory and nonswitch B cells p<0.001. Interestingly, the strong positive correlation between plasmablasts and transitional Bregs at T6 is associated with their significant frequency reduction at the same time point. Stratification according to donor type into living (G1) and deceased (G2) donors and evaluation of subset B frequencies showed a significant reduction in the naive cell population in both G1 and G2 groups p = 0.039 and p = 0.036, respectively at T6. However, only in group G2 a significant reduction of transitional Bregs p = 0.001 and plasmablasts p = 0.001 was detected. B subsets differed significantly between time points or groups did not correlate with age, gender or dialysis vintage.
Conclusions: B cell subsets analysis in kidney transplant recipients with good function, showed that both the deceased donor and living donor recipient groups had lower frequencies of naïve cells 6 months after transplantation. In addition, only the deceased group maintained low frequencies of transitional Bregs and plasmablasts, while the remaining subsets remained unchanged.

P154 ATHEROSCLEROSIS AND INTRARENAL RESISTANCE INDEX IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Atherosclerosis of the aortoiliac vessels can adversely affect kidney perfusion after kidney transplantation. Atherosclerosis severity can be determined using the calcium score (CaScore). Potential problems with post transplantation kidney perfusion can be determined using the intrarenal resistance index (RI). This study investigated the association between aortoiliac CaScore and RI in kidney transplant recipients.
Methods: Kidney transplant recipients (2004-2019), for whom the CaScore and RI were determined, were included in this dual-center cohort study. CaScore was measured in 3 aortoiliac segments using non contrast CT imaging. RI was determined using Doppler ultrasound. Multivariable linear regression analyses were performed between the CaScore and RI, adjusted for confounding variables.
Results: Mean age of the 389 included patients was 59 (±13) y. Mean RI (unitless) was 0.71 (±0.09) and median CaScore (unitless) was 3340 (399-7833). In univariable linear regression analyses with RI as the dependent variable, CaScore (β = 0.011; P < 0.001) was positively associated with RI. Moreover, recipient age (β = 0.014; P < 0.001), history of diabetes (β = 0.029; P = 0.003), recipient history of vascular interventions (β = 0.032; P = 0.002), prior dialysis (β = 0.029; P = 0.003), deceased donor transplantation (β = 0.042; P < 0.001), donation after cardiac death (β = 0.036; P = 0.001), an increase in cold ischemia time (β = 0.011; P < 0.001), and the Comprehensive Complication Index (β = 0.006; P = 0.002) were also positively associated with RI, whereas preoperative recipient diastolic blood pressure (β = -0.007; P = 0.030) was inversely associated. In multivariable analyses, CaScore and RI remained significantly (P = 0.010) associated, independent of adjustment for potential confounders. Furthermore, in univariable linear regression analyses, multiple graft function characteristics were associated with RI.
Conclusions: A significant association was found between CaScore and RI, independent of adjustment for multiple potential confounding factors, leading to a better insight into the development and interpretation of RI. Aortoiliac atherosclerosis should be considered when interpreting the RI and determining the possible cause of malperfusion and graft failure after kidney transplantation.

P155 COVID-19 EFFECT ON KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE COHORT STUDY

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Background: Kidney transplant recipients in immunosuppression are at particularly high risk of serious Covid-19 disease. Both the disease itself, as well as the reduction of the dosage of immunosuppression medications, may affect graft function after the recovery from the disease. In this retrospective cohort study, we investigated the role of Covid-19 disease on transplant function in vaccinated and not vaccinated recipients.
Methods: We recorded the vaccination status before the onset of Covid-19 disease in 544 patients followed in our clinic. eGFR and proteinuria were recorded in 101 patients before and 6-12 months after they had contracted the Covid-19 disease.
Results: Out of 544 patients, 156 (28.7%) have contracted Covid-19 and from those infected, 121 (77.6%) had been vaccinated with at least 2 doses of the COVID-19 vaccine. In 101 infected patients (48±14 years old), eGFR was similar before Covid-19 and after recovery [52.4(25.9) vs 54.5(26.9) ml/min/1.73m^2], and proteinuria also remained stable [180(261) vs 176(243) mg daily]. No significant differences were observed when we examined particularly the not vaccinated patients (46 out of 101, 45,5%) at the time of infection, as eGFR was similar before and after recovery [57.7(31.2) vs 57.8(34.5) ml/min/1.73m^2] and proteinuria increased only slightly after the infection [170(216) vs 119(199) mg, p=0.75].
Conclusions: Graft function, as assessed by eGFR and proteinuria, was not affected, in the long term, by Covid-19 disease in kidney transplant recipients, independent of their vaccination status.

P157 LIVER OR THYROID CANCER IN LIVING LIVER DONORS SHOULD BE MONITORED AFTER DONOR HEPATECTOMY

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Background: Living liver donors (LLDs) are screened for transmissible diseases including cancer. Outcomes following donation are excellent, but concern exists regarding the development of malignancy, and cancer risk is unknown. We investigated the actual cancer incidence of LLDs compared with a matched healthy control group from the general Korean population using data from the Korean National Health Insurance Services (NHIS).
Methods: 12,372 LLDs who donated a liver graft between 2002 and 2018, and were registered in the Korean Network for Organ Sharing. They were compared to matched healthy control group selected from the Korean NHIS.
Results: Cancer diagnosis was identified in 175 LLDs (1.4%) and 1,014 controls (0.8%). The incidence of liver and thyroid cancer in the LLD group is higher than in the healthy control group. The incidence of 11 specified cancers incidence was not different between the two groups.
Conclusions: Present study suggests that liver and thyroid cancer screening in the LLDs should be routinely required after donor hepatectomy.

P158 THE EVACADE STUDY: DD-CFDNA FOR DIAGNOSIS OF ACUTE REJECTION IN KIDNEY TRANSPLANTATION ON BEHALF OF THE SPANISH WORKING GROUP ON TRANSPLANT IMMUNOLOGY

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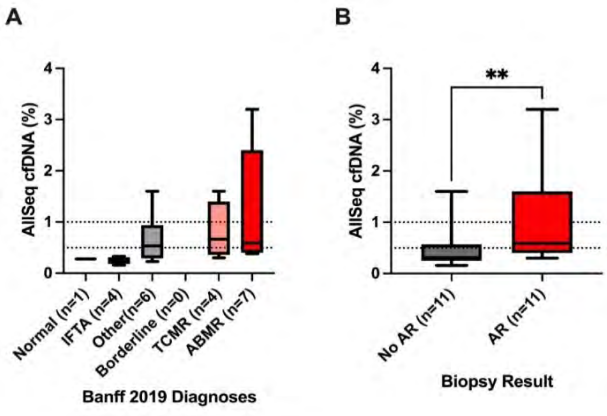
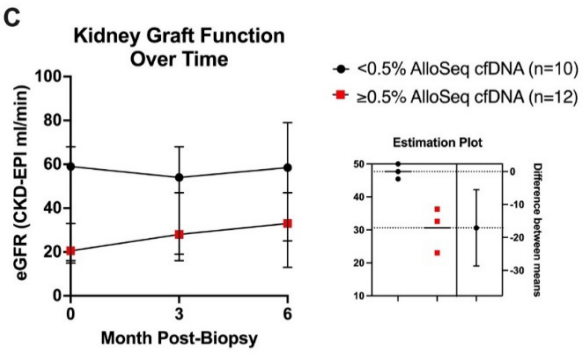
Background: Noninvasive surveillance with routine monitoring of donor-derived cell-free DNA (dd-cfDNA) after kidney transplantation may identify the risk of allograft injury. The availability of standardized high-throughput methodologies across centres might open the opportunity to conduct dd-cfDNA testing in a clinical routine basis with short turn-around times. We aimed to validate the clinical performance of dd-cfDNA as a surrogate marker of active acute rejection (aAR) for the identification of allograft injury, based on histology Banff 2019 criteria diagnoses, in kidney transplant recipients (KTr) with a follow-up of 6 months to assess clinical outcomes
Methods: The EvAcADE is a multicentric cross-sectional study enrolling KTr at clinical suspicion of allograft injury undergoing indication biopsy. Since January 2022, 42 patients have been included from twelve different Spanish Renal Transplant Units. So far, dd-cfDNA data were available from 22 patients for trend analysis. Overall, blood was drawn paired with biopsy at each site, whereas dd-cfDNA fraction from plasma samples was quantified in a centralised laboratory using the AlloSeq® cfDNA assay (CareDx®). The U-Mann Whitney and unpaired T tests were used, accordingly, with $p<0.05$ as statistically significant
Results: 50% (n=11) of the indication biopsies had histology classified as rejection. Antibody-mediated (ABMR) and T-cell mediated (TCMR) rejection had higher levels of dd-cfDNA compared to other Banff categories (IFTA, pyelonephritis, BKV, PTLD, recurrent or *de novo* glomerulonephritis, pyelonephritis or drug-induced interstitial nephritis) (Fig1A). dd-cfDNA at the time of biopsy was significantly elevated in patients with aAR compared to those without aAR (0.57 % vs 0.31%, p=0.008) (Fig1B). Elevation of dd-cfDNA (≥0.5%) was significantly correlated with reduced estimated glomerular filtration rate (eGFR) (p=0.01) (Fig1C)
Conclusions: Testing for dd-cfDNA fraction in plasma efficiently discriminates aAR at the time of clinical presentation. Both ABMR and TCMR elevated dd-cfDNA levels. dd-cfDNA values ≥0.5% were associated with declined renal graft function. Laboratory testing for dd-cfDNA could be a feasible and interesting tool to non-invasively predict clinically significant events and renal allograft injury





P159 NEUTROPHIL-TO-LYMPHOCYTE RATIO AND FRAILTY: HIGHLY PREDICTIVE TOOLS FOR CYTOMEGALOVIRUS INFECTIONS IN KIDNEY TRANSPLANT PATIENTS

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Background: Cytomegalovirus (CMV) infection is the most common viral complication after kidney transplant (KT) which is associated with significant morbidity, graft rejection, failure & mortality in KT recipients. Medical frailty has been associated with poorer post-operative outcome. Neutrophil-to-lymphocyte ratio (NLR), a novel inflammatory marker, has also been associated with worse prognosis in KT. Yet, there is limited data investigating the relationship of these variables with CMV infection risk in KT recipients.
Methods: A single-centre, retrospective study of KT recipients was conducted between April 2017 to December 2017. Data on the recipient characteristics, frailty (5-point Modified Frailty Index) at the time of transplantation, inflammatory markers up to 3 days post-transplant, patient outcomes including CMV incidence were recorded up to 1 and 3-year time points. Area under curve of NLR (AUCNLR) on day of KT to day 3 after KT were calculated as a single numeral value for each individual recipient. Mann-Whitney & Chi-square test were used to analyse the relationship between the variables & 2-month CMV infection.
Results: Of 92 KT recipients included in this study, CMV infection occurred in 29 (31.5%) patients. There is a significant difference in AUCNLR between the CMV & non-CMV group (*p=0.016*) with a cut-off value of 41.4. There is also significant association between frailty and CMV (*p=0.008*) with a cut-off frailty score of 2. When stratified by AUCNLR and frailty, statistical significance is demonstrated across all 4 groups (*p<0.001*) (Table 1).
Conclusion: Preliminary analysis suggests frailty & reduced NLR are associated with a higher risk of post-transplant CMV infection in KT patients. Our findings corroborate the existing research in that frailty is linked with worse post-operative outcomes. NLR from 0-3 days and MFI score at index admission are readily accessible tools for clinicians to predict CMV infections – a potential for personalised and stratified management.

Table 1: Outline of patient cohort's CMV outcomes based on classification of AUCNLR & frailty

Total Cohort	2-month CMV incidence		Percentage of CMV-positive patients
	Yes	No	
AUCNLR<41.4, Frail (MFI-5 >2)	7	1	87.5%
AUCNLR<41.4, Non-frail	11	20	35.6%
AUCNLR>41.4, Frail	4	7	36.4%
AUCNLR>41.4, Non-frail	7	35	16.7%
Total	n = 92		p < 0.001

P160 THE IBOX SCORE AS A PREDICTIVE FACTOR IN A RETROSPECTIVE KIDNEY RETRANSPLANT COHORT

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Background: Predicting kidney allograft survival as precise as possible and within a time frame which is still allowing potential intervention to save the graft and the patient's wellbeing is absolutely desirable. Several factors impacting long-term outcome after kidney transplantation are known, but there are hardly any clinical applicable scores available. The iBox algorithm, developed by the Paris Transplant Group, predicts individual long-term kidney allograft survival for 3, 5 and 7 years.
Methods: The iBox algorithm, including time from transplant, eGFR, proteinuria, anti-HLA donor-specific antibody MFI and biopsy result was applied retrospectively to kidney retransplantations (2nd and 3rd transplants) performed at the Medical University of Innsbruck. The iBox score was calculated with values and parameters on postoperative day 7, 6 and 12 months post-transplant. Donor, recipient and transplant demographics were collated; Cox regression and Kaplan-Meier survival analyses were performed.
Results: Ninety-five retransplants, 75 2nd and 20 3rd, were analysed. Median recipient age was 49 (21-73) and median donor age was 48 (0-73) years. Mean±SD recipient and donor BMI were 22.9±3.2 and 26.3±5.7 kg/m^2. Median panel reactive antibodies were 43 (0-100)%. Mean±SD cold ischemia time was 15.6±4.8 hrs; mean±SD anastomosis time was 28±7 min. Nineteen (20%) kidneys were from ECD donors. Thirty-six (37.9%) patients experienced delayed graft function. Mean±SD eGFR at month 12 was 48.4±15.4 ml/min/1.73m^2; mean±SD serum creatinine at month 12 was 1.5±0.8 mg/dl. Overall, 16/95 (17%) patients lost their kidneys; median graft survival was 6 (1-20) years. Univariate analyses revealed month 6 and 12 iBox scores, eGFR and serum creatinine at month 12, donor age, ECD, donor BMI and anastomosis time as significant. Multivariate analyses detected the month-12 iBox score as the most important factor influencing graft survival, besides anastomosis time, and eGFR at month 12 (table 1). Graft survival stratified for an iBox score of more or less than 90% at month 12 was significantly better for the >90% group; log rank p=0.002 (figure 1).
Conclusions: In our cohort, the iBox score significantly predicts graft survival after a 2nd or a 3rd kidney retransplant. These findings have to be validated in a prospective study.

Table 1.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
don_BMI	.054	.037	2.089	1	.148	1.055	.981	1.135
WIT	.129	.052	6.247	1	.012	1.138	1.028	1.259
ECD	.628	.802	.614	1	.433	1.875	.389	9.031
crea_M12	1.290	.822	2.461	1	.117	3.632	.725	18.194
GFR_M12	.063	.029	4.745	1	.029	1.066	1.006	1.128
predi_M12_year7	-6.414	1.769	13.139	1	<.001	.002	.000	.053

P161 EARLY GRAFT FUNCTION USING PREDICTED DONOR RENAL CORTICAL VOLUME WITH CT IMAGE ANALYSIS

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Background: Recent advances in CT image analysis technology have contributed to the improvement of diagnostic performance and preoperative evaluation in various fields. For the kidneys, renal and renal cortical volumes can be estimated, allowing quantitative and objective evaluation. While graft nephron mass and donor-recipient size ratio are known to affect early renal function after living donor transplantation, this study aimed to identify donor and recipient factors from CT images that correlate with early renal function after living donor transplantation and to develop a prediction model for early renal function.
Methods: We evaluated 160 pairs of donors and recipients who underwent living donor renal transplantation at the Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital from April 2020 to December 2021. Three items, actual kidney weight, predicted renal volume and predicted renal cortical volume measured using Volume Analyzer based on CT images, were used as donor factors, and five items, preoperative weight, ideal weight, height, body surface area, and BMI, were used as recipient factors. These factors and serum creatinine levels at 1 month postoperatively were analyzed using Pearson correlations, and a predictive model of serum creatinine levels at 1 month postoperatively was created by multiple regression analysis.
Results: The recipient's early postoperative serum creatinine level correlated best with the donor's predicted renal cortical volume and recipient weight ratio, and a linear equation was calculated to predict early transplant renal function.
Conclusions: Donor renal cortical volume calculated from CT image analysis provides a reasonable prediction of early post-transplant graft renal function.

P162 SERIOUS ADVERSE REACTIONS AND SERIOUS ADVERSE EVENTS ANALYSIS IN ORGAN DONATION AND TRANSPLANTATION NETWORK FROM 2012 TO 2021

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Background: In the clinical risk management of our donation and transplantation network, serious adverse reactions (SARs) and serious adverse events (SAEs) are classified as follows: -serious adverse event: undesired and unexpected event that might cause the transmission of disease, disability or death; -serious adverse reaction: unintended response that causes disease, disability or death; -near miss: potentially serious adverse event that does not occur by chance or as intercepted in time; - sentinel event: particularly serious event or reaction that can lead to serious harm or death, denoting a system malfunction. At the notice, we assign a score to each event or reaction as the product of the values assigned to severity and likelihood of repetition. This score defines the seriousness of event or reaction related to its severity. With the help of a related color code, we identify the actions to implement in the corrective action. The aim of the study is to analyze the impact SAEs and SARs had on our organ donation and transplantation network from 2012 to 2021.
Methods: Data related to SAEs and SARs reported in the period 2012-2021 have been analyzed, detailing type of event reported, type of risk associated to the event (neoplastic, infectious, organizational, others), seriousness/severity of the event, phase of the process in which the event occurred, type of donor involved (deceased donor/living donor) and organs involved.
Results: In the period 2012-2021, 283 adverse SAEs and SARs have been reported. In most cases (68%) it was an adverse event. The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). In 10 years only 8 events have been classified of greater severity (3% of all the detections). Retrieval, back table surgery and transplantation were the most represented stages (35, 45 and 37 respectively), involving in 99% donation after brain death. In 51% kidney was organ concerned.
Conclusions: Reporting SARs and SAEs guarantees high quality and safety of donation and transplantation as long as it gives the chance to act quickly in order to correct system malfunction and prevent the recurrence of the event.

P163 SCOPING REVIEW OF CURRENT DEVELOPMENTS OF RADIONOMICS IN KIDNEY TRANSPLANTATION

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Background: Radiomics is increasingly applied to the diagnosis, management, and outcome prediction of various urological conditions. The purpose of this scoping review is to evaluate the current evidence of the application of radiomics in kidney transplantation, especially its utility in diagnostics and therapeutics.
Methods: An electronic literature search on radiomics in the setting of transplantation was conducted on PubMed, EMBASE, and Scopus from inception to 23 September 2022. A total of 13 studies were included.
Results: This review shows that radiomics in transplantation is in its initial stages of development and reveals the directions in which radiomics is developing its utility. Technology such as Optical coherence tomography (OCT) is a non-invasive procedure to build high-resolution optical cross-section images of the kidney cortex in situ and in real-time, which can provide histopathological information of donor kidney candidates for transplantation and to predict post-transplant function. Although the correlation of CT volume with renal function is well established, there are limited studies on radiomics for assessment of donor suitability. The most widely studied clinical utility of radiomics in kidney transplantation is its use as an adjunct to diagnose rejection, potentially reducing the need for unnecessary biopsies or guide decision for earlier biopsies to optimize graft survival. Contrast-enhanced ultrasound (CEUS) using microbubble-based contrast agents coupled to T cell- specific antibodies such as anti-CD3 and nuclear imaging using various labelled antibodies have been used to diagnose acute rejection in the renal allograft. This shows that radiomics has the potential to augment current clinical decision in the evaluation and management of both transplant donors and recipients.
Conclusions: Although radiomics in kidney transplantation is still in its infancy, it has the potential for large-scale implementation. Its greatest potential lies in the correlation with conventional established diagnostic evaluation for living donors and potential in predicting and detecting rejection and graft failure post operatively.

P164 FAILURE TO RESCUE RATE TO BETTER ANALYZE SURGICAL COMPLICATIONS AFTER 500 PEDIATRIC LIVING DONOR LIVER TRANSPLANTATIONS

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Background: This work reviews our monocentric series of pediatric living donor (LD) liver transplantations (LT) and tries to evaluate the potential interest of the failure to rescue (FTR) concept for surgical complications.
Methods: Between 1993 and 2022, a total of 792 primary pediatric LT were performed in our center, of which 500 LDLT (median 1.9 years; range 0.1-16.5 years). Main pre-LT diagnoses were biliary atresia (n=325, 65%), cholestatic diseases (n=55, 11%), metabolic diseases (n=45, 9%), liver malignancies (n=44, 8.8%) and other diagnoses. The repartition of left vs full-left liver graft was 98.5% (n=194) vs 1.5% (n=3) before 1-year old at LT, 96.8% (n=211) vs 3.2% (n=7) between 1- and 5-years old at LT, and 40% (n=34) vs 60% (n=51) after 5 years old at LT. All medical records of LDLT were retrospectively reviewed; minimal/median follow-up were 4 months / 7 years. The patient/graft survival, retransplantation rate and arterial/portal/biliary complications rates were analyzed with special interest for FTR (death after a complication). The FTR rates were calculated for the most frequent complications, for patients (FTRp) and grafts (FTRg).
Results: Overall 1- and 5-year patient survival were 94.5% and 92.1%, with a total of 40 deaths. In terms of graft survival, the 1- and 5-year rates were 92.7% and 89.8%, with 13 retransplantations. The 3- and 12-month retransplantation rates were 1% and 1.8%. The hepatic artery complications rate was 3.6% (n=18/500) with 14 thromboses and 4 extrinsic compressions; portal vein complications rate was 11.2% (n=56/500) with 32 thromboses and 24 stenoses; biliary complications rate was 20.2% (n=101/500) with 55 anastomotic strictures, 35 biliary leakages and 11 intra-hepatic stenoses with or without anastomotic strictures. Overall 4-month FTRp and FTRg were 10.8% (n=8/74) and 8.1% (n=6/74). Four-month FTRp / FTRg were 21.4% (n=3/14) / 14.3% (n=2/14) for hepatic artery thrombosis, 15.4% (n=2/13) / 15.4% (n=2/13) for portal vein thrombosis and 0% (n=0/15) / 0% (n=0/15) for anastomotic biliary stricture.

Conclusions: Our data suggests that the FTR concept would offer a tool for analyzing the missing link between patient morbidity and mortality. We think that the precise analysis of causes of FTR would allow quality improvement of post operative care in the field of pediatric LDLT.

P165 DONATION AFTER CARDIOCIRCULATORY DEATH IN PATIENTS OLDER THAN 70 YEARS

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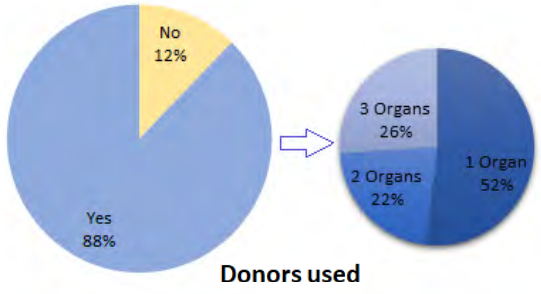
Background: Organ transplantation improves the quality of life and increases the life expectancy of patients with end-stage organ failure. The demand of organs for transplant is continually increasing given the aging population. In Spain, more than a decade ago, controlled asystole donation (CAD) emerged as a strategy to solve the shortage of organs available for transplant. Despite, there is not a stablish age limit in controlled asystole donors, exists an "unconscious bias" to reject asystole organs by age criteria. The main objective of this study is to determine if CAD in patients over 70 years of age is feasible in terms of the effectiveness of the donation and number of organs per real and used donor.
Methods: Retrospective observational study including donors in controlled asystole older than 70 years from November 2014 to December 2022 in a tertiary care hospital.
Results: During the study period, a total of 57 real controlled asystole donors were collected. Of the sample studied, the median age was 74.4 ± 2.6 years, being a most men (59.6%). Regarding to cardiovascular risk factors, 59.6 % patients suffered from arterial hypertension, 22.5% from diabetes and 21.1% from dyslipidemia. The most frequent blood type included was 0+ (50.9%) followed by A+ (35.1%) and B+ (8.8%). The median length of stay in the critical care unit before donation was 7 [1; 38] days. The analysis of the data showed an effectiveness of 87.7%, 50 donors used out of the total number of patients included. A total of 40 livers and 50 kidneys were valid and transplanted on their appropriate receptors. In 45.6% of the total of sample it was possible to use one organ, in 19.3% two organs and in 22.8% three organs, assuming a rate of 1.52 organs per real donor and 1.74 in donor used.
Conclusions: The effectiveness of the CAD in this age group is high (87.7%), similar to the Spanish average in previous years (87%). The rate of organs per donor it exceeds 1.5 organs by transplanted donor, which is enough to not dismiss a potential controlled asystole donor based solely on age criteria.



P166 NAÏVE T CELL-DEPLETED HEMATOPOIETIC GRAFT COMBINED WITH SOLID ORGAN TRANSPLANTATION AS STRATEGY TO INDUCE TOLERANCE

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Induction of tolerance by donor hematopoietic stem cell transplantation together with SOT is an active approach to avoid the chronic use of pharmacological immunosuppression and their adverse effects.
Objective: To present a model for inducing transient mixed chimerism in 2 patients undergoing SOT employing a non-myeloablative conditioning regimen and a partially T cell-depleted graft consisting of CD34+ hematopoietic progenitor cells and CD45RA− memory lymphocytes
Methods: Bone marrow harvesting was performed on the iliac crest and lumbar and dorsal vertebrae of the deceased donor for patient #1 and mobilized leukoapheresis from sibling donor for patient #2. First we obtained the enriched by CD34+ selection using the CliniMACS system (Miltenyi Biotec) and afterwards the CD45RA+ cell depletion. Lineage-specific chimerism analysis and Immune cell recovery was monitored
Results: Patient #1 15-year-old boy with intestinal epithelial dysplasia. After two previous intestinal trasplants. T cell depleted bone marrow graft from the same fully HLA mismatched deceased donor was done. After the infusion of CD34+ cells and CD3+CD45RO+ T cells, any degree of graft versus host disease has been observed, as well as no sign of rejection, with chimerism between 0,05 and 5,1%. Tacrolimus was withdrawal after 8 months. The patient receive only sirolimus as immunossupresor to maintain drug concentrations at 6 ng/ml. No signs of rejection were detected after 36 months of follow-up. Patient #2 49-year-old woman diagnosed with chronic kidney failure secondary to rapidly progressive glomerulonephritis. She had received three kidney graft previously. We performed CD34+ haematopoyetic progenitors and CD45RA- memory lymphocytes infusion in match related HLA living donor kidney transplant. Mixed hematopoietic chimerism was demonstrated during the first 3 months after SOT of between 0.1% and 40% of CD3+ cells. The patient continued on monotherapy with tacrolimus. The patient did not have acute rejection, graft versus host disease, viral reactivations during the 24 months of follow-up.
Conclusion: We describe for the first time the use of non-myeloablative conditioning and a CD45RA$^-$ T cell-depleted graft to induce transitory mixed chimerism using both hematopoietic progenitors and a solid organ, for tolerance induction purposes.

P167 MANAGEMENT OF BKV INFECTION AND NEPHROPATHY IN KIDNEY TRANPLANT RECIPIENTS; NINE YEARS OF EXPERIENCE

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Background: The treatment options, other than immunosuppressive dose reduction are very limited for BKV infected kidney transplant recipients. In this study, current treatment options, especially changing the standard treatment to everolimus/low-dose tacrolimus, were evaluated in patients who developed BKV infection or nephropathy after kidney transplantation (Ktx).
Methods: Data of patients with kidney transplantation between October 2013 and March 2022 were evaluated retrospectively in terms of BKV replication, development of BKV nephropathy and efficacy of treatment modalities. Serum BKV PCR was monitored monthly for the first six months and then every three months. The treatment plan was everolimus/low-dose tacrolimus shift in the first line after then, IVIG, Leflunamide or Cidofovir, depending on the clinical situation.
Results: A total of 646 patients were evaluated, 61 patients (9.4%) who had BKV replication (mean age 47.3±12.3 years, 67.2% males) were identified. Living donor Ktx was 91.8%, induction treatment was mostly anti-thymocyte globulin (90.2%). Everolimus/low-dose tacrolimus exchange was applied in all patients with BKV replication, complete response was obtained in 73.8% of patients and BKV PCR became negative, partial response (BKV PCR >50% regression) was observed in 13.1% of patients. Nine patients did not respond to first-line treatment; complete response was obtained with IVIG in one patient and partial response with IVIG + Leflunamide in one another. Various combinations of cidofovir, IVIG/Leflunomide were used in a total of seven patients, partial response in only one patient, impaired allograft function in three patients, and allograft loss in three patients. Allograft function was preserved according to the basal creatinine level (1.16±0.36mg/dl vs. 1.58±1.06mg/dl, p=0.81) in those who responded to treatment in the first step.
Conclusions: Replacing standard immunosuppressive therapy with everolimus/low-dose tacrolimus/steroid is the most effective approach in BKV infection developing after kidney transplantation. Early intervention with frequent BKV replication monitoring is appropriate for treatment effectiveness. Current treatment options seem unlikely to be successful in patients who do not benefit from first-line immunosuppressive changes.

P169 ASSESSMENT OF DD-CFDNA IN KIDNEY TRANSPLANTATION AS A MARKER OF GRAFT INJURY – A PROSPECTIVE STUDY

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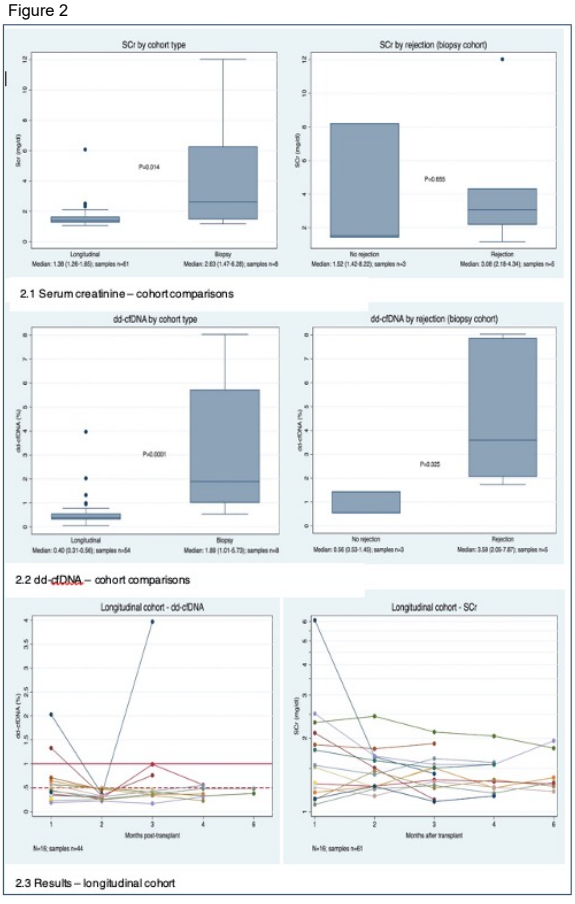
Background: Cell-free DNA (cfDNA) refers to DNA fragments originating from donor organ cell injury and death, increasing donor derived-cfDNA (dd-cfDNA) plasma levels - a correlation between this increase and graft injury was shown previously.
Methods: We prospectively assessed dd-cfDNA role as a kidney graft injury marker, defining 2 cohorts: longitudinal cohort (LC), with samples collected from all *de novo* kidney transplant recipients at months 1, 2, 3, 4, 6, 9 and 12 post-transplant; biopsy cohort (BC), with samples collected at biopsy time for clinical indication and 4 and 8 weeks afterwards.
Results: Twenty-four patients were included (8 from BC). Median age was 57 years (IQR 42-60). Remaining characteristics are listed in figure 1. As expected, dd-cfDNA was higher in BC and remained low and stable in most LC patients (figure 2). In 44 LC samples, only 3 had dd-cfDNA > 1%: one sample (2,03%) was miscollected only 5 days after transplant with delayed graft function, so tubular injury may be culprit, though persistent elevation at month 3 (4%) in the same patient remains unexplained. In other sample, a dd-cfDNA of 1.4% at month 1 coincided with COVID infection. In the 8 BC patients there was a clear dd-cfDNA segregation between rejection status (median 3,59% with *vs* 0,56% without; p=0,025). This wasn't observed with serum creatinine (sCr). In those with rejection (5/8), dd-cfDNA at biopsy varied between 1.73-8.03%, all reducing to <1% at 1 month. Four of these 5 had *de novo* donor-specific antibodies (DSA). In the only antibody-mediated rejection case, dd-cfDNA normalized during follow-up, as DSA and proteinuria disappeared. The highest dd-cfDNA case (8.03%) had the lowest graft function by end of follow-up (sCr 4.39 mg/dL). The only non-rejection biopsied case with a dd-cfDNA > 1% (1.45%), had contemporaneous significant BKV viremia (peak 52k copies), successfully treated with stable renal function and dd-cfDNA reduction.
Conclusions: In our data, dd-cfDNA was higher when dysfunction was caused by rejection and outperformed sCr distinguishing stable (LC) from injury (BC) cases. Reduction of dd-cfDNA after biopsy did'nt correlate with function improvement. Furthermore, the magnitude of the elevation may correlate with rejection severity, *de novo* DSA and prognosis. This needs validation with more cases and follow-up.

Figure 1

	Total; N=24	Longitudinal; N=16	Biopsy; N=8	P
Age, median (IQR)	57 (42-60)	57(47-62)	48 (38-59)	0.312
Female R, n (%)	10 (42)	6 (38)	4 (50)	0.673
Retransplant, n (%)	5 (21)	3 (19)	2 (25)	1
Living donor, n (%)	7 (29)	5 (31)	2 (25)	1
Preformed DSA, n (%)	3 (13)	2 (13)	1 (13)	1
Number of dd-cfDNA (total)	62	44	18	-
Number of dd-cfDNA, median (IQR)	3 (2-3)	3 (2-4)	2 (2-3)	0.324
Indication for biopsy	-	-	7: graft dysfunction; 1: proteinuria	-
Months since KT, median (IQR)	1.2 (0.9-3.4)	1.0 (0.7-1.2)	9.4 (3.4-13.6)	**<0.001**
Scr*, median (IQR)	1.54 (1.27-2.42)	1.42 (1.23-1.99)	2.63 (1.47-6.28)	0.062
Proteinuria*, median (IQR)	0.26 (0.20-0.66)	0.24 (0.20-0.40)	0.51 (0.22-4.05)	0.150
Acute rejection, n	-	-	5	-

Figure 2



P170 EX VIVO NORMOTHERMIC CIRCULATION (PNEV) OF GRAFTS FROM DCDS. AN EXPERIMENTAL STUDY OF BIOCHEMICAL AND METABOLIC CONDITION

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Background: Organs from donors after circulatory deaths (DCD) show an increased susceptibility to prolonged periods of warm and cold ischemia resulting in increased rates of delayed graft function and non-functioning grafts. Efforts should be directed towards improving the criteria for their use and optimizing their viability during preservation. Ex vivo normothermic perfusion (EVNP) would maintain the aerobic metabolism of the graft by providing it with oxygen and nutrients.
Methods: In a porcine model, kidneys were exposed to 30 minutes of warm ischemia and randomized to 1 of 2 study groups with a short (4 hours) or long (18 hours) period of static cold storage (SCS) followed by a 2-hour period of EVNP using a cardiopulmonary bypass and blood perfusion solution. Viability assessment included renal and tubular function, acid-base balance, histology, oxygen consumption and Hosgood viability score (macroscopic appearance of the graft, renal blood flow and urine output) that determines low (1-2), moderate (3-4) or high risk (5). Renal damage molecules (KIM1, NGAL), inflammation (NFkB, iNOs) and cell stress response (SOD1) were estimated by immunohistochemistry.
Results: Data are presented for 12 grafts undergoing PNEV. HyperGlu [437.0 (428.0; 461.0)] mg/dl, hyperNa [163.0 (141.0; 168.0)] mEq/L and hyperosmolarity [269.5 (267.3; 271.8)] characterized blood perfusion solution. Oxygen consumption reached a maximum in the first hour of PNEV (7.0-8.5 mlO2/min/100g) and decreased markedly in the second hour (4.8-4.9 mlO2/min/100g), accompanied by a progressive increase in lactate and a deterioration in the macroscopic appearance of the graft. Severe alkalosis and hypocapnia resulted in increased oxidative stress. SOD1 staining also increased after normothermic preservation indicating strong antioxidant response of the tubular cells. However, histological study showed minimal tubular changes and increased Bowman's space as a sign of oedema. The grafts had a viability score of at least, 4 points corresponding to a "moderate" risk.
Conclusions: The need for cardiovascular by-pass equipment and the use of blood-preserving solution poses logistical challenges that limit the clinical application of EVNP. Optimization of PNEV should result in a decrease in the risk score of grafts for transplantation.

P171 SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT IPSILATERAL VERSUS CONTRALATERAL, A SINGLE UNIT EXPERIENCE

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Background: In simultaneous pancreas kidney transplantation (SPK) grafts are conventionally implanted controlaterally (cSPK), with the pancreas allograft (PG) on right iliac fossa and kidney allograft (KG) on the left. Ipsilateral implant (iSPK) of both grafts on the right side has been previously described but remains underutilised, potentially due to concerns regarding technical complications. We aimed to assess feasibility, safety and outcomes of an iSPK implantation technique.
Methods: A retrospective analysis of a contemporaneous database of SPK transplants was perfomed. Grafts laterality was noted (iSPK or cSPK) with implantation decision dependent on surgeon preference and recipient factors. Recipients' characteristics, surgical outcomes and graft and patient survival rates were compared.
Results: 162 SPKs were performed (cSPK n=126 and iSPK n=36) between 2015-21. Recipients' demographics, indications, diabetic burden and comorbidities were comparable between the groups. Cold and and warm ischaemia times, intraoperative time, rates of complications, reoperation and readmission comparison showed no statistically significative difference between the 2 groups (p=NS). Survival rates for grafts (iSPK=97.2% vs cSPK=91.2%, p=NS) and patient (iSPK=97.2% vs cSPK=98.4%, p=NS) at 1 year follow-up was comparable as well.
Conclusions: In our experience iSPK appears to be a safe and feasible alternative, with comparable outcomes to cSPK. With increasing experience, iSPK could be offered to a larger number of recipients as there are no deterious effects on KG outcome. iSPK may provide benefit in reduction of operative time coupled with preservation of the contralateral side for future transplants, impacting on longer term patient longevity.

P172 EARLY DETERMINATION OF FAST TACROLIMUS METABOLIZER STATUS IDENTIFY RISK OF REJECTION AND ALLOGRAFT SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Fast tacrolimus metabolizers kidney transplant recipients have a lower allograft function, but determination of Metabolic Status (MS)' patients can be difficult to assess in real life setting due to dosages modifications during the first months post-transplantation. We investigated allograft outcomes and function (eGFR) evolution depending on MS (Fast metabolizers: MS+ or not: MS), and the reproducibility of MS status during the first-months post-transplantation.
Methods: eGFR up to 5-years post transplantation was analysed using a linear mixed effect model at T*=1-month (main analysis); we also studied sub-cohorts at T*=2 to 6-months. Long-term allograft survival, occurrence of biopsy proven acute rejection (BPAR) and *de novo* Donor Specific Antibodies (dnDSA) were also assessed after adjustment on confounding variables.
Results: 1979 patients were analysed at T*=1-month, 44.9% were MS+, this status was reproducible during the first months for >80% of them. The 10-years allograft survival was significantly reduced for MS+ patients at T*=1-month (83.4%, 95%CI = [80.1% to 86.8%] vs 74.2%, 95%CI = [69.4% to 79.3%]). MS+ patients had a higher risk of occurrence of BPAR (HR = 1.40, CI95% = [1.09; 1.81], p = 0.0088), and a trend to a higher risk of dnDSA (HR = 1.32, CI95% = [0.97; 1.78], p = 0.0747). The confounder-adjusted mean eGFR at T*=1-month was lower for MS+ (-3.97 ml/min, 95%CI = [-5.55;-2.40]). Moreover, their eGFR increase between one and six months was reduced and their long-term eGFR kinetic was also worst.
Conclusions: MS+ status' deleterious effect on allograft occurs since the first month due to BPAR and probably to tacrolimus nephrotoxicity. Physicians may consider an immunosuppression adaptation in the early post-transplantation period in these patients.

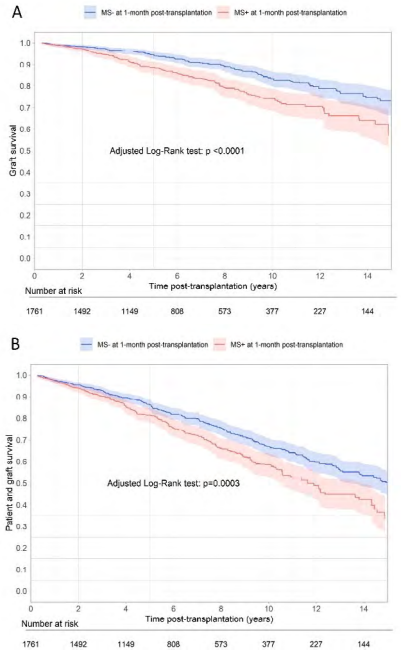

Figure. A Confounder-adjusted death-censored graft survival according to the MS status at 1-month post-transplantation estimated from the weighted Kaplan-Meier estimator in the cohort with a baseline set at T*=1-month post-transplantation. B. Confounder-adjusted patient and graft survival according to the MS status at 1-month post-transplantation estimated from the weighted Kaplan-Meier estimator in the cohort with a baseline set at T*=1-month post-transplantation.

P173 EVOLUTION OF HUMORAL RESPONSE TO SARS-COV-2 VACCINATION AFTER KIDNEY TRANSPLANTATION IN PATIENTS PREVIOUSLY VACCINATED WHILE ON THE WAITING LIST

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Background: Humoral response following mRNA vaccine is broadly acceptable in hemodialysis patients, contrary to kidney transplant recipients (KTR), due to their immunosuppressive status. We retrospectively studied anti-spike IgG titer evolution after transplantation for patients previously vaccinated while on waiting-list.
Methods: All KTR from 2 French university hospital vaccinated previous to transplantation with available serological assessement at the time of transplantation and afterward were included. Evolution of anti-spike IgG titer in absence of immune event (i.e. booster vaccine and/or Covid-19 infection) was investigated, as for the safety and efficiency of vaccine boosters during the first six month post-transplantation.
Results: 121 KTR were included in the analysis, among whom 50 received a booster during the first 6 months post-transplantation. In absence of any immune event, anti-spike titer decreased by 37.9% at M1, 44.4% at M3 and 63.9% at M6 post-transplantation; however, not reaching negativity in any patient. In those who received a booster vaccine after transplantation and with available serological assessement afterward, only 20% did not presented an increase in anti-spike titer. Allograft rejection occurred in 10.8% (n = 14) of the cohort; but only one patient out of seven presented a rejection after the vaccine booster. 35 patients presented a SARS-Cov-2 infection during the follow-up, only 3 of them required oxygen supportive care (8.6%), none of them died.
Conclusion: Humoral response of Covid-19 mRNA vaccines strongly decrease immediately after kidney transplantation, however remaining positive. Administration of vaccine booster in the first six-month post transplantation was safe and broadly efficient despite immunosuppressive therapies.

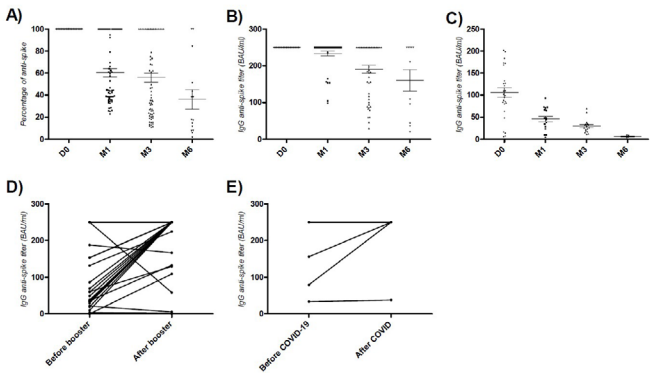

Figure. A) Evolution of the anti-spike titer (%), in absence of immune event during the first 6 months post-transplantation. B) Evolution of the anti-spike titer (BAU/ml) in absence of immune event in the HIGH POS sub cohort. C) Evolution of the anti-spike titer (BAU/ml) in absence of immune event in the LOW POS sub cohort. D) Impact of mRNA vaccine booster when administered during the first 6 months E) Impact of Covid-19 when occurring in the first 6 months post transplantation.

P174 ASSOCIATION BETWEEN HLA MOLECULAR MISMATCH AND HISTOLOGICAL REJECTION IN KIDNEY ALLOGRAFT

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Background: Conventional HLA serologic mismatch does not provide detailed risk of histologic rejection in kidney allograft. We hypothesized that molecular level of HLA mismatch load can predict future rejection at histologic level.
Methods: We assessed the association between molecular HLA mismatch load and Banff scores from kidney biopsies performed within 2-year after kidney transplant (KT). High resolution HLA typing was performed on 71 donor and recipient pairs from a previously reported prospective multicenter trial. HLA Matchmaker software was used to assess eplet mismatch and antibody mismatch load. Logistic regression was used to estimate the odds ratio for 1-unit change in HLA mismatch scores and Banff scores.
Results: Increased HLA class I eplet mismatch load is significantly associated with increased Banff tubulitis (t) scores (OR 1.04 [95% CI 1.00-1.08], P = 0.04) (Table 1A). The higher degree of HLA class II eplet mismatch is significantly associated with Banff t scores (OR 1.05, 95% CI [1.02-1.07], p=0.001), interstitial inflammation (i) (OR 1.04, 95% CI [1.01-1.07], p=0.01), glomerulitis (g) scores (OR 1.05, 95% CI [1.00-1.10], p=0.046), and arteriolar hyalinosis (OR 1.03, 95% [CI 1.00-1.07], p=0.04) (Table1B).
Conclusions: The degree of HLA class I and II elplet mismatch is associated with histologic evidence of rejection. Future study in a bigger cohort will be needed to address personalized immunosuppression approaches to prevent rejection depending on the HLA eplet mismatch load.

Table 1 A) Association between HLA Class I Eplets Mismatch Load and Banff Scores

Banff Lesion Scores	OR (Odds Ratio)	95% CI (low and high)	P value
t	1.04	1.00-1.08	0.04*
i	1.03	0.99-1.07	0.17
C4d	1	0.90-1.09	0.92
v	0.95	0.80-1.13	0.57
g	1	0.94-1.06	0.92
ptc	1.02	0.97-1.06	0.48
mm	1.01	0.98-1.05	0.44
ah	1.04	1-1.10	0.06
ct	1.00	0.97-1.04	0.84
ci	1.02	0.99-1.05	0.21
TG	1.07	0.83-1.38	0.61

Table 1B) Association between HLA Class II Eplet Mismatch Load and Banff Scores

Banff Lesion Scores	OR (Odds Ratio)	95% CI	P value
t	**1.05**	**1.02-1.07**	**0.001***
i	**1.04**	**1.01-1.07**	**0.01***
C4d	1.05	0.98-1.13	0.16
v	1.04	0.92 -1.17	0.53
g	**1.05**	**1.00-1.10**	**0.046***
ptc	1.03	0.99 -1.06	0.10
mm	1.03	1-1.05	0.05
ah	**1.03**	**1.00-1.07**	**0.04***
ct	1.01	0.98-1.03	0.56
Ci	1.02	1-1.04	0.1
TG	1.14	0.90-1.45	0.29

P175 METABOLIC ACIDOSIS INCREASES MORTALITY AND PROGRESSION OF CHRONIC GRAFT FAILURE IN PATIENTS LONG TERM AFTER KIDNEY TRANSPLANTATION

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Background: Metabolic acidosis (MA) is frequently diagnosed in patients after kidney transplantation (KTx). Results of both experimental and clinical studies suggest that MA may contribute to faster progression of chronic kidney disease. Data on such relationship in KTx patients are very limited. The aim of this clinical, single center, retrospective, observational study was to examine the relationship between MA and both mortality and renal outcomes in patients long term after KTx.
Methods: Blood HCO_3^- was measured in 486 patients (290 male; 196 female) aged 48 ± 12 years at least one year after KTx and subsequently all patients were observed during 7 years. MA was defined as the blood HCO_3^- concentration lower than 22 mmol/L. The endpoints in Kaplan-Meier survival curves analysis were death and initiation of dialysis therapy or retransplantation. Differences in survival curves were analyzed with log-rank test and were consider as significant when p<0.05. Relative risks (RR) were presented with 95% CI.
Results: MA was diagnosed in 57 (12%) patients being long term after KTx. The Kaplan-Meier curves analysis have shown that patients with MA earlier reach both endpoints during the follow-up (log-rank p=0.01 for death and p=0.001 for dialysis or retransplantation). In patients with MA the risks of initiation of dialysis therapy or retransplantation was significantly higher than in patients without MA [RR=2.51 (1.71-3.68), p<0.001]. Risk of cumulative endpoint of the study (death and initiation of dialysis therapy or retransplantation) was also higher in patients with MA [RR=2.28 (1.73-3.00), p<0.001].
Conclusions: MA increases mortality and progression of chronic graft failure in patients long term after kidney transplantation.

P176 LIVER GRAFT REDUCTION THROUGH EX-VIVO RIGHT POSTERIOR SECTIONECTOMY: SINGLE CENTER EXPERIENCE IN PREVENTING LARGE-FOR-SIZE SYNDROME

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Background: Transplantation of an extremely large liver into a small recipient can lead to Large for Size Syndrome (LFS) characterized by graft compression, impaired graft perfusion, and dangerous increase of intraabdominal pressure and consequently high risk of graft loss. To address this issue, in particular in situations of non-splittable grafts, one possible solution is to reduce the size of the transplanted liver. Especially the reduction of the right lobe of the liver has been shown to be effective in preventing LFS when significant size-mismatch between donor and recipient is expected. Recently, Pu et al. described an *ex-vivo* technique for performing graft reduction through a right posterior sectionectomy (RPS), reporting positive results in five patients. In this regard, we want to share our own experience using this graft reduction technique.
Methods: Single center retrospective analysis of reduced size dead donor liver transplantations (DDLT) performed during the period January 2018 to April 2022 using the *ex-vivo* RPS technique in young and pediatric recipients.
Results: In the study period, 7 patients underwent reduced-size DDLT through the *ex-vivo* RPS technique. Median age of recipients was 8 (range 2-18), with a M/F ratio of 1/6. Median weight and height were 36 kg (range 11-73) and 141 cm (range 89-163) respectively, and median body mass index (BMI) was 18 (range 13-27). All but one patient was transplanted as high urgency and received grafts through primary allocation. Grafts were non-splittable and had median ET-DRI score of 1.17 (range 1,09-1,89) as whole liver, and 1.99 (range 1,64-2,84) as partial liver. Median Graft-to-Recipient Weight Ratio (GRWR) was 4.7 (range 2,2-10,9) before and 2.2 (range 1,1-5,5) after RPS. Only one patient required delayed fascial closure. There were no cases of LFS postoperatively. One patient died 34 days after transplantation due to brain edema and herniation, and another patient required re-transplantation 22 days after initial transplantation due to severe ITBL and graft failure. Remaining patients had normal functioning grafts at their last follow-up.
Conclusions: The *ex-vivo* RPS-technique represents in our opinion a feasible surgical strategy to prevent LFS, in particular in small recipients and in the setting of high urgency or impossibility to split the graft.

P177 EFFECT OF RECONSTRUCTION TYPE OF DUAL ARTERIES ON LONG-TERM OUTCOME IN LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Dual renal arteries (DRA) in living donor kidney transplantation (LDKT) are causing technical challenges. Various reconstruction methods are applicable depending on the anatomy. One group has reported that the end-to-side DRA reconstruction method was inferior to other methods in graft survival. We tried to analyze the outcome according to the reconstruction method in the case of the DRA in LDKT.
Methods: Among the 374 patients who underwent LDKT at SNUBH from 2005 to 2021, 79 donors had DRA. Cases with 3 or more renal arteries were excluded. In the case of DRA, they were reconstructed to 5 different methods. (figure 1A). If two arteries were of similar size, they were connected side-to-side to make a single lumen (n=11), or each artery was connected to an internal or external iliac artery respectively (n=15). Additionally, we used internal iliac artery (IIA) and its branch for DRA anastomosis (n=29). If one artery was smaller than the other artery, the smaller artery was connected to the main renal artery end-to-side fashion (n=9), or the small artery was anastomosed to the inferior epigastric artery (n=15). The outcomes of each group were compared to the control group, a single renal artery (SRA) anastomosis (n=280).
Results: As for the short-term result, post-operative GFR did not differ among all six groups (p=0.167). (figure 1B). The 10-year graft survival was significantly lower in end-to-side and side-to-side groups compared to the SRA group (p<0.01 each). (figure 1C). The graft survival of IIA anterior and posterior division group did not show a significant difference compared to SRA group (p=0.878). (figure 1D). There was no significant difference in patient survival according to reconstruction type (p=0.162).
Conclusions: Our study showed that long-term graft survival was decreased in end-to-side and side-to-side reconstruction groups. This suggests that the reconstruction of those two methods should be avoided in DRA transplantation. Further study needs on the possible cause of these two methods being inferior to the others.

Figure 1A

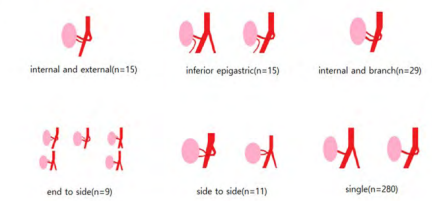


Figure 1B

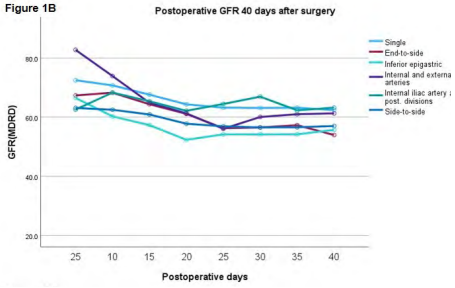


Figure 1C

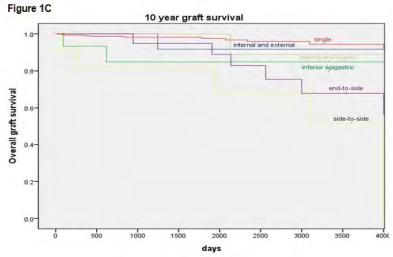
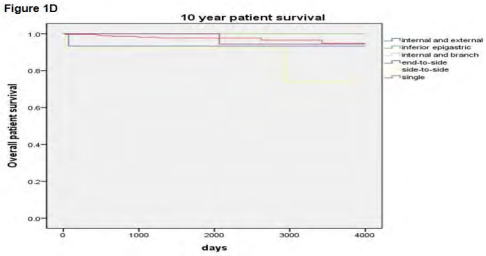


Figure 1D



P180 THE PREVALENCE OF DYSLIPIDEMIA BEFORE AND AFTER SUCCESSFUL LIVER TRANSPLANTATION

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Background: Liver transplantation (LTx) is the only successful treatment for end-stage liver disease. Long term results of LTx not only depend upon graft survival but it may be also affected by superimposed cardiovascular morbidities. This single center, retrospective clinical study was aimed to assess the prevalence of lipid disorders in patients before and after successful LTx.
Methods: One hundred eleven patients (mean age 49.7±12.2 years) who underwent LTx because of liver cirrhosis and survived at least 2 years with functioning graft were included in this study. The prevalence of dyslipidemia was assessed before and two years after LTx in relation to etiology of liver disease, including alcohol toxicity, viral infections or autoimmune diseases.
Results: The prevalence of hypertriglyceridemia before and at least 2 years after LTx was in the whole studied group 13.5% and 40.5%, respectively (P<0.001). Similarly hypercholesterolemia and hypertriglyceridemia together with hypercholesterolemia was noted before and after LTx in 17.1% and 51.4% (P<0.001) and 7.2% and 27.9%, (P<0.001), respectively. In patients with the autoimmune cause of liver cirrhosis the prevalence of dyslipidemia was significantly lower than in patients with the alcoholic liver disease: hypertriglyceridemia (18.5% vs 66.7%, respectively; p<0.001), hypercholesterolemia (29.6% vs 70.0%, respectively; p=0.002) and hypertriglyceridemia together with hypercholesterolemia (14.8% vs 46.7%, respectively; p=0.009).
1. The prevalence of dyslipidemia is significantly increased in patients after LTx in comparison to the pre-transplant results. 2. High prevalence of dyslipidemia is especially common in patients transplanted due to alcoholic liver cirrhosis and may contribute to the increased risk of cardiovascular complications in these patients.

P181 IMPACT OF HUANG'S CLASSIFICATION ON MANAGEMENT OF BILIARY STRICTURES IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Biliary complications remain the Achilles heel of living donor liver transplantation (LDLT). The anatomical variations in donor biliary anatomy have been shown to impact post-transplant biliary complications. The objective of this study was to assess the frequency of various anatomical variations and rates of successful management in patients who developed biliary complications.
Methods: All patients who underwent a right lobe graft LDLT at our centre between 2012 and 2018 were reviewed. Patients with incomplete data were excluded. Out of these, patients with biochemical and radiological evidence of post-transplant biliary stricture formation were included in the study (n=78). Huang classification was used for identification of graft biliary anatomy. We looked at clinical resolution rate for biliary strictures.
Results: Median age was 53 (14-70) and median follow up was 24 months. Among 78 patients who developed biliary strictures, the right lobe donor anatomy was Huang A1 in 50 (64.1%), A2 in 4 (5.1%), A3 in 16 (20.5%), and A4 in 8 (10.3%) grafts. Only 9 (30.8%) patients needed percutaneous biliary intervention after ERCP. The stricture resolution was seen in 49/50 (98%) patients with A1 biliary anatomy and 100% in A2 and A4 anatomy. Only 14/16 (87.5%) patients had resolution of strictures in the A3 Huang group. Patients in the A3 group required a median of 3 (1-10) ERCPs and 3/16 (18.8%) needed percutaneous biliary drainage.
Conclusions: Huang A3 graft biliary anatomy might be associated with lower rates of stricture resolution requiring multiple endoscopic and percutaneous biliary interventions.

Table 1: The frequency and outcomes in anatomical variants of the biliary system based on Huang's classification.

Anatomical Variant	Frequency Number (%)	Stricture Traversed Number (%)	Median number of ERCPs (range)	Percutaneous transhepatic biliary drainage Number (%)	Stricture Resolution Number (%)
Huang type A1	50 (64.1)	43 (86)	04 (1-8)	06 (12)	49 (98)
Huang type A2	04 (5.1)	04 (100)	2.5 (2-4)	00 (0)	04 (100)
Huang type A3	16 (20.5)	11 (68.75)	03 (1-10)	03 (18.8)	14 (87.5)
Huang type A4	08 (10.3)	05 (62.5)	03 (1-9)	00 (0)	08 (100)

P183 CLINICAL OUTCOME OF LUNG TRANSPLANTATION IN CONNECTIVE TISSUE DISEASE RELATED INTERSTITIAL LUNG DISEASE

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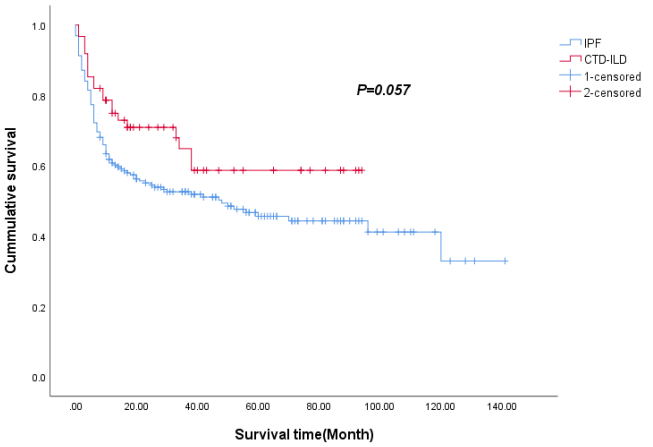
Background: Interstitial lung disease(ILD) is account for about half of the cause of lung transplantation. Idiopathic pulmonary fibrosis(IPF) is most common idiopathic interstitial pneumonia, other interstitial lung disease also ended to lung transplantation. Connective tissue disease(CTD) may affects the pulmonary system as interstitial lung disease. Although their severity and prevalence differ for each disease, some of them ended to death or lung transplantation. CTD patients are usually accompanied by other comorbidities, and transplantation in those patients is still challenging.
Methods: The electronic medical records of lung transplantation patients from January 2010 to December 2021 are reviewed and analyzed retrospectively. The clinical characteristics of CTD-related ILD(CTD-ILD) were compared with those of IPF.
Results: Total 400 patients underwent lung transplantation during the study period. CTD-ILD (n=61, mean age,51.1 years) were younger (P=0.004) than IPF (n=194, mean 29.4) and more like to be female(P<0.01). The myositis (n=17, 27.9%) was most common subtype followed by systemic sclerosis (n=15, 24.6%), rheumatoid arthritis (n=13, 21.3%), Sjögren's disease (n=11, 18%) and mixed connective tissue disease (n=2, 3.3%). The 5-year survival of transplantation associated CTD-ILD (58.7%) was not significantly (p=0.057) different from that of IPF (45.6%). The multivariate cox-regression analysis reveals that the age (Hazard ratio 1.05, P <0.001) at transplantation was associated with the mortality, not the pre-transplantation diagnosis(P=0.302).
Conclusions: The lung transplantation in connective tissue disease-related interstitial lung disease showed comparable clinical outcome with that of idiopathic pulmonary fibrosis.

Figure1. Kaplan-Meier cumulative survival curves for idiopathic pulmonary fibrosis(IPF) and connective tissue disease-related interstitial lung disease(CTD-ILD)



P184 48HR NORMOTHERMIC MACHINE PERFUSION WITH URINE RECIRCULATION FOR DISCARDED HUMAN KIDNEY GRAFTS: A CASE SERIES

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Background: Normothermic machine perfusion (NMP) has reshaped organ preservation in recent years. Despite great success in liver, lung and heart preservation, the role of NMP in renal transplantation has not been clearly defined. In this preclinical study, prolonged normothermic perfusions of discarded human kidney grafts were performed in order to investigate its feasibility, perfusion dynamics and identify potential quality and assessment indicators.
Methods: Five human discarded kidney grafts were perfused normothermically for 48-hours using the Kidney Assist device with a red-blood-cell based perfusate. For fluid management, urine recirculation was applied. Perfusion dynamics, perfusate and urine composition as well as pro- and anti-inflammatory markers were measured and analyzed.
Results: Donor age ranged from 41 to 68 years. Four kidneys were from brain dead donors, one from a donor after cardiocirculatory death. Four donors died due to a cerebrovascular accident, one due to anoxic brain injury. All kidney grafts were successfully perfused for 48-hours. Median arterial flow ranged from 405 to 841 mL/min. All kidneys excreted urine until the end of perfusion. While sodium levels were consistently lower in urine compared to perfusate samples, this was only seen for chloride and potassium in a single organ (KTX 2). Lactate metabolization was recorded in two organs (KTX 2 and 5). AST, LDH as well as pro-inflammatory cytokines increased over time, especially in kidneys KTX 3 and 4. Injury marker dynamics differed between different donor types and donor history.
Conclusions: Ex-situ normothermic machine perfusion of discarded human donor kidneys is feasible for 48-hours applying urine recirculation. Urine production was achieved throughout the perfusion irrespective of donor demographics. Lactate metabolization, pH and injury marker dynamics in prolonged perfusion might be indicators for organ quality.

Table 1. Demographics

	KTX 1	KTX 2	KTX 3	KTX 4	KTX 5
Donor Age (years)	62	68	51	41	65
Donor type	DBD	DBD	DCD	DBD	DBD
Cause of death	CVA	CVA	CVA	anoxic brain injury	CVA
Creatinine (mg/dL)	0.9	1.06	1.17	1.98 (RRT)	0.74
CIT total (hours)	27	19.5	19	28	11.5
Reason for discard	malignancy	poor organ quality	poor perfusion	poor perfusion	poor organ quality
Remuzzi Score	0	3	3	2	5
Comment				VV-ECMO sepsis	

P185 THE QUESTIONABLE BURDEN OF AB0 INCOMPATIBLE KIDNEY TRANSPLANTATION

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Background: AB0 incompatible kidney transplantation has become a genuine treatment method for end-stage renal disease. Non-inferiority in the long term graft function compared to AB0 compatible transplantation has been shown. However, the assumed burden due to complications owing to increased immunosuppression inherent to AB0 incompatible transplantation has not yet been quantified. The aim of this study was to determine if AB0 incompatible recipients have additional morbidity and whether this burden is justified or whether kidney paired donation programs should be advocated.
Methods: From January 2000 to March 2020 45 AB0 incompatible living kidney transplantation were performed at a tertiary care hospital. Patients were matched with AB0 compatible recipients according to sex, age, underlying disease, year of transplantation and duration of dialysis. Number and duration of readmissions, surgical complication rates according to Clavien-Dindo and its comprehensive complication index (CCI), kidney function, occurrence of new onset diabetes as well as tumour incidence were analysed.
Results: Readmission rate during the time span from transplantation to March 2020 was not significantly higher in AB0 incompatible recipients. The median difference in length of hospital stay for readmissions CCI during primary hospital stay and CCI for readmissions at 3, 6, 12 and >12 months after transplantation were comparable. Incidence of tumour and new onset diabetes after transplantation was not increased in incompatible recipients.
Conclusions: AB0 incompatible recipients do not suffer from a higher burden compared to AB0 compatible recipients. We currently recommend not delaying transplantation in AB0 incompatible pairs.

P187 PLASMA FGF21 CONCENTRATION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Fibroblast growth factor 21 (FGF21) is a protein hormone involved in the regulation of energy expenditure. Results of clinical studies suggest that plasma FGF21 concentration increases with the progression of chronic kidney disease (CKD). The aim of the present clinical study was to analyze the effect of successful kidney transplantation (KTx) on plasma FGF21 concentration and to study the factors related to plasma FGF21 concentration in patients long-term after KTx.
Methods: The first part of the study, i.e. the 6 months prospective observation, included 40 CKD patients directly before KTx [26 women and 14 men aged 47.0 (39.2 – 54.0) years]. In the second part of the study 184 patients long-term after KTx [72 women and 112 men aged 52.0 (48.0 – 54.0) years] and 50 healthy subjects (HS) [28 women and 22 men aged 52.0 (48.0 – 58.0) years] were enrolled.
Results: In CKD patients directly before KTx plasma FGF21 concentration were significantly higher than in HS [1013.0 (689.6–1635.8) pg/ml vs 239.5 (219.0–294.5) pg/ml respectively; p<0.001]. At 14, 30 days and 6 months after KTx, a significant decrease of plasma FGF21 was observed [322.5 (197.3–579.6) pg/ml; 355.0 (268.5–547.6) pg/ml; 344.0 (264.1–405.6) pg/ml (p<0.001), respectively]. In patients long-term after KTx, a negative correlation was found between plasma FGF21 concentration and estimated glomerular filtration rate and a positive correlations between plasma FGF21 concentration and BMI and serum concentration of triglycerides, insulin, interleukin 6, CRP and cystatin C.
Conclusions: 1. Plasma FGF21 concentration in CKD patients measured directly before KTx is higher than in HS. 2. Successful KTx leads to a significant decrease of plasma FGF21 concentration. 2. Plasma FGF21 concentration in patients long-term after KTx is related to the degree of graft function impairment and degree of metabolic abnormalities of these patients.

P188 PROGNOSTIC BIOMARKERS IN KIDNEY TRANSPLANTATION: A META-EPIDEMIOLOGICAL STUDY

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Background: Despite the increasing number of biomarkers studies published in the transplant literature for the past 20 years, very few have proved clinical benefit and have been implemented in clinical practice. We hypothesized that suboptimal design, data, methodology and reporting might have contributed to this phenomenon. Our goal was to perform a meta-epidemiological study of the prognostic biomarker studies in kidney transplantation.
Methods: We formed a consortium of experts in systematic reviews, nephrologists and methodologists. A systematic literature search was performed in Pubmed, Embase, Scopus, Web of Science, and Cochrane Library between 2005 and 2022. All original studies investigating the association between a biomarker and kidney-allograft failure were included. Any uncertainty in the full text assessment was resolved through weakly group discussions. Reviewers performed the critical appraisal of the studies with 45 recorded items for each study including: i) study basic characteristics, ii) transparency indicators, and parameters related to iii) the biomarker, iv) methods, v) results, vi) results interpretation.
Results: A total of 7,372 publications were screened and 804 studies met the inclusion criteria. A total of 1143 biomarkers were identified among the included studies. Most biomarkers were from blood (n=821, 71.8%), intra-graft (n=169, 14.8%), or urine (n=81, 7.1%). The number of studies per year was increasing. The top three countries in terms of publications were the USA (n=168 studies, 20.9%), France (n=66, 8.2%), and Germany (n=54, 6.7%). The median number of patients included was 232 (IQR: 96-629). The median follow-up post-transplant was 4.8 years (IQR: 3.0-6.2). 595 studies (74.0%) used data from a single center. Only 38 (4.7%) studies were externally validated. 346 studies (43.0%) did not adjust their biomarker for key prognostic factors. Data sharing, code sharing, and registration occurred in 71 (8.8%), 9 (1.1%), and 37 (4.6%) studies, respectively. 158 studies (20.0%) emphasized the clinical relevance of the biomarker while non-significant.
Conclusions: Biomarker kidney transplant studies lack validation, rigorous design, methods and interpretation, and transparency. Higher standards are needed for biomarker research.

P189 INCREASED TACROLIMUS TROUGH LEVELS IN KIDNEY TRANSPLANT RECIPIENTS WITH COVID-19

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Background: Kidney transplant recipients (KTRs) with coronavirus disease-19 (COVID-19) have similar clinical manifestations to general population. However, KTRs are more vulnerable to develop severe forms and the mortality rate is higher in this category compared to general population, this is due partly to the use of immunosuppressive agents. The variability of tacrolimus levels in patients infected with SARS-COV-2 virus is unknown. The purpose of this study is to determine the impact of COVID-19 infection on tacrolimus trough concentrations (C0) in KTRs.
Methods: In this single-center retrospective observational study, data were collected from patient medical records, and therapeutic drug monitoring database. Tacrolimus C0 of 25 KTRs (n=25) during COVID-19 infection were compared to their prior-to and post-infection values. Patients were stratified based on presence or absence of diarrhea as symptom. The use of concomitant macrolides during COVID-19 infection was noted.
Results: The median tacrolimus C0 during COVID-19 infection was elevated (9,6 ng/ml) compared to prior-to (6,6 ng/ml, p = 0.003), and post-infection (5,5 ng/ml, p < 0.001). There was no difference in median tacrolimus C0 in the patients with or without diarrhea (9,4 ng/ml vs 10,3 ng/ml, p>0,05). No difference was noted in tacrolimus levels in KTRs concomitantly receiving macrolides.
Conclusions: KTRs infected with SARS-COV-2 virus can be overexposed to tacrolimus. Therapeutic drug monitoring is recommended during COVID-19 infection for all patients even those without diarrhea, to minimise toxicity of immunosuppression.

P190 THE OUTCOMES OF FISTULA TRACT EMBOLIZATION FOR ANASTOMOTIC BILIARY LEAKAGE AFTER LIVING DONOR LIVER TRANSPLANTATION

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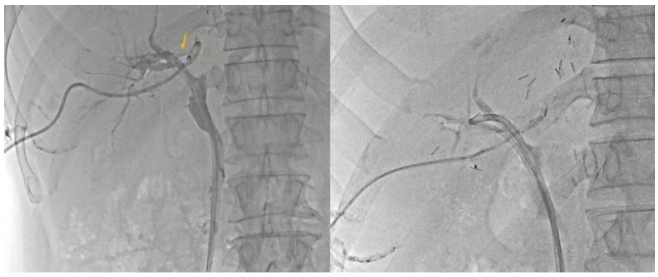
Background: Postoperative bile leak is one of troublesome complications after living donor liver transplantation (LDLT). It usually needs percutaneous drainage (PCD) and interventional biliary stenting although minor leak may be resolved spontaneously. However, a long-standing PCD deteriorates the quality of life of the patient. This study shows our experience on early PCD removal after tract embolization despite large amounts of drainage.
Methods: We retrospectively reviewed the medical records of patients who underwent LDLT in Seoul National University Bundang Hospital between March 2012 and December 2021. When post-transplant bile leak developed at the biliary anastomosis site, we usually inserted PCD for intra-abdominal bile collection and placed biliary stent at leakage site through the endoscopic or transhepatic approach. Although PCDs were removed after bile leakage was resolved, we also tried to remove PCD early after fistula tract embolization in some patients with a high output biliary leakage if the controlled fistula tract was formed. We investigated the outcomes of this strategy.
Results: Among 118 LDLT patients, bile leak occurred in 12 (10.2%) patients. All patients with bile leak received endoscopic or radiologic interventions for biliary stenting and 9 patients (75%) also needed PCD insertion. In 4 patients, PCDs were removed after bile leak was resolved. However, 5 patients (55.5%) had a lasting amount of bile leakage before removal of PCD. The median amount of bile leakage right before PCD removal was 20(1.5-165)cc/day Those patients had PCD during 22 days of the median duration before removal. The internal biliary stents were removed endoscopically 1-3 months after PCD removal. In this treatment strategy, there were neither severe complications and nor recurrent bile leak requiring re-insertion of PCD.
Conclusions: This case series shows that PCD for bile leakage after LDLT could be removed early with tract embolization following internal stent insertion. It does not increase the morbidity of patients and can improve their quality of life. However, because this study was just case series with small number of patients, the results should be validated with large scale studies.

Fig 1.> Fistulogram and embolization



P191 DONORS' AGE MODIFIES THE IMPACT OF PRE-DONATION ESTIMATED GLOMERULAR FILTRATION RATE ON CENSORED GRAFT SURVIVAL

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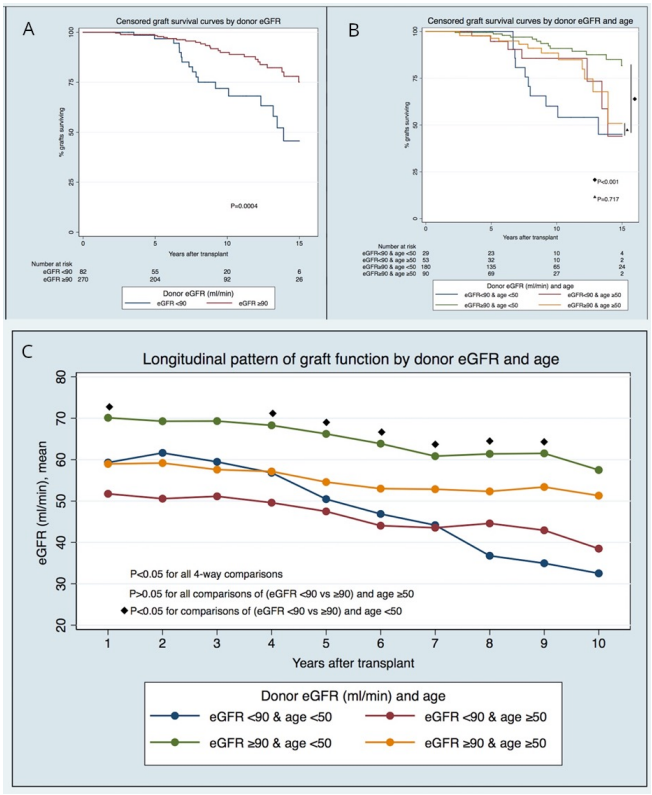
Background: A living donor (LD) kidney transplant (KT) is the preferred treatment for ESRD, but not all LD organs are equal. We sought to evaluate the effects of clinical characteristics of LD associated with worse graft outcomes in our cohort, namely age, pre-donation estimated glomerular filtration rate (eGFR), hypertension, dyslipidemia, smoking, proteinuria, and obesity.
Methods: We studied 352 recipients (R) of LDKT from 1998 to 2020, followed until death, graft failure (GF), or attaining 15 years (Y) of follow-up. Firstly, considering R and KT variables, we identified independent predictors of censored (C) GF through a stepwise analysis with backward elimination of variables with a P-value ≥0.05. Then, adjusting for these predictors, we explored the aforementioned LD variables as predictors of censored GF in a multivariable Cox model. Lastly, using the same model, we analyzed the interaction between eGFR and LD age categories for the prediction of censored GF.
Results: Most of the R were males (67%), with a mean age of 40.4±13.6 Y. The R from LD with higher eGFR (> 90) were significantly younger (39.6±13.1 vs 43.1±14.6, p=0.04) and had significantly better-censored graft survival (GS) at 15y after KT (75% vs 46%, p<0.001). In younger LD (age <50), R from LD with eGFR<90 experienced the greatest risk of CGF, with adjusted HR [95% CI) of 3.370 [1.362-8.343], compared to recipients from LD with eGFR≥90. Differently, when LD were older (age ≥50), no difference in the risk of GF was observed between eGFR categories [eGFR <90 vs ≥90: adjusted HR 1.661 (0.623-4.429)]. The longitudinal pattern of graft function by LD eGFR and age showed, since the first years after KT in R from younger D, significant differences between those with lower and higher eGFR while that differences did not hold in R from older LD. Importantly, none of the remaining LD factors evaluated were independent predictors of CGF.
Conclusions: In our cohort, pre-donation eGFR was associated with post-KT outcomes but LD's age significantly interacted with this effect. Only in younger LD had an eGFR <90 impact on GS drawing attention to the need for an age-adjusted eGFR cutoff for LD admissibility. The dissimilarity in outcomes driven by pre-donation renal function between younger and older LD may result from different pathophysiologic mechanisms being measured as eGFR.

Table 1.

	Total N=352	eGFR<90 ml/min/1.73m2 N=82 (23%)	eGFR≥90 ml/min/1.73m2 N=270 (87%)	P
Recipient				
Age, Mean±SD	40.4±13.6	43.1±14.6	39.6±13.1	**0.040**
F Sex, n (%)	117 (33)	24 (29)	93 (34)	0.384
CKD etiology, n (%)				0.614
DM	9 (3)	3 (4)	6 (2)	
CGN	171 (49)	43 (52)	128 (47)	
Cystic disease	38 (11)	8 (10)	30 (11)	
Urologic	46 (13)	9 (11)	37 (14)	
Unknown	63 (18)	11 (13)	52 (19)	
Others	25 (7)	8 (10)	17 (6)	
Donor				
Age, mean±SD	46.8±10.7	52.8±9.5	44.9±10.4	**<0.001**
Age ≥50, n (%)	143 (41)	53 (65)	90 (33)	**<0.001**
F Sex n (%)	244 (69)	55 (67)	189 (70)	0.615
IBMI ≥30, n (%)	33 (9)	10 (12)	23 (9)	0.317
Predonation SCr, median(IQR)	0.72 (0.64-0.88)	0.90 (0.80-1.02)	0.69 (0.61-0.78)	**<0.001**
Predonation eGFR, mean±SD	100.5±14.7	79.7±8.4	106.8±9.5	**<0.001**
Hypertension, n (%)	53 (15)	19 (23)	34 (13)	**0.019**
Dyslipidemia, n (%)	46 (13)	21 (26)	25 (9)	**<0.001**
Smoking habits n (%)	56 (16)	9 (11)	47 (17)	0.163
ProtU 0.15-0.5 g/g, n (%)	98 (28)	23 (28)	75 (28)	0.962
Transplant				
Previous transplant, n (%)	64 (18)	18 (22)	46 (17)	0.312
HLA-incompatible, n (%)	26 (7)	7 (9)	19 (7)	0.649
ABO-incompatible, n (%)	15 (4)	2 (2)	13 (5)	0.535
HLA AB MM, mean±SD	2.03±1.18	1.98±1.18	2.04±1.18	0.648
HLA DR MM, mean±SD	0.97±0.68	0.99±0.69	0.96±0.68	0.776
Acute rejection, n (%)	47 (13)	12 (15)	35 (13)	0.697
Years of follow-up Median(IQR)	7.4 (4.9-11.5)	6.6 (4.5-9.5)	7.8 (5.1-12.0)	**0.041**
Predictors of censored graft failure				
	HR	95% CI		P
Pre donation eGFR<90 ml/min 1.73m2	2.406	1.255-4.613		0.008
Donor age ≥50 years	1.991	1.015-3.906		0.045
Hypertension	1.080	0.390-2.991		0.883
Dyslipidemia	0.618	0.206-1.854		0.390
Smoking habits	1.440	0.571-3.631		0.440
Donor BMI ≥30Kg/m2	2.062	0.742-5.730		0.165
Proteinuria 0.15-0.5g/24h	1.371	0.666-2.821		0.391
Acute rejection	2.228	1.078-4.605		0.031
CKD due to GNF	3.927	1.834-8.392		<0.001
Retransplant	3.573	1.747-7.009		<0.001
Recipient age	0.949	0.915-0.985		0.006
Interaction of pre-donation eGFRxDonor age				
GFR<90 vs ≥90 & IdD<50	3.370	1.362-8.343		0.009
GFR<90 vs ≥90 & IdD≥50	1.661	0.623-4.429		0.311
Adjusted to the same variables of the previous analysis				



P192 URINARY LEVELS OF V-SET IG DOMAIN-CONTAINING 4 (VSIG4) ARE ASSOCIATED WITH CHRONIC CHANGES IN TRANSPLANT KIDNEYS

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Background: Chronic allograft dysfunction has been linked to interstitial fibrosis in transplant kidneys, which negatively impacts graft outcomes. Recently, the protein V-set Ig domain-containing 4 (VSIG4) has been found to regulate inflammation and drive epithelial-mesenchymal transition in various diseases. However, its role in kidney transplantation remains unclear. This study aimed to determine the significance of urinary VSIG4 levels in kidney transplant patients who underwent biopsy.
Methods: A total of 43 patients (24 males, 19 females, average age 47.0 ±14.5 years) were divided into three groups based on their chronicity index (1-4, 5-8, and >9) as determined by the 2019 Banff classification. The chronicity index is the sum of the scores for interstitial fibrosis, tubular atrophy, chronic vasculopathy, and chronic glomerulopathy, with the latter being double-counted, and has a maximum score of 15. Urinary VSIG4 levels were measured using ELISA and adjusted for urine creatinine levels.
Results: The mean serum creatinine was 2.37 ± 2.54 mg/dL, and eGFR was 40.9 ± 17.8 ml/min/m2. Results of the Kruskal-Wallis test showed that urinary VSIG4 levels (ng/mgCr) were significantly different among the three groups analyzed: lower group median (IQR), 3.66 (1.30, 4.97); middle group: 9.46 (4.77, 21.9); higher group: 21.2 (11.3, 34.8), p = 0.038). Spearman's rank test was used to analyze correlations between urinary levels and other clinical parameters. A significant correlation was found between urinary VSIG4 levels and the total chronicity index (r = 0.327, p = 0.03). The levels were negatively correlated with the eGFR (r = -0.295, p = 0.049) and positively correlated with BUN (r = 0.034, p = 0.045). However, urinary VSIG4 levels did not differ according to the total activity score.
Conclusions: In conclusion, urinary VSIG4 levels are associated with chronic changes in the transplant kidney. Given the relationship between the chronicity index and allograft loss, the levels may serve as a marker for graft outcome.

P196 FUNCTIONAL OUTCOMES AFTER ALEMTUZUMAB THERAPY FOR T-CELL MEDIATED, ANTIBODY-MEDIATED AND MIXED KIDNEY TRANSPLANT REJECTION

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Background: Lymphocyte-depleting therapy is advised for severe or glucocorticoid-resistant T cell-mediated rejection (TCMR) and is one of the recommended modalities for treating antibody-mediated rejection (ABMR). Alemtuzumab has been used off-label for these indications; however, its efficacy for the treatment of different subtypes of kidney transplant rejection has not been compared. We present the functional outcomes of different subtypes of kidney transplant rejections in a large cohort of alemtuzumab-treated patients.
Methods: Clinical data of patients treated with alemtuzumab for severe kidney transplant rejections between January 1st 2012 and January 1st 2022 were retrospectively evaluated by type of rejection. The cause-specific cumulative incidence of graft loss with death as competing risk was calculated. The trend in estimated glomerular filtration rate (eGFR) over time was modelled with a linear mixed effects model.
Results: During the study period, alemtuzumab was given for 216 unique, biopsy-proven rejections. There were 138 TCMR, 47 ABMR and 31 mixed-type rejections. Baseline characteristics are provided in Table 1. Cumulative incidences of graft loss per rejection subtype are depicted in Figure 1. Graft loss was comparable during the first five years of follow-up, with five-year cumulative incidences of 35.8% [95%-CI 26.7 to 45.0] for TCMR, 39.1% [95%-CI 23.8 to 54.4] for ABMR and 42% [95%-CI 22.9 to 61.1] for mixed-type. After the first five years of follow-up, significantly more grafts were lost after mixed-type rejection, with ten-year cumulative incidences of 78% [95%-CI 56.3 to 99.4] versus 37.3% [95%-CI 27.9 to 46.8] (TCMR) and 39.1% [95%-CI 23.8 to 54.4] (ABMR). Kidney function over time tended to decrease and decline faster after mixed-type rejection, but this result was not statistically significant.
Conclusions: Graft survival after alemtuzumab therapy for different types of kidney transplant rejection is comparable during the first five years, but long-term graft survival is worse for patients with mixed-type rejection. We hypothesize that this late graft loss is due to gradual loss in kidney function by ongoing immunological activity in the kidney transplant. Current data were insufficient to support this hypothesis via linear mixed effects modelling.

		Rejection subtype			Statistic[1]
		TCMR (n = 138)	ABMR (n = 47)	Mixed-type (n = 31)	P-value
Age of recipient	Median (IQR)	57.00 (43.25, 65.00)	54.00 (34.50, 63.50)	43.00 (27.00, 63.50)	0.10
Recipient sex	Female/Male	50/88	21/26	16/15	0.23
Previous transplantations	1/2/3 or more	113/16/9	29/9/9	23/7/1	0.02
Pre-emptive Tx	No/Yes	94/44	39/8	22/9	0.14
PRA actual in %	0-10/10-50/50-100	126/5/7	27/10/9	21/5/5	<0.01
	Unknown or missing	0	1	0	
PRA historic in %	0-10/10-50/50-100	100/11/25	20/2/24	14/4/13	<0.01
	Unknown or missing	2	1	0	
Donor age	Median (IQR)	56.00 (46.25, 64.00)	53.00 (43.00, 59.50)	48.00 (38.00, 63.00)	0.10
Donor type	DBD/DCD/Living	18/36/84	9/12/26	6/9/16	0.72
Timing of rejection	Early/Late	91/47	34/13	14/17	0.05

Table 1: Baseline characteristics of biopsy-proven rejections

[1] Kruskal-Wallis (continuous variables) or Fisher's exact (categorical variables) test

Tx: Transplantation; PRA: Panel reactive antibody; DBD: Donation after brain death; DCD: Donation after circulatory death; HLA: Human leukocyte antigen. Early rejection: rejection within 3 months after transplantation.

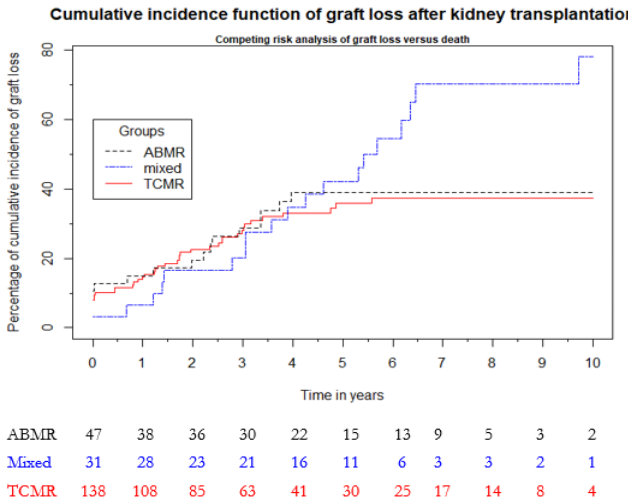

Figure 1 Cumulative incidence of graft loss between different subtypes of rejection

P197 SYSTEMATIC REPORTING AND INVESTIGATION OF POSSIBLE INFECTION OF DONOR ORIGIN IN DECEASED ORGAN DONATION IS ESSENTIAL FOR BEST TRANSPLANTATION PRACTICE

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Background: Post-transplant events that may have an impact on allograft recipients must be centrally reported to our national organ donation and transplantation organisation; this should be done as soon as a donor-related transmission event becomes a possibility. Notification triggers prompt dissemination of information to transplant centres and initiates a systematic investigation. A report with findings, actions, and recommendations is essential; co-operation from all stake holders and a multi-disciplinary approach are key to improved practice and better patient outcomes.
Methods: The outcome of extensive investigations over a period of 10 years, where donor-derived transmission of infection was deemed to be possible, probable, or proven is hereby summarised. The methods used may vary depending on the pathogen involved, and good knowledge of the specific disease process is required.
Results: During this period 14,949 donors enabled 38,380 organ transplants, with an approximate 0.3% rate of donor-related transmission of infection events per proceeding donor. The agents most implicated were Human Herpes Viruses, mainly herpesvirus type 1,2, and 8, followed by Hepatitis E Virus (table 1); of note, herpesvirus type 8 alone was responsible for a quarter of all cases and was the most frequent imputable pathogen. Cases where the donor was excluded as possible source of infection in the recipient, or where imputability could not be ascertained, are not included in this summary.
Conclusions: Although infrequent, unintended transmission of infection of donor origin may be associated with significant recipient morbidity and mortality. It is essential that all those involved in organ donation and transplantation remain attentive to potential occurrences, so that they can be detected, notified, and appropriately managed. Critical analysis of these events is important for the identification of possible deficiencies, need for change and learning. In our practice, this is continuously used to inform best practice and guidance.

Table 1: Number of events investigated (2012-2022) and the corresponding implicated infectious agent, where recipient infection of donor origin was classed as proven, probable, or possible

Implicated Organism	Imputability grade		
	Proven	Probable	Possible
Candida albicans	1		
Cytomegalovirus		2	
Halicephalobus gengivalis	1		
Hepatitis B virus		1	2
Hepatitis C virus	2		
Hepatitis E virus	8		
Herpes simplex virus type 1 or 2	2	5	
Herpes virus type 8	10		
Herpes virus type 6			1
Leishmania donovani	1		
Mycobacterium tuberculosis		1	
Parvovirus B19		1	1
Strongyloides stercoralis		1	

Note: Figures denote number of events investigated and not number of recipients involved in each event.

P198 EARLY RESULTS OF A SCREENING PROGRAM FOR SKIN CANCER IN LIVER TRANSPLANT RECIPIENTS: A COHORT STUDY

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Background: Skin cancers are the most common type of cancers reported in liver transplant recipients with greatly increased risk compared to the general population, likely due to immunosuppressive treatment. Timely and regular dermatological assessment may reduce rates of advanced skin cancer. However, evidence for use of screening programs in liver transplant recipients is lacking. The aim of the study was to describe the early results of a screening program for skin cancer in Danish liver transplant recipients initiated in 2018.
Methods: In this prospective cohort study, we included liver transplant recipients enrolled in a skin cancer screening program four years after initiation (January 1st, 2018 to December 31st, 2021) in our center. Overall prevalence and incidence of skin cancer and preneoplastic lesions were determined. Risk factors were assessed using Cox-regression analyses.
Results: Of 245 liver transplant recipients, 219 (89.6 %) were referred to a screening program for skin cancer at a specialized dermatological department. In 32 (15.4 %) liver transplant recipients, 118 skin cancers / preneoplastic lesions were diagnosed during the screening period. The incidence rate of skin cancer / preneoplastic lesions was 100.3 per 1000 person-year. Age at transplantation and time since transplantation were independently associated with increased risk of skin cancer / preneoplastic lesions.
Conclusions: Early results from a screening program for skin cancer in liver transplant recipients demonstrated a high referral rate to dermatological assessment with a prevalence and incidence comparable to the literature. Later data with additional follow-up is needed to provide more insight into the effects of the screening program.

P200 FACTORS THAT INFLUENCE THE DEVELOPMENT AND IMPLEMENTATION OF PREHABILITATION FOR KIDNEY TRANSPLANT CANDIDATES: A MIXED-METHODS CONTEXTUAL ANALYSIS

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Background: The overall fitness of kidney transplant candidates (KTCs) is often compromised due to chronic kidney disease, comorbidities and dialysis. Prehabilitation, comprised of exercise, nutritional and psychological interventions, may be an effective way to improve the overall fitness of KTCs. However, implementation of a multicomponent intervention is challenging. This study aimed to gain insight into contextual and implementation related factors that are of influence on the development and implementation of prehabilitation for KTCs.
Methods: A contextual analysis using the Context and Implementation of Complex Intervention Framework was performed to gain a deeper understanding of current practices, preferences, possible barriers and facilitators for prehabilitation by using qualitative and quantitative methods. In-depth interviews (n=22) and focus group meetings (n=5) were performed with KTCs, their significant others, kidney transplant recipients and healthcare providers (HCPs). In addition, a survey (n=87) was conducted among waitlisted KTCs.
Results: In current practice, care for KTCs has a medical focus. In addition, dieticians and social workers are often involved. Both KTCs and HCPs indicated that little attention is paid to physical activity. Ninety-two percent of the KTCs encountered one or more problems regarding physical activity, nutritional status and/or psychological wellbeing. Perceived barriers to engage in healthy life style behaviors were mainly fatigue and a lack of motivation and/or knowledge. Perceived facilitators included social support and guidance from a healthcare professional. Furthermore, 79% of the KTCs indicated that they felt the need for a prehabilitation program, in which 73% would like to improve their strength and endurance, 48% to obtain a healthy nutritional status and 30% to cope with stress and/or fatigue. The majority of KTCs (64%) preferred a personalized, home-based-training program, with guidance from a healthcare professional.
Conclusions: The high percentage of KTCs encountering physical and psychological problems, the limited attention for physical activity in current practice and the felt need for prehabilitation, suggests that prehabilitation may be a promising intervention to improve the overall fitness of KTCs before transplant.

P203 PRE-TRANSPLANT PROPORTIONS OF POLYFUNCTIONAL DONOR-REACTIVE T CELLS ARE ASSOCIATED WITH ACUTE T-CELL MEDIATED REJECTION OF THE KIDNEY TRANSPLANT

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Background: Acute T-cell mediated rejection (aTCMR) still remains a clinical problem after kidney transplantation despite significant improvements in immunosuppressive regimens. Polyfunctional T-cells, i.e. T-cells producing multiple pro-inflammatory cytokines, are believed to be the most relevant T-cells in an immune response. The aim of this study was to determine whether pre-transplant proportions of polyfunctional donor-reactive T-cells are associated with aTCMR.
Methods: In a case-control study, 49 kidney transplant recipients with a biopsy-proven aTCMR in the first year after transplantation were included, as well as 51 controls without aTCMR. Circulating donor-reactive T-cells were identified by the expression of CD137 using a multiparameter flowcytometric assay following a short-term co-culture with donor antigen-presenting cells. Proportions of interleukin (IL)-2, tumor necrosis factor (TNF)-α and interferon (IFN)-γ cytokine producing cells and combinations thereof were determined. Polyfunctional donor-reactive T-cells were further characterized by dissection into different T-cell subsets encompassing the spectrum of naïve to terminally-differentiated effector T-cells.
Results: Prior to kidney transplantation, proportions of donor-reactive CD4+ (0.03% versus 0.02%; P<0.01) and CD8+ (0.18% versus 0.10%; P<0.01) CD137high-expresssing (CD137++) T-cells were significantly higher in recipients with a biopsy-proven aTCMR versus non-rejectors. Polyfunctionality was higher (P=0.03) in this subset of CD137-expressing T-cells. These cells were predominantly of the EM/EMRA-phenotype, with polyfunctional donor-reactive CD137++CD4+ T-cells predominantly co-expressing CD28 whereas approximately half of the polyfunctional CD137++CD8+ T-cells co-expressed CD28. In addition, at the time of aTCMR, polyfunctional donor-reactive CD137++ CD4+, but not CD8+, T-cells, were specifically decreased by 75% compared to before transplantation in recipients with as well as those without an aTCMR.
Conclusions: Prior to transplantation, the proportion of polyfunctional donor-reactive CD137++ T-cells is associated with the occurrence of a biopsy-proven aTCMR within the first year after transplantation.

P205 VIGILANCE DATA IN ORGAN DONATION AND SOLID ORGAN TRANSPLANTATION IN GERMANY: DONOR-DERIVED DISEASE TRANSMISSION FROM 2016-2022

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Background: Diligent reporting and analysis of all serious adverse event (SAE) and serious adverse reaction (SAR) cases can help to identify risks of transmitting donor-derived disease to transplant recipients. The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is the delegated body assigned by the German Federal Ministry of Health responsible for the management of the national SAE/SAR system.
Methods: A team of qualified physicians of the DSO analyzed all SAE and SAR reported from January 1st 2016 to December 31st 2022. In case of a possible transmission of a disease to one or more recipients, an assessment of imputability was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC).
Results: Between 2016 and 2022, 21060 organs were transplanted from 8519 donors. In the same period, the DSO received 543 SAE/SAR reports. 52 of the 543 reports (9,6%) were proven or probable (P/P) transmissions of infectious diseases, malignancies or other diseases to 74 recipients. 17 of 74 (17/74; 23 %) recipients died due to the transmitted disease. Infections were the most frequently reported P/P disease transmission occurrences (28/52; 54%). 16 cases (16/52; 31%) were P/P transmissions of malignancies to 22 recipients resulting in 11 attributable deaths (11/22;50 %).
Conclusions: Donor-Derived disease transmission is a rare event (52/8519; 0,6 %), but when it occurs can lead to significant morbidity and mortality, especially when malignant diseases are transmitted. Reporting of SAE and SAR can identify possible risks in organ donation and solid organ transplantation and help to improve donor characterization and to increase awareness of transmission events.

	Total reports	P/P Donors	Total recipients From P/P Donors	Total recipients with transmission from P/P Donors*	Total Deaths from Transmission**
Malignancy	145	16	43	22 (51%)	11 (50%)
Bacteria	169	12	43	20 (47%)	0 (0%)
Fungus	114	10	41	11 (27%)	2 (18%)
Virus	48	6	23	12 (52%)	3 (25%)
Parasite	5	1	4	1 (25%)	1 (100%)
Other	62	7	23	8 (35%)	0 (0%)
Total	543	52	177	74 (42%)	17 (23%)

*%= recipients with transmission/recipients from P/P donors. **%= deaths from transmission/total recipients with transmission.

P206 MULTIPARAMETER ANALYSIS OF ALLOREACTIVE T CELLS IDENTIFIED BY ACTIVATION-INDUCED MARKERS (AIMS); DIFFERENT AIMS RECOGNIZE SPECIFIC T CELL SUBSETS

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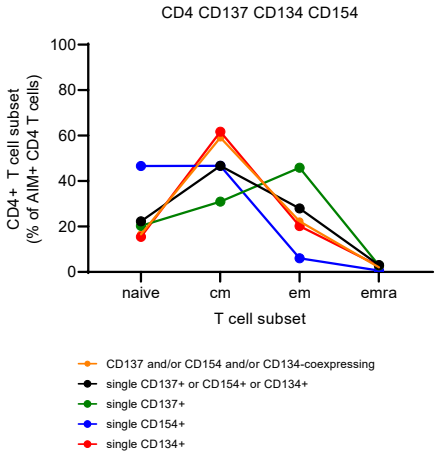
Background: Expression of activation-induced markers (AIMs) after T-cell receptor-mediated activation is used to identify alloreactive T cells but whether these markers recognize similar subsets of alloreactive T cells is largely unknown.
Methods: Alloreactive T cells were characterized following a short-term co-culture of responders peripheral blood mononuclear cells (PBMCs) with allogeneic CD3-depleted PBMCs or autologous CD3-depleted PBMCs as a negative control (background signal). T cells were analyzed by multi-parameter flow-cytometry using a combination of monoclonal antibodies directed to commonly used AIMs (CD69, CD134, CD154 and CD137) and CD45RA and CCR7 for T cells subset analysis (naïve, central memory (CM), effector memory (EM) and terminally differentiated CD45RA-expressing effector memory (EMRA)). Both supervised and unsupervised data analysis (FlowSOM) were performed.
Results: Median proportions of CD137, CD154 and CD134 total (including single as well as co-expressing other AIMs) alloreactive CD4 T cells amounted to 0.34%, 0.52%, 0.16%, respectively with a low background signal. CD69 expression on CD4+ T cells was high (median 4.16%) with a substantial background (median 3.24%). CD137 expression was preferentially found on EM ($P<0.05$) while CD154 and CD134 were preferentially found on CM cells ($P<0.05$). Of all CD137-expressing CD4+ T cells 36.3% were EM versus 19.6% and 7.1% for CD134- and CD154-expressing CD4+ T cells, respectively, with minimal overlap between EM alloreactive CD4+ T cells identified by different AIMs. Proportions of alloreactive CD4+ T cells co-expressing AIMs (59%) were higher in the CM subset when compared to single-AIM expressing (47%) ($P<0.05$). Alloreactive CD8+ T cells can be best detected using CD137, as CD134 and CD154 were hardly expressed.
Conclusions: AIMs are differentially expressed according to the differentiation status of alloreactive CD4+ T cells but in general overlap between these different AIMs is surprisingly low. Identification of alloreactive CD4+ T cells by AIMS should therefore include at least CD137, CD134 and CD154.



P207 REMAINING STEROID FREE ONE YEAR AFTER KIDNEY TRANSPLANTATION

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Background: Steroid-free regimen (SFR) is welcome in kidney transplantation (TX) to avoid steroid related side effects. However, the approach is not always suitable, for some patients from the beginning after TX, while for some the initial SFR plan ought to be abandoned afterwards, mostly to ensure sufficient immunosuppression (IS). To examine the proportion of kidney transplant patients planned for SFR and proportion of those remaining on SFR at 1 year after kidney TX and to determine reasons for or against SFR, both at planning and after initially planned for SFR.
Methods: We undertook a retrospective study of all patients that underwent kidney TX from 2013 to 2021 at University Hospital Merkur, Zagreb, Croatia. The TX center performs protocol kidney transplant biopsies (BX) at months 2, 6 and 12. The data were taken from medical records.
Results: Total of 460 patients (66 % males; median age 53 years, 15 – 78) were analyzed. SFR was planned in 57 % of them, but only 24 % of the planned (or 14 % of all) were on SFR at 1 year after TX. The most common reason against SFR plan were PRA ≥ 8 % with or without retransplantation (in 15 % of all) or simultaneous TX of pancreas or liver (as preference of TX center, in 10 % of all), then IgA nephropathy or other glomerulitis, or other less frequent reasons. The most common reason not to start a planned SFR was delayed graft function (in 44 % of the planned SFR). Acute rejection (diagnosed by indication or by protocol BX in 21 % of the planned SFR) was the most frequent reason for breaking SFR, following by leukopenia (in 5 % of the planned SFR) and other less frequent reasons.
Conclusions: SFR plan was suitable for more than a half of kidney transplant candidates, while other needed higher IS from the beginning of the TX mostly because of human leukocyte antigen sensibilization or simultaneous kidney with pancreas or kidney with liver TX. Only a quarter of the planned SFR remained on SFR at 1 year after the TX, the majority not fulfiling the plan due to DGF or rejection. Eventually, 1 year after TX there were totally 14 % patients on SFR. Protocol BX of kidney transplant are of great help in supporting remaining on SFR or indicating abondoning it. Despite the high attrition from the SFR intention, still 14 % of patients might have benefit from SFR.

P208 MICROSURGICAL ANASTOMOSIS BETWEEN LOWER POLAR ARTERY AND INFERIOR EPIGASTRIC ARTERY IN KIDNEY TRANSPLANT: SINGLE CENTRE EXPERIENCE

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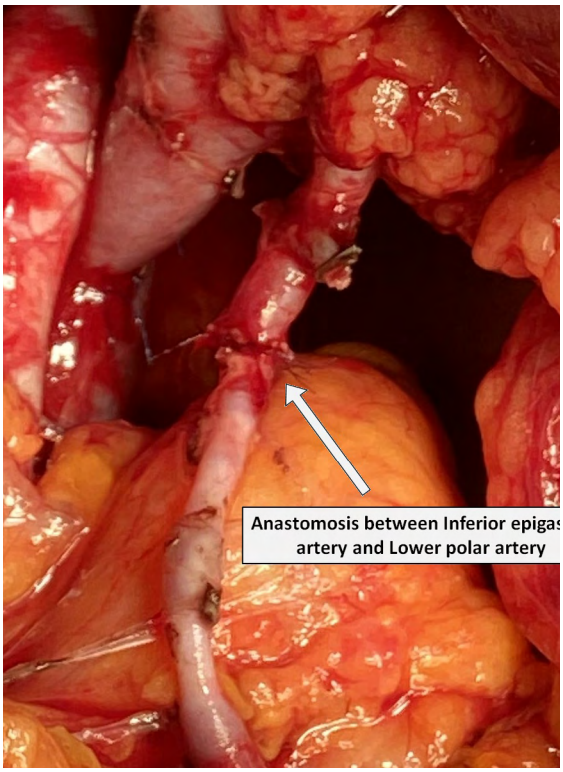
Background: The reported incidence of multiple renal arteries (MRA) is approximately 20%, and roughly 6% of them are lower polar arteries (LPA). The LPA supplies the upper urinary tract, therefore at kidney transplantation (KT) reconstruction of LPA is essential to avoid necrosis of the ureter. Among the possible reconstructive techniques for LPA, its anastomosis with recipient's inferior epigastric artery (IEA) has been seldomly described in literature, with approximately 10% experiencing vascular or urological complications such as arterial thrombosis, partial infarction, urinary fistula, and graft loss.
Methods: Single-centre retrospective analysis of 9 KTs (7 living donors, 2 deceased donors) with LPA-IEA anastomoses, focused on postoperative complications, and patient and graft survival. The IEA was exposed before approaching recipient's iliac vessels. The LPA-IEA anastomosis was performed after main vessels were anastomosed and declamped, thus reducing ischemic time according to sequential reperfusion technique. The LPA-IEA anastomosis was performed end-to-end with 7-0 Prolene single stitches, using 5x magnifying loupes with glasses. Doppler US was performed intraoperatively, before discharge, and at follow-ups (FU) with blood exams.
Results: Recipients' demographics: average age and BMI respectively 45.5 years and 26.5, 4 males and 5 females, all AB0 compatible (A=4, AB=2, 0=2, B=1). Average FU was 76.3 months (4 - 139). Neither vascular complications nor ureter necrosis occurred. Other complications: acute rejection treated with steroids (n=1), delayed graft function (n=1), lymphocele (n=1). Patient and graft survivals were 100% at most recent FU, and mean creatinine levels within acceptable range.
Conclusions: Reconstruction of LPA is mandatory in KTs. The LPA-IEA anastomosis, when accurately performed (i.e., microsurgical technique), carries excellent and durable results.



P209 INTRAOPERATIVE MEASURES OF VASCULAR FLOW IN LIVER TRANSPLANT. WHAT CAN THEY REALLY FORESEE?

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Background: The increase in orthotopic liver transplantation (OLT) along with the organ shortage calls for success in every transplant we perform. The goal of our study is to determine the relation between hepatic artery and portal vein flows and the implications in short and large term outcomes.
Methods: A retrospective observational unicentric study was performed, including 126 OLT patients between January 2019 and October 2022. Factors recorded included: demographic characteristics, comorbidities of the recipient, intraoperative variables, postoperative morbidity and mortality and graft and patient survival. Following successful implantation and at point of hemodynamic stability hepatic artery and portal vein flows were measured. Qualitative measures were described using frequencies and percentages. Quantitative measures were expressed as mean ± standard deviation (SD) or median and interquartile range. For the statistical analysis we used Student's t and Mann-Whitney U tests and Spearman correlation value. Results were considered significant when the corresponding p-value was less than 0.05.
Results: A total of 126 patients were included with a median follow up of 12 months. The mean hepatic artery flow (HAF) was 351 ml/min whereas the portal vein flow (PVF) was 1750 ml/min. Neither HAF, PVF, nor the length-of-stay in intensive care unit or hospitalization show a significant correlation. Also, biliary, suprahepatic or portal complications were not affected by HAF or PVF. However, the HAF was statistically significant (P= 0.005) for the arterial complications. There were differences between allograft and patient survival after 3, 6 and 12 months considering PVF as a significative predictor. Similarly, PVF was also a significative predictor of reoperations, with a percentage in our sample of 20.64%. The mortality rate was 15.08%.
Conclusions: According to our results PVF is a reference standard that can statistically significantly predict patient and graft survival at 3, 6 and 12 months after OLT. More prospective and larger studies are required in order to establish a cutoff point in PVF that can serve us as guidance to achieve better results in every OLT.

P210 PATIENTS' EXPERIENCES OF PATHWAY CARE AFTER KIDNEY TRANSPLANTATION: FINDINGS FROM AN ITALIAN ETHNOGRAPHIC RESEARCH

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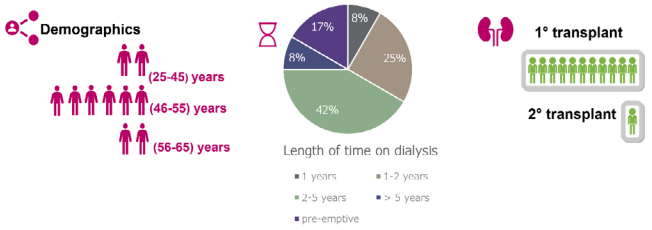
Background: Adherence to immunosuppressive therapy is essential in patients who have received a kidney transplant to prevent organ failure. Therefore, it is crucial to consider the patient's perspective to recognize the factors that compromise a patient's adherence to treatment. This qualitative ethnographic research has aim to identify the possible factors that may promote or, conversely, may impact "adherent" behavior, such as unmet needs, to benefit the supportive care process for transplant patients.
Methods: Twelve adult patients receiving transplant in the previous two years were interviewed via face-to-face video recording at a time and place based on participants' preferences. The interviews were conducted using a semi-structured approach to collect and analyze cultural meanings associated with the condition and its treatment, with a focus on how patients behaved during immunosuppressive therapy. A thematic analysis of the interview texts was to find common themes within the data by identifying interpretive categories and subcategories about the organization, clinical and psychological care, and relational and social factors, and was performed by expert researchers.
Results: Two main categories of patients were identified, depending on whether the illness was viewed as a part of the person's identity or as an "alternate" stage of life relative to "regular" life. Patients who view their illness as an identifying attribute are more likely to "normalize" it as an essential component of who they are. The transplant recipients were generally satisfied with their transplant education, but they identified communication gaps in all areas of the transplant process, including the transplant waitlist, surgery, life changes post-transplant and immunosuppressive therapy and its effects/consequences. The main categories of unmet needs by the current assistive care process for transplant care are needs related to self-awareness, for information on the disease and lifestyle. Moreover, there emerged the need for patients to receive better psychological support and communication with HCPs.

Conclusions: The results suggest that it is relevant improving HCPs attention to patients' psychosocial, communication and relational needs and might become integral for improving patient transplant outcome.



P211 MESENCHYMAL STEM CELLS INFUSION DURING LIVER RESECTION AND TRANSPLANTATION – REGENERATION AUGMENTATION AND IMMUNE MODULATION: CASE REPORT

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Background: Mesenchymal stem cells (MSCs) have been demonstrated exciting therapeutic effects in drug-induced liver failure, while only a few studies have been reported in liver surgical models. We have previously shown that intraportal local infusion of allogeneic adipose tissue MSCs during liver transplantation (LT) is safe and feasible with promising immunomodulatory effect.
Case description: The patient M., 54 yo, was diagnosed with right liver lobe mass (histologically – alveococcosis) required right extended hemihepatectomy with future liver remnant of 14%, demanded ALPPS procedure. To augment liver regeneration, intraportal infusion of 20 million MSCs into the left portal vein during the 1st and 2nd stage of ALPPS procedure was performed (FLR volume increased by 64% between LR stages; posthepatectomy liver failure was not observed). On the 45th postoperative day (POD) after LR, left hepatic vein stenosis (pressure gradient 28 mmHg) was revealed; successful endovascular stent placement was performed. On the 178 POD, inferior vena cava (IVC) stenosis (just before the entrance in the right atrium) with Budd-Chiari syndrome was diagnosed. Despite successful endovascular IVC stent placement and pressure gradient decrease (from 12 to 3 mmHg), no clinical improvement was happened and subsequent deterioration of portal hypertension (ascites, esophageal varices) was observed. The patient was listed on LT. 10 months after LR, LT was performed (intraoperative features: 20l of ascites, pericardotomy for upper caval anastomosis; bloodloss 3 l). Due to the high risk of acute kidney injury and infectious complications, an alternative immunosuppressive therapy with local intraoperative intraportal infusion of 20 million MSCs and systemic intravenous (on the 0 POD and 4th POD; 2 million MSCs per kg), low-dose Tacrolimus (Mycophenolate avoidance till the 7th POD) were prescribed. Neither infectious nor immunological complications were detected. No portal vein thrombosis or other MSCs infusion complications were revealed.
Conclusion: Clinical intraportal MSCs infusion during major hepatectomy and liver transplantation is feasible and safe intervention with no severe adverse events revealed. Allogeneic adipose tissue MSCs may provide as regenerative as immunomodalatory effects in liver surgery.

P212 LONG-TERM PRESERVATION OF KIDNEYS BY MEANS OF CRYOPERFUSION: THE NEXT STEP IN ORGAN PRESERVATION?

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Background: In contrast to cell lines and small biopsies, cryopreservation of whole organs brings extra hurdles such as temperature gradients and ice crystal formation that potentially damages cell viability. Cryopreservation during continuous organ perfusion could counteract these aspects by homogeneously distributing temperature and cryoprotectant agents. This study aimed to generate first pilot data on renal cryoperfusion at -15ºC.
Methods: Porcine kidneys were subjected to 30 min of warm ischemia and randomized into a control and a cryoperfusion group. Control kidneys were preserved with hypothermic machine perfusion (HMP) at 0-8°C for 24h and cryoperfusion kidneys were first preserved 3h in HMP, followed by 6h of cryoperfusion at -15°C and then 15h in HMP overnight. During cooling, the concentration of cryoprotectant agent (CPA) was increased from 10% to 35% in steps, and during rewarming the CPA was sequentially diluted back to the starting concentration. The next day, both kidneys underwent 4h of normothermic machine perfusion (NMP) for viability assessment.
Results: After cryoperfusion, none of the kidneys displayed macroscopic signs of ice crystal formation. During NMP, cryopreserved kidneys produced significantly more urine (p=0.0286) and had significantly lower flow rates (p=0.0004) per 100g. Kidneys which underwent the cryoperfusion protocol had a higher total mass gain after NMP (p=0.0085), suggesting increased edema. Perfusate lactate concentration, electrolyte balance, and oxygen consumption in both groups were similar, indicating that cryoperfused kidneys did seem to function within a normal range during NMP. Injury markers ASAT and LDH at the end of perfusion were not statistically different between groups (p=0.1508 and p=0.2222, respectively).
Conclusions: Although our cryoperfusion protocol still requires multiple protocol improvements, these pilot results suggest, for the first time, that kidneys cryoperfused at -15°C still hold some functionality after reperfusion without inflicting major cellular injury. This suggests that cryoperfusion could potentially show to be a viable long-term preservation technique for whole-organs, which in turn could lead to better donor-recipient matching, and worldwide organ exchange.

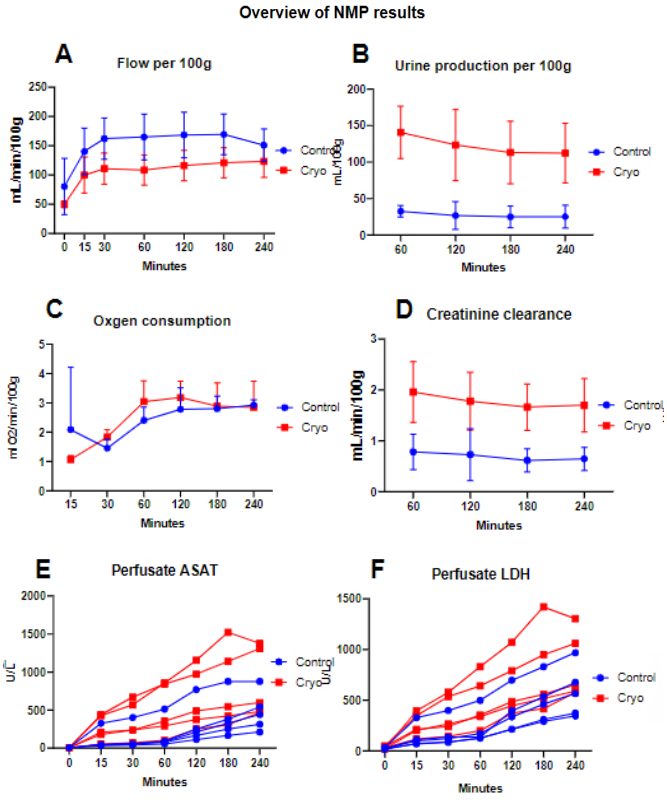

Figure 1: **(A)** Grouped longitudital representation of flow rate (mL/min) per 100g of tissue; **(B)** Grouped longitudital representation of urine production (mL) per 100g of tissue; **(C)** Grouped longitudital representation of calculated oxygen consumption (mLO2/min) per 100g of tissue; **(D)** Grouped longitudital representation of calculated creatinine clearance (mL/min) per 100g of tissue; **(E)** Individual longitudital representation of perfusate ASAT concentration (U/L); **(F)** Individual longitudital representation of perfusate LDH concentration (U/L);

P213 AWARENESS CAMPAIGN FOR ORGAN DONATION THROUGH SOCIAL MEDIA AND PODCASTS: AN INNOVATIVE APPROACH

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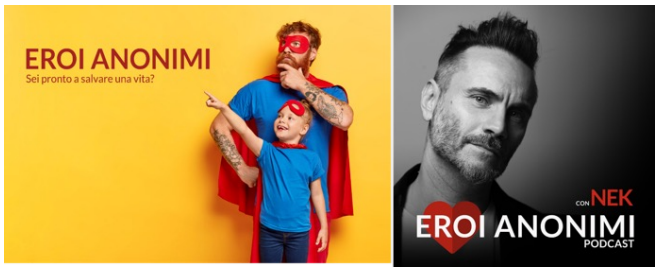
Background: Organ donation is a critical aspect of healthcare and raising awareness on its importance is crucial to increase the number of donors. Despite its importance, there is often a lack of public awareness and understanding of the process. This project aimed to increase awareness of organ donation through a multi-faceted communication campaign utilizing a web site, social media and podcast.
Methods: The campaign was designed to target a broad audience (people 25-54 years) and provide accessible, engaging information on organ donation. Social media platforms (Facebook, Instagram) were utilized to spread awareness and promote educational content, through infographics, questions and answer and emotional videos. A podcast series was also produced, featuring interviews with transplant medical experts, organ living donors, and recipients. A transplant stories' patients tell themselves and by a famous Italian artist were used to convey the message in a podcast format. The impact of the awareness campaign was evaluated based on the number of listeners, time spent listening of the podcast, and web site visualization and social media followers.
Results: The focus of the communication campaign was on the important role of donors ("Anonymous Heroes") and the public calling "Are you ready to save a life?". The number of podcast listeners was over 15.300. The average time spent listening to the podcast was over 80% indicating high engagement and interest among the listeners. Podcast series reached 6th position nationwide among all podcasts in the health and wellness category. Furthermore, a web site visits, from June 2020 to January 2023, around 40.000 and 953.774 people has reached from social. In the same period in Italy, thanks to all communication campaigns, donation declarations of willingness to donate has reached the largest absolute number of consents.
Conclusions: This approach highlights the potential of social media and podcast as effective tools for increasing public awareness and understanding of organ donation. The use of transplant patient stories and famous artists can help to personalize and amplify the message, leading to greater engagement and impact.



P214 HORMONAL PROFILE OF FEMALES INFLUENCES INTESTINAL REPERCUSSIONS IN POTENTIAL BRAIN-DEAD DONORS

Fernanda Yamamoto Ricardo-da-Silva*[1], Marina Vidal-Dos-Santos[1;2], Roberto Armstrong-Jr[1;2], Cristiano de Jesus Correia[1], Luiz Felipe Pinho Moreira[1], Ana Cristina Breithaupt-Faloppa[1]

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Background: Female donors' organs have been associated with worse prognostics after transplant, which seems to be associated with the hormonal imbalance produced by brain death (BD). Female sex hormones are known to regulate the inflammatory response. As such, here we investigated the effects of previous sex hormones reduction, like menopause, on gut inflammation using a BD model in female rats.
Methods: Female Wistar rats were separated in 4 groups: BD - high estradiol concentration rats (proestrus phase to heat period) underwent BD and were maintained for 6h, BD-OVx - ovariectomized rats (10 days before BD induction day) and underwent BD (6h), Control - non-manipulated rats, Control-OVx - ovariectomized rats not submitted to BD. Serum was analyzed for VEGF, TNF-α, IL-1β, IL-6 and MIP-1α concentrations. Intestine was removed for histopathological analysis; analysis of neutrophil presence/activity (myeloperoxidase - MPO) and microvascular permeability. Mesentery was exposed for blood flow analysis, and sampled for immunohistochemistry and PCR analysis (eNOS, iNOS and ET-1).
Results: Both BD and BD-OVx had greater intestine leukocyte infiltration (BD: 0.23±0.01, BD-OVx: 0.23±0.02, Control: 0.16±0.01, Control-OVx: 0.13±0.01 cell/μm²; P<0.0001), reduction of villus height (BD: 398.9±18.1, BD-OVx: 348.7±19.8, Control: 453±31.1, Control-OVx: 433.1±20.9 μm; P=0.03) and increased MPO activity compared to respective controls, accompanied by the increase of serum TNF-α, IL-1β, IL-6 and MIP-1α. Comparing BD and BD-OVx groups, intestinal injury, serum TNF-α and MIP-1α were higher in BD-OVx. Conversely, microvascular permeability (BD: 97.3±18, BD-OVx: 50±3.4 μg/mg of dry weight; P=0.09) and blood flow was increased in BD. On mesentery, eNOS had greater protein expression in BD and BD-OVx compared to their controls, and gene expression was higher in BD-OVx compared to BD. iNOS was also increased in BD-OVx group, and ET-1 gene was higher in BD compared to BD-OVx.
Conclusions: BD produced a systemic inflammation that altered intestine integrity in female rats. Menopause like model (ovariectomy) had greater villus injury associated with iNOS increase, besides BD induced acute drop of female hormones has worsened the intestinal edema. Grant 2023/00728-6, 2021/13020-6, São Paulo Research Foundation (FAPESP).

P216 DONOR-DERIVED CELL-FREE DNA AND GENE EXPRESSION PROFILE IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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Background: Rejection is the major cause of graft failure after pancreas transplantation, but pancreas biopsy is a risky technique. Molecular biomarkers, such as donor-derived cell-free DNA (dd-cfDNA) and gene expression profile (GEP), have emerged as an alternative to monitor graft rejection in other solid organ transplants. We hypothesized whether these techniques could complement the non-invasive diagnostic performance of currently available biomarkers of pancreas graft dysfunction.
Methods: We performed a longitudinal analysis of samples from 38 pancreas transplant recipients. Plasma was collected in PAXgene tubes pre-transplant, and afterwards at 1h, 24h and 7 days post-transplant, and at time of pancreas biopsy – either per protocol at 3 weeks and 12 months, or for clinical indication. The Allonext assay was used to report the dd-cfDNA as a % of the donor-derived fraction as compared with total cfDNA by using panels of >500 SNPs. GEP was analysed with the TruGraf® algorithm, which analysed differential expression of 120 genes. GEP results were provided as a probability score normalized on a 0–100 scale. The TruGraf® assay has a previously defined probability threshold of 50 to differentiate the TX (no rejection) from the not TX phenotype.
Results: Dd-cfDNA increased significantly during the first hour after pancreas transplantation (4.30±2.53%), and reduced progressively (at 24h 2.41±1.79%, at 1 week 0.65±0.47%, at 3 weeks 0.47±0.28%). Patients with biopsy-proven acute rejection (P-BPAR) episodes presented higher values of dd-cfDNA (2.1±2.46% vs 0.50±0.88%; p<0.027). In patients with pancreas acute rejection, GEP diagnosed the rejection episode in 58.8%, with a sensitivity of 74.1% (95% CI 53.7-88.9) and a specificity of 83.3% (95% CI 59.8-92.5) and with negative predictive value of 86.7% (95% CI 77.3-92.6). Sub-clinical rejection (lipase <3xs normal) was diagnosed in 57.1%, with a specificity of 86.1% (95% CI 71-95). The combination of both parameters presented a negative predictive value of 82.3% (67-91%), with thirteen patients with P-BPAR (72.2%) presenting either test positive.
Conclusions: Dd-cfDNA and GEP can improve the detection of pancreas acute rejection episodes. GEP may provide non-invasive monitoring for sub-clinical rejection of the pancreas. graft.

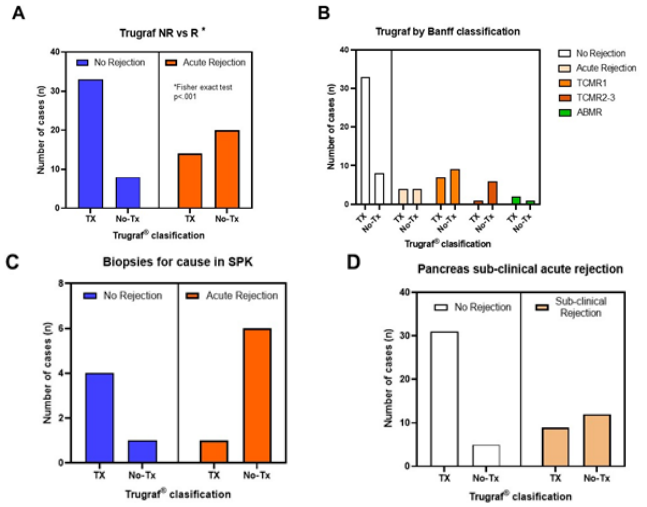

Figure: Trugraf® classification **A)** according to the diagnosis of acute rejection in the biopsy-matched cases evaluated, and **B)** according to the Banff classification scheme. **C)** Trugraf® discrimination ability biopsies performed for cause in recipients of SPK. **D)** Trugraf® discrimination in patients with sub-clinical (lipase <3xs/normal) pancreas acute rejection. SPK – simultaneous kidney-pancreas transplant.

P217 SARCOPENIA BUT NOT FRAILTY IS ASSOCIATED WITH A SPECIFIC METABOLOMIC SIGNATURE IN KIDNEY TRANSPLANT CANDIDATES

Maria Jose Perez Saez[1], Francisco Madrid[2], Alex Gomez-Gomez[2], Noemi Haro[2], Dolores Redondo-Pachón[1], Vanesa Davalos[1], Ester Marco[1], Marta Crespo*[1], Oscar Pozo[2], Julio Pascual[1]

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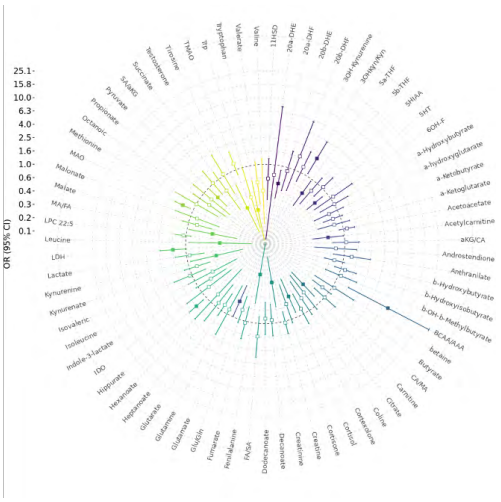
Background: Sarcopenia and frailty are conditions frequently neglected in the evaluation of kidney transplant (KT) candidates. They might contribute to poor health outcomes after transplantation. Our aim was to analyze which metabolites were associated with frailty and sarcopenia in a cohort of KT candidates.
Methods: Frailty and sarcopenia, measured by Physical Frailty Phenotype and EGWSOP-2 criteria, respectively, were evaluated. Serum samples were analyzed through targeted metabolomics. Seventy-five metabolic markers were tested utilizing weighted logistic regressions. The models were adjusted by age, sex, body mass index, diabetes mellitus, type of renal replacement therapy and family/social support. The Benjamini–Hochberg procedure was applied to control the false discovery rate.
Results: 173 KT candidates (72.3% male, mean age 60.7 ± 13.1 years) were evaluated. Regarding frailty and sarcopenia, 66.5% of KT candidates presented with any grade of frailty (57.8% were pre-frail and 8.6% were frail) and 27.2% with sarcopenia. Patients with frailty (both pre-frail and frail patients together) were more frequently female (77% of women vs. 62.4% of men presented with any grade of frailty, p=0.047) but same age as robust ones (61.04 vs 60 years, p=0.078). Similarly, sarcopenia was more frequently detected in women (41.6 vs. 21.6% in men, p=0.008). Phenylalanine, creatinine, serotonin, tyrosine, carnitine, and tryptophan were associated with sarcopenia (Figure). No metabolite was associated with frailty in this cohort.
Conclusions: Frailty and sarcopenia are frequent among KT candidates and women are at special risk for both of them. Although frailty was not associated with any specific metabolic pattern, sarcopenia was found to have a metabolic signature associated with the metabolism of phenylalanine, tyrosine and tryptophan. This metabolic signature might serve as therapeutic target for pharmacological and non- pharmacological treatments in the context of CKD patients.

Metabolite	OR (95% CI)	FDR-corrected p-value
Phenylalanine	0.186 (0.064-0.509)	0.0014
Creatinine	0.245 (0.099-0.575)	0.0016
Serotonin	0.589 (0.416-0.820)	0.0021
Tyrosine	0.256 (0.101-0.619)	0.0031
Carnitine	0.430 (0.241-0.753)	0.0033
Tryptophan	0.212 (0.073-0.589)	0.0035



P218 EFFICACY OF DESENSITIZATION IN INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION

Constantino Fernández Rivera[1], Catuxa Rodriguez Magariños[1], Marta Blanco Pardo*[1], Diego Sierra Castro[1], Maria Calvo Rodriguez[1], Tamara Ferreiro Hermida[1], Sara Domenica Erraez Guerrero[1], Leticia Garcia Gago[1], Andres Lopez Muñiz[1], Mercedes Cao Vilariño[1]

[1]Complexo Hospitalario Universitario A Coruña, Nephrology, A Coruña, Spain

Background: Kidney transplantation is the best therapeutic option for renal replacement therapy in patients with chronic renal failure but a lot of these patients are highly sensitized, and their transplantation options include joining specific lists, undergoing desensitization protocols, or entering cross-transplant programs. The aim of this study is to known the probability of kidney transplantation after desensitization in patients with incompatible HLA kidney transplantation
Methods: We studied all patients HLA incompatible with living donor that received a desensitization protocol with Rituximab, plasma exchange or immunoadsorption and CMV specific immunoglobulins and Immunosuppression with tacrolimus, mycophenolic acid derivatives and steroids. Efficacy of desensitization was to achieve a cross-match by CDC negative, flow cytometry negative and MFI of DSA < 1000.
Results: We analyzed 38 patients, median age 46,2±13 years old, 20(52,6%) women),Time in wait list 72±80months (seven patients were pre-emptive),CPRA 72.2±26%), RIS(relative intensity score) 8±6.7, number of mismatches (A,B,DR) 3.5±1,3, number of total antibodies 1.55±0,75. MFI Class I 7272±3920, MFI Class II 6422±4066. Cross-match positive before conditioning were CDC in 19, flow cytometry in 10 and presence of DSA in 9.
We achieve the objective in 29 patients (76.3%). These patients had MFI Class I lower (p< 0,001), RIS 5.9±4 vs 15±7.9 (p=0,008), age 48.7±13.1 years old (p=0,048). The percentage of patients with efficacy of desensitization was lower in those that cross-match was positive by CDC comparing with flow cytometry and DSA: 42%, 0% and 11.1% respectively (p=0.024).In ROC curves MFI Class I area 0,966 (p<0.01) with a sensibility of 87% and 1-specificity 0.48 for MFI Class I 9718.
Conclusions: Higher levels of MFI in Class I, RIS and cross- match positive by CDC are factors conditioning the efficacy of desensitization using this protocol.

P221 EVALUATING THE USE OF CONTINUOUS GLUCOSE MONITORING (CGM) EARLY AFTER KIDNEY TRANSPLANTATION

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Background: Prediabetes and Post Transplant Diabetes mellitus (PTDM) affect about 20-30% of kidney transplant recipients (KTR) and have been associated with an increased risk for cardiovascular morbidity and mortality in this population. Despite the poor performance of fasting plasma glucose (FPG) and HbA1c in detecting prediabetes and PTDM, the systematic integration of the “gold standard” oral glucose tolerance test (oGTT) remains challenging. The goal of this study was to evaluate the prognostic and diagnostic capacity of CGM regarding PTDM and prediabetes in the early phase after kidney transplantation.
Methods: CGM with the “Free Style Libre Pro IQ Sensor” was carried out in 21 KTR from day 10 to day 90 post transplantation. On day 90 a blood sample with FPG and HbA1c was drawn and an oGTT performed.
Results: Three months posttransplant, one patient developed PTDM (by all aforementioned diagnostics), twelve patients prediabetes (5 by oGTT, 8 by HbA1c, 8 by FPG) and eight showed no abnormality in the glycemic tests performed. One dropout war registered due to patient inconvenience with the sensor. CGM mean glucose from day 10 to day 90 was highest for the PTDM-patient, followed by the prediabetic and the normoglycemic ones. There were no sensor-associated adverse events.
Conclusions: Prediabetes and PTDM are highly prevalent at day 90 post kidney transplantation. CGM-metrics from day 10 to day 90 show an association with glycemic testing at day 90, though higher patient numbers are needed for conclusive statistical analyses. Importantly, feasibility and tolerability of the CGM were excellent allowing the general applicability in the transplant population.

P222 CALCINEURIN-INHIBITOR-FREE IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION IMPROVES RENAL FUNCTION: A SINGLE CENTER EXPERIENCE

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Background: Calcineurin inhibitor (CNI)-associated nephrotoxicity after liver transplantation (LT) is inevitable; however, the safety of both CNI-sparing protocols and CNI-free immunosuppression is still under debate. Thus, this retrospective analysis was designed to evaluate effects of CNI-discontinuation after long-term follow-up of liver transplant recipients.
Methods: 453 outpatients are currently being followed up after LT in our center. 35 (7.8%) of those were switched to CNI-free immunosuppression after 63 (4-125) months for renal (n=25) or neurological (n=1) impairment or the occurrence of cancer (n=9) to monotherapy with Everolimus (n=10), Sirolimus (n=7) or to Everolimus combined with Mycophenolate Mofetil (n=18). Target trough levels of Everolimus or Sirolimus were 4-6 ng/ml.
Results: While serum creatinine decreased by 17.7% after 6 months of CNI-free immunosuppression from 1.7± 0.6 mg/dl to 1.4 ±0.4 mg/dl the CCr increased by 11.7% from 65.9±11.3 ml/min to 74.6±13.7 ml/min. Most interestingly, kidney function recovered best in patients with serum creatinine of <2 mg/dl. Non-biopsy proven mild rejection occurred in only one patient (2.8%). Two patients (5.7%) were switched back to CNI for proteinuria. The infection rate was comparable in both groups.
Conclusions: CNI-free immunosuppression is safe and has a positive effect especially in patients with serum creatinine of <2 mg/dl.

P224 PROGNOSTIC VALUE OF CREATININE REDUCTION RATIO AT DAY 2 AFTER KIDNEY TRANSPLANTATION

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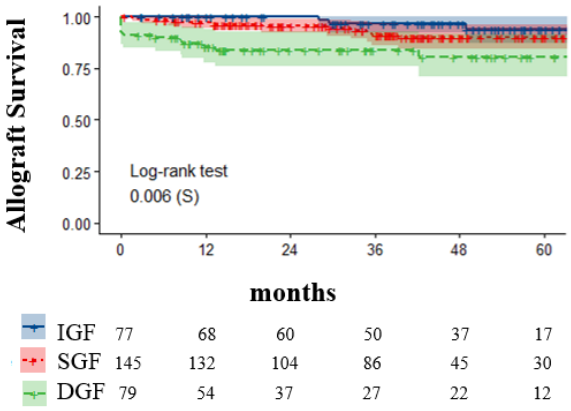
Background: Slow graft function [SGF] after kidney transplantation can be identified by a low Creatinine Reduction Ratio calculated at POD2 [CRR2], a subtle marker of how allograft function recovers, using the immediate trajectory of serum creatinine (SCr) instead of a threshold value.
Methods: CRR2(%) is defined by ([Cr1-Cr2]x100)/Cr1), where Cr1 is POD1 SCr (collected the first morning following transplantation) and Cr2 the SCr 24H after. In a monocentric, retrospective study, including all patients receiving a kidney transplant (taken from a deceased donor) between 2016 and 2021, we analyzed the outcome of patients with delayed graft function [DGF, defined by the need of dialysis by POD7], SGF (defined by a CRR2<30% and no need for dialysis), or immediate graft function [IGF, defined by a CRR2>30% and no need for dialysis). Patient and graft survival were computed over time using a Kaplan-Meier analysis, and a Cox model was used to quantify the impact of graft functions on the risk of graft loss or death.
Results: Among the 301 patients included in the study, 79 (26.2%) developed DGF, 145 (48.2%) recovered SGF, and 77 (25.6%) had an IGF. Median follow-up was 41.4 (Q1;Q3=19.9;58.0) months. Graft survival was significantly different between groups (Log-rank test, p=0.006) (Figure). Compared to IGF, DGF tripled the risk of graft loss (OR 3.26, 95%CI=[1.16;9.19], p=0.025). Likewise, patient survival was significantly influenced by the mode of graft function recovery: compared to IGF, SGF was associated with an OR of 3.65 for the risk of death (95%CI=[1.08;12.28], p=0.037), and DGF with an OR of 6.70 (95%CI=[1.96;22.88], p=0.002).
Conclusions: CRR2 is a swift, precise, and relevant marker for the quality of graft function recovery. It discriminates SGF (incidentally, the commonest trajectory of recovery) from IGF and DGF with respect to functional and vital outcomes.



(number of patients at risk)

P225 OPTIMIZING PATIENT THRIVING DURING THE TRANSPLANT PROCESS

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Background: Over 900,000 transplants have been conducted in the United States to date. Although transplantation is viewed as the optimal treatment for end-stage organ disease, many patients report mental health needs due to symptoms of anxiety, depression, and high levels of stress amongst others. These symptoms have been observed pre- and post-transplant, signifying the value of mental health interventions to help patients successfully navigate the steps to transplant as well as post-transplant to enhance their quality of life.
Methods: Informed by clinical practice and research, current practices and interventions used for managing the mental health needs of transplant patients are presented using case study examples as well as supporting research about the usefulness of these practices for different organ types. Additionally, a review of research on strength-based approaches for enhancing patients' qualify of life and coping during the transplant process is addressed.
Results: Findings revealed the importance of early mental health symptom identification, such as depressive symptoms given the potential for negative physiological and psychological outcomes. Evidence-based interventions such as cognitive behavioral therapy, acceptance and commitment therapy, and behavioral modifications have been effective for symptom reduction, improving medication adherence and reducing post-graft failure. Strength-based strategies such as resilience, and interventions focused on increasing patients' positive attitudes have been found to be beneficial, although this area is understudied.
Conclusions: Transplant-specific mental health providers are integral to the transplantation process as they are valuable for mitigating the mental health concerns co-occurring pre- and post-transplantation. Effective interventions can be advantageous for improving patients' outcomes and quality of life. Future work in this area should focus on groundbreaking evidence-based practices for helping patients and consider the cultural relevance of these practices. Also central to the provision of optimal mental health care is harnessing strengths that are already prevalent in this patient population.

P226 IS IMPLANTABLE DOPPLER PROBE USEFUL AS A VASCULAR MONITORING DEVICE IN KIDNEY TRANSPLANT PATIENTS: A RETROSPECTIVE COHORT, SINGLE CENTRE STUDY

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Background: Vascular complications account for 30-35% of the total kidney grafts lost during the first three months after implantation. Early detection of vascular complications allows an opportunity for a prompt intervention that is critical to reducing graft loss. This study aims to evaluate the usefulness of implantable Doppler probe as a vascular monitoring device in kidney transplant patients.
Methods: Implantable Doppler probe is used intermittently for the postoperative monitoring of kidney transplant patients at our centre. We conducted a retrospective description of prospectively maintained medical data by comparing the clinical outcomes in the kidney transplant patients that had postoperative Implantable Doppler probe monitoring against those with standard care clinical observation. The medical data of 324 kidney transplant patients at our unit between Jan 2016 and Oct 2021 was studied and divided into two groups. Group 1 consisted of 194(60%) kidney transplant patients with the postoperative Implantable Doppler probe monitoring while Group 2 comprised 129(40%) kidney transplant patients with standard care clinical observation. The groups were compared in terms of the number of vascular complications identified, the number of departmental ultrasound scans required postoperatively, and the 03-month graft loss.
Results: Overall, in all patients, vascular complications were identified in 13.5%, and the resultant graft loss was 2.1%. Both the groups were similar in demographical characteristics. In Group 1 more vascular complications were identified (17.5% vs. 9.3%; RR = 1.88), fewer ultrasound scans were requested in the first 24 hours postoperatively (71.1% vs. 83.7%; RR = 0.84), and lower graft loss (1.5% vs. 3.1%; RR = 0.48) was recorded as compared to Group 2. All probes were removed safely after 72 hours, and no complication related to the device was reported.
Conclusions: The monitoring device may be used as an additional adjunct for graft monitoring in kidney transplant patients. Further controlled studies are warranted to evaluate this device in clinical practice.

P227 PPI CONSULTATION ON THE PROTOCOL DEVELOPMENT OF A STUDY INVESTIGATING THE FEASIBILITY OF THE IMPLANTABLE DOPPLER PROBE IN KIDNEY TRANSPLANTATION

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Background: The shortage of organs available for donation is the most limiting factor in kidney transplant practice today. In the continuous quest to reduce graft loss due to vascular complications, new monitoring technologies are being investigated. A related study is proposed to assess the feasibility of a novel blood flow monitoring device, the Implantable Doppler (ID) probe in kidney transplant surgery.
Methods: This Public Patient Involvement consultation was aimed at exploring the views and expectations of the stakeholders (kidney transplant recipients, surgeons, clinicians, and nurses with direct experience of the ID probe) on the protocol development of the feasibility study. Its objective was to reveal areas of improvement in the study protocol, understand the perceptions of stakeholders regarding research in the postoperative graft surveillance, identify potential confounding factors to the research and challenges to implementation of ID probe in clinical practice. Semi-structured interviews containing open-ended questions were conducted with the stakeholders (n = 12). Thematic analysis of the data was done at the latent level by an inductive approach using a six-phase guide by Braun and Clarke using NVivo 12 software.
Results: Three key themes emerged. (1) Experiences with the ID probe as a monitoring device reflected that it was well received by the patients. However, there was a clinical equipoise among the healthcare professionals. (2) Recognition of the need for research in the early postoperative graft monitoring displayed the stakeholder's understanding regarding the role of a blood flow monitoring device to improve the surgical outcomes. (3) Recommendations for the smooth conduct of the proposed study includes suggestions for improvement in the study protocol, informative sessions for the patients and nurses, and innovative ideas to improve the monitoring device.
Conclusions: The PPI consultation provided valuable insights to inform the research design of the proposed feasibility study. Useful strategies and a patient centred approach identified were incorporated to mitigate the potential challenges to the conduct of the research.

P228 COMPARISON OF COVID-19 AFTER KIDNEY TRANSPLANTATION BEFORE AND AFTER THE OMICRON VARIANT EPIDEMIC IN JAPAN

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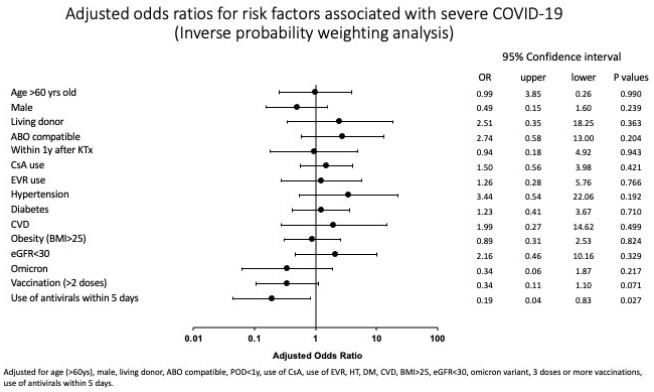
Background: With the emergence of the Omicron variant, the novel coronavirus infection (COVID-19) has evolved into the largest epidemic wave both domestically and internationally. The Omicron variant has been reported as more infectious and less severe in the general population, but its characteristics and clinical course in kidney transplant recipients are not clear.
Subjects: Patients who developed COVID-19 in the first to fifth domestic waves (April 2020 to December 2021: predominantly wild-type, alpha, and delta variants, n=27) and the sixth to seventh waves (January to August 2022: predominantly omicron variant, n=132) among the 1,498 kidney transplant recipients who were receiving care at our hospital as of June 2022.
Results: The incidence in the sixth to seventh waves was 9.7 times higher than in the first to fifth waves (1.2% vs. 11.6%, p<0.01). The sixth to seventh waves had significantly fewer patients who needed oxygen therapy (48.2% vs. 6.8%, p<0.01) and more patients who received three or more doses of the vaccine (18.5% vs. 81.8%, p<0.01). In the inverse probability weighting analysis, the use of antivirals within 5 days of onset was associated with a decreased risk of needing oxygen therapy (adjusted OR 0.19, 95%CI [0.04-0.83], P=0.03).
Conclusions: In the sixth to seventh domestic waves by the Omicron variant since January 2022, the incidence of COVID-19 increased, but the severity decreased in kidney transplant recipients as well as in the general population. Even during the Omicron endemic, early treatment with antivirals is important for recipients.



P229 URINE-DERIVED STEM CELL ATTENUATED RENAL FIBROSIS AFTER ISCHEMIA REPERFUSION VIA KLOTHO ACTIVATION

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Background: After renal IRI, regeneration and recovery of the renal tubular cell occurs. However, if the renal repair process is maladaptive, it progresses to renal fibrosis. The role of stem cells in kidney regeneration or fibrosis has not been fully elucidated. we evaluated the urine drived stem cells(UDSC) for renal inflammation and fibrosis after renal ischemia reperfusion(IR).
Methods: 10 week old balb/c nude male mice were used. sham, sham with UDSC, IR, IR with UDSC. UDSC were infused 3 times via tail vain at 6,7,8th day after renal IR. Urine NGAL/creatinine(Cr) were checked. The kidneys tissue were harvested at day 14 day. In vitro, TGF-β treated HK2 cell were co-cultured with UDSC. Klotho siRNA silencing was performed in UDSC.
Results: Urinary NGAL/Cr were significantly increased in IR mice after 14 day IR, compared to sham mice. Urinary NGAL/Cr significantly decreased in UDSC treated IR mice, compared to IR mice. In H&E stain, renal tubulo-interstitial injury were significantly decreased in UDSC treated IR mice, compared to IR mice. In masson trichrom stain, renal fibrosis area were were significantly decreased in UDSC treated IR mice, compared to IR mice. The renal expression of TGF-β, α-SMA, and collagne IV were significantly decreased in UDSC treated IR mice, compared to IR mice. The renal expression of Klotho were increased in UDSC treated IR mice, compared to IR mice. in vitro, UDSCs were stem cells that expressed Klotho protein more strongly than other mesenchymal stem cells (MSCs). UDSCs also suppressed fibrosis by inhibiting transforming growth factor (TGF)-β in HK-2 human renal proximal tubule cells in an in vitro model. Klotho siRNA silencing reduced the TGF-β-inhibiting ability of UDSCs.
Conclusions: UDSC attenuate renal fibrosis after renal IR. Klotho-secretion of UDSC play a role in these anti- fibrotic effects.

P230 DELETION OF PTP4A1 AMELIORATE RENAL FIBROSIS INDUCED BY UUO IN MICE

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Background: Inhibitors of protein tyrosine kinases(PTP) has been investigated as potential anti-fibrotic agents. PTP4A1 belongs to a sub-class of three prenylated PTP. PTP4A1 has known as promoting growth and migration of tumor cells. The role PTP4A1 has little known in kidney. We evaluated whether the PTP4A1 could be target of renal fibrosis.
Methods: 10 week old male background PTP4A1 KO mice and wild type mice were divided into 4 groups; wild, PTP4A1 KO, wild with UUO, and PTP4A1 KO with UUO. Mice were sacrificed at 7 days after surgery and kidney tissue were collected. Molecular study and Histologic examination were performed.
Results: PTP4A1 KO with UUO mice showed decrease of renal tubule-interstitial damage and fibrosis compared to wild type UUO mice. PTP4A1 KO with UUO reduced the renal expression of α-SMA and TGF-β in UUO kidney, compared to wild type with UUO mice. Wild type with UUO kidney showed decrease of renal expression of E-cadherin, compared to sham mice. However, PTP4A1 KO UUO showed increase of renal expression of E-cadherin, compared to Wild type UUO mice. In vitro, silencing of PTP4A1 in TGF-β treated HK2 cell showed increase of E-cadherin and decrease of hosphorylation of AKT and GSK3ß
Conclusions: PTP4A1 KO ameliorate renal fibrosis in UUO kidney.

P231 THE LONG-TERM RISKS OF KIDNEY DONATION (RENAL RESERVE, HYPERTENSION): OBSERVATIONS FROM A 15-YEAR FOLLOW-UP PERIOD AT THE MILITARY MEDICAL ACADEMY

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Background: The research papers published over the past decade have increased the knowledge concerning the long-term risks after kidney donation. We conducted a retrospective study in our kidney donors in the period from 2004. to 2020., taking into account the renal reserve assessment and the frequency of occurrence and/or worsening of hypertension.
Methods: Our study was conducted as a retrospective case-control study. It included all living kidney donors who underwent donor nephrectomy since 2004 and for whom the medical documentation was available. The parameters of interest were observed before donor nephrectomy, 6 months post-op and 1, 5, 10 and 15 years post-op as well. The control group consisted of donor nephrectomy patients themselves.
Results: The average age of our patients at the time of donation was 55.87, with almost two thirds of them under the age of 60. After donor nephrectomy, the kidney function is decreased. In the first year, a statistically significant decrease in total glomerular filtration (eGFR CKD EPI) was registered, while in the later observed period a partial recovery was achieved. Out of our 108 patients, 44 (40.74%) did not have hypertension during the selection period, nor did they develop it during the follow-up. In 20 patients (18.52%), de novo hypertension developed in the follow-up period. Hypertension was constantly present in 42 patients (38.89%), while 2 patients (1.85%) with hypertension verified prior to donation, were found not to have it after donor nephrectomy. At the beginning of the follow-up period, we observed that, in the group of patients who did not have hypertension prior to donation, the eGFR CKD EPI was lower, compared to the group of patients who had had prior hypertension.
Conclusions: In our study, the donor's age hasn't been proved to be a significant factor which impacts the average time span preceding the occurence of chronic kidney disease (CKD). In patients under the age of 45, not a single CKD was developed. In patients aged 60 and over, 32% developed CKD. Hypertension in the follow-up period was not the reason for faster deterioration and/or the onset of CKD compared to patients without hypertension. Kidney donors are ideal for studying the relationship between the reduced renal reserve and the risk of cardiovascular disease (CVD) occurence.

P232 PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS IN A BELGIAN COHORT OF LUNG TRANSPLANT CANDIDATES: THE PROGRESS STUDY

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Background: Lung transplant (LT) candidates are at high risk of osteoporosis (OP), due to both their respiratory condition and frequent oral glucocorticoids use. However, few is known on the prevalence and management of OP in LT candidates. This study aims to evaluate the prevalence and therapeutic management of OP in LT candidates and to determine the risk factors associated with OP.
Methods: We included 198 patients patients (103 women) among 388 screened for LT at CHU UCL Namur between January 1998 and December 2020. We collected data on bone mineral density (BMD), measured by Dual-energy X-ray absorptiometry (Hologic) at the lumbar spine, total hip and femoral neck, fragility fracture (FF), and OP risk factors along with other factors suspected of affecting BMD such as inhaled (i) glucocorticoids (GCs) use, pulmonary function tests, hypoxemia and pulmonary disorder type.
Results: OP, as defined by BMD values (T-score ≤ -2.5) and/or FF, was observed in 118 patients (59.6%), among which 54 (45.8%) had only a T-score ≤ -2.5, while 36 (30.5%) had only an FF, with predominant vertebral fractures (77.8%). OP patients were older (median [IQR]) (59.0 years [54.2-62.0] vs 57.0 [53.0-62.0]) and had lower body-mass indexes (mean ± SD) 22.2 ± 4.6kg/m² vs 24.3 ± 4.6kg/m² than non-OP. Seventy-eight OP patients (66.1%) reached the ten-year probability of major osteoporotic fracture intervention threshold. Among them, 53 received only calcium and/or vitamin D and 25 an add-on therapy, mostly a bisphosphonates (n=23, 92.0%). Thirty-six OP patients (30.5%) were untreated. OP patients was more prevalent in COPD patients (n=102/153, 66.6%%) than in those with ILD (n=12/33, 36.3%) or any other pulmonary diseases (n=4/12, 33.3%). Finally, OP patients used more iGCs, had lower FVC and severely impaired FEV1/FVC ratio. Oral GCs treatment was associated with FF, regardless of the daily dosage.
Conclusions: Most of LT candidates have OP. OP diagnosis before LT in these patients is crucial for a better management of their bone fragility risk after transplantation. GCs use is a major OP risk factor in this category and should raise awareness on related risks of OP.

	All Patients (n=198)	OP patients (n=118)	Non-OP (n=80)
Age, y (median and IQR)	58.0 (53.3-62.0)	59.0 (54.2-62.0)	57.0 (52.0-62.0)
BMI, kg/m² (mean ± SD)	23.1 ± 4.7	22.2±4.6	24.3±4.6
GCs use, n (%)	154 (77.8)	94 (79.7)	60 (75.0)
iGCs use, n (%)	155 (78.3)	99 (83.9)	56 (70.0)
COPD, n (%)	153 (77.3)	102 (86.4)	44 (55.0)
FEV1, % PV (median and IQR)	23.0 (19.0-35.0)	22.0 (19.0-28.0)	28.0 (20.0-52.7)
FVC, % of PV (median and IQR)	60.0 (49.0-75.0)	58.0 (48.0-71.0)	64.0 (50.0-77.2)
FEV1/FVC ratio (median and IQR)	41.0 (35.0-57.0)	40.0 (35.0-48.0)	49.5 (35.7-93.2)
T-score ≤ -2.5, n (%)	54 (27.3)	54 (45.8)	NA
FF, n (%)	36 (18.2)	36 (30.5)	NA
T-score ≤ -2.5 and FF, n (%)	28 (14.1)	28 (23.7)	NA
Risk factors for OP, OR (CI) – p value			
BMI	NA	0.43 (0.20-0.92) p = 0.03	NA
GCs use	NA	1.31 (0.66-2.57) p = 0.44	NA
iGCs use	NA	2.23 (1.13-4.48) p = 0.02	NA
FVC	NA	0.49 (0.25-0.94) p = 0.03	NA
FEV1/FVC ratio	NA	0.38 (0.17-0.86) p = 0.02	NA
COPD	NA	3.62 (1.83-7.42) p = 0.0003	NA

Abbreviations. BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FF, fragility fracture; FVC, forced vital capacity; iGCs : inhaled glucocorticoids; IQR, interquartile range; GCs, oral glucocorticoids; NA, not applicable; OP, osteoporosis; OR, odds ratio; PV, Pulmonary volume; SD, standard deviation; y, years

P233 REDUCTION OF ORGAN ALLOCATION TIMES

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Background: Optimizing the time in need to allocate organs is a priority to rationalize timing in the articulate and complex process of donation and transplantation. For this purpose, on February 14th 2022 the protocol named "Reduction of organ allocation times project" has been introduced. The main aspects entered by the protocol were: identification of a minimum data set, organ-specific, in need for the evaluation; identification of a procedure as long as to permit transplant centers rapid and easy access to data; identification of a procedure with the aim of rationalizing transplant centers' evaluation of the organs. The goal of this paper is to compare the average organ allocation time before and after the use of the protocol.
Methods: From February 14th 2022 to August 14th 2022 organ allocation times were evaluated for about 22% of actual DBD donors (145 donors casually selected). A proportional stratified sample has been considered. In the priority organ allocation scheme of the donors selected, recipients enlisted on a national allocation organ programme for at least one thoracic organ, liver, kidneys and eventually pancreas, had to occur. In order to calculate allocation times the time of the first organ offered and the time of the last organ accepted have been taken into consideration. The resulting average allocation time has been confronted with the one calculated taking into account a similar sample (casually selected) of 2021, the year prior to the protocol entry.
Results: During the period in which the protocol has been used, the average organ allocation time was 292 minutes (median: 251 minutes), while during the previous period, it was 364 minutes (median: 334 minutes).
Conclusions: The analysis shows how the entry of the protocol strikes its goal with an average reduction of the time needed for the organ allocation process up to 72 minutes. However, continuous effort in order to reduce more the allocation times in order to make the process smoother and prompter is necessary.

P234 FUTURE-PROOFING DECEASED DONOR KIDNEY TRANSPLANTATION: FIRST RESULTS OF A UNIQUE COLLABORATIVE BETWEEN FIVE TRANSPLANT CENTRES IN A METROPOLITAN AREA

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Background: Deceased donor kidney transplantation (DDKT) is unpredictable; any transplant centre (Ctr) may receive many offers in a short timeframe for which there may not be enough capacity (CAP) to transplant (Tx) in a timely fashion. Such situations pose logistical and ethical challenges. Prolonged cold ischaemia times (CIT) with adverse outcomes may result. Declining an offer could result in patients losing out on a unique Tx opportunity. There may however be a neighbouring Ctr with surplus CAP. To identify and utilise this CAP, a system for the safe transfer and transplantation of patients and organs between 5 Ctrs in a metropolitan area was proposed in 2018. We here describe the initial activity and outcome of the resulting collaborative.
Methods: Prospectively collected data on DDKT performed by this collaborative was obtained from National Health Service Blood and Transplant and the five collaborating centres, then retrospectively analysed.
Results: 16 patients were transplanted over 21 months during the ongoing coronavirus pandemic (COVID-19). Ctr CAP and computer systems failure were the reasons for utilisation of the collaborative. 10 kidneys (63%) were from donation after brainstem death. Median kidney donor risk index was 1.18 (interquartile range 0.56). Median kidney donor profile index was 68% (44). 8 kidneys (50%) were extended criteria. 4 donors (25%) had acute kidney injury. 12 patients (75%) were first Tx recipients. 3 patients (19%) were highly sensitised (calculated reaction frequency ≥ 85%). Median waiting time was 1075 days (955). Median recipient body mass index was 24.4 (4.7). Median CIT was 13.12 hours (4.99). 7 patients (44%) had delayed graft function. Median length of stay was 7.5 days (7.5). 3 patients (19%) died within 6 months after Tx. 7 patients (44%) suffered post-operative complications. 2 patients (13%) required re-operation. Median creatinine was 270 µmol/L at seven days (146), 121 µmol/L at 3 months (80), 144 µmol/L at 6 months (97) and 108 µmol/L at 12 months (78).
Conclusions: Our experience demonstrates the feasibility of a unique Tx collaborative by sharing CAP between five centres for DDKT. Morbidity and mortality have been affected by COVID-19. These patients may otherwise not have received their Tx. We hope to foster greater harmonisation as the collaboration continues.

P235 EXTENDING THE USE OF WEB PORTAL FOEDUS TO UNITED KINGDOM ORGANIZATION (NHS) AND EUROTRANSPLANT IN 2022

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Background: From 2015, almost all European countries have been using the FOEDUS web portal to manage organ exchange offers. These offers increase the availability of suitable organs for the patients awaiting for organ transplantation around Europe. From January 2022, United Kingdom health system (NHS) and Eurotransplant joined and started using the portal. The aim of the paper is analyzing the effect of their involvement on the organ exchange flow on FOEDUS.
Methods: We compared the data regarding organs offered and transplanted in the years 2021 and 2022, thanks to the use of FOEDUS portal. We considered in detail the type of organ and organization that made the offer, and the type of organ and organization that accepted the offer and eventually transplanted the organ.
Results: In 2022, a total number of 386 organs were offered through FOEDUS web portal, while, in 2021, 285 organs were offered, registering an increase by 35 %. Excluding kidneys and multivisceral organs offers, all the other organ offers improved significantly. In particular, we observed a significant increase for lungs and small bowel offers, which increased about by 86% and 145% respectively. To date, UK-NHS has not started using the FOEDUS portal yet, to offer organs abroad; on the contrary, Eurotransplant stated offering up to 80 organs and resulting the leading organization offering organs abroad (21 % of the total offers). In 2022, a total of 97 organs offered and accepted through the portal were actually transplanted, compared with 57 transplanted in 2021, with an increased by 70%. Considering the data of the new organizations participating in the program, UK-NHS performed 4 transplants and Eurotransplant 27. In 2022, as well as in 2021, Italy was the Country that performed the higher number of transplants with organ accepted through the FOEDUS portal: 23 in 2021, 29 in 2023.
Conclusions: Extending the use of the FOEDUS web portal to other organizations is an advantage for the patient enlisted for organ transplantation as long as we proved to increase the number of organ offers and transplants among Europe. The allocation rule based on the principle first comes first serves improved the chance to find the more suitable recipient in the shortest time.

P236 ASSOCIATION BETWEEN ADULT DBD KIDNEY OFFER DECLINE RATES AND RISK-ADJUSTED WAITING TIMES IN THE UNITED KINGDOM

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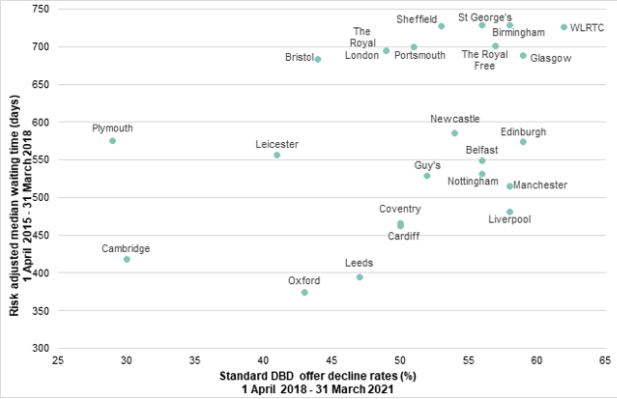
Background: Deceased organ donor age and co-morbidities are increasing, meaning that donated organs are more challenging to successfully transplant. There is a variation in appetite for accepting donor offers across the 23 adult kidney transplant centres in the UK[1]. We explore whether 'risk appetite' predicts the average time that a patient waits for a standard criteria[2] DBD donor kidney transplant.
Methods: Data were extracted from the UK Transplant Registry held by NHS Blood and Transplant as published in the NHSBT Kidney Annual Report 2020/21[1]. Offer decline rates were calculated by centre using adult kidney- only offers from standard criteria DBD donors, between 1 April 2018 and 31 March 2021, who had at least one kidney retrieved, offered directly and on behalf of a named individual patient and resulted in a transplant. Adult risk-adjusted[3] median waiting times by centre were calculated for patients listed between 1 April 2015 and 31 March 2018 using a Cox-proportional hazards model. The Pearson's correlation coefficient was used to measure the association between centres offer decline rate and risk-adjusted median waiting time.
Results: The overall decline rate in the UK for an adult standard criteria DBD donor kidney offer was 53%, ranging from 29% to 62%. The median risk-adjusted waiting time to transplant for adult patients registered on the kidney-only waiting list is 563 days, ranging from 374 days to 729 days. Figure **1** shows a significant linear relationship between offer decline rate and waiting time (r=0.4, p=0.05). This is a positive relationship, with a higher offer decline rate associated with a longer waiting time.
Conclusions: Risk-adjusted waiting time and offer decline rates increase together even for these apparently favourable donor offers. This may lead to patients being disadvantaged, depending on the centre where they were listed.
[1]https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/26790/kidney-annual-report-2020-21.pdf. [2] Donors aged < 60 or aged 50 to 59 with one or fewer donor characteristics: hypertension, creatinine >130 µmol/l or death due to intracranial haemorrhage. [3] Risk-adjusted for age at registration, sex, ethnicity, highly sensitised, blood group, dialysis status, matchability score, renal disease.

Figure 1: Adult kidney adjusted waiting time by DBD standard offer decline rates



P238 THE EFFICACY OF FERROPTOSIS INHIBITION IN KIDNEY ISCHEMIA REPERFUSION INJURY AND TRANSPLANTATION: A SYSTEMATIC REVIEW

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Background: Ferroptosis, a new form of iron-dependent cell death, plays a role in organ injury resulting from ischemia and reperfusion injury (IRI). Several ferroptosis inhibitors have been described. Here, we report the results of our systematic review on the evidence of ferroptosis inhibition on outcomes in experimental models of renal IRI and transplantation, with specific attention to their efficacy against organ injury and on organ function.
Methods: Using two concepts of "ferroptosis" and "ischemia reperfusion injury", a broad search strategy was build and used to screen multiple databases (Pubmed, Embase, Web of Science, Cochrane).
Results: After screening 1786 records and 1753 records after snowballing, 18 articles were included (mice: 10; rat: 4; rabbit: 3; dog: 1; pig: 1). The majority of studies (16/18, 89%) showed improved outcomes with ferroptosis inhibition. Ferrostatin-1 (radical trap, 5/18, 28%) and deferoxamine (iron chelator, 9/18, 50%) were most frequently studied. Ferrostatin-1 inhibition improved outcome in all studies, deferoxamine in 7/9 (78%) studies. Emerging evidence suggests that novel inhibitors with improved pharmacodynamics or specific targets in ferroptotic pathways are protective as well (8/18, 44%). Especially, inhibitors protecting the anti-oxidant system, direct or indirect, are increasingly studied (5/18, 28%) and can effectively reduce renal injury (5/5, 100%). Interestingly, combination treatments with inhibitors of necroptosis or other damaging pathways proved to be superior to ferroptosis inhibition alone, which is consistent with the multifactorial nature of IRI.
Conclusions: Ferroptosis inhibition can significantly improve kidney function and protect against IRI. These findings confirm that ferroptosis inhibitors have the potential to reduce IRI in kidney grafts. Further translation to clinically relevant models is important.

P240 CARDIOVASCULAR EVENTS AFTER KIDNEY TRANSPLANTATION AND LONG-TERM OUTCOMES

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Background: Over the past decades , improvement in kidney transplant (KT) survival is more pronounced in the short term than in the long term. Cardiovascular (CV) events are the leading cause of nongraft-related mortality in KT recipients in the long term. Detection of potential risk factors (RF) of CV events are essential for improving KT outcomes.
Methods: A total of 184 patients undergoing KT from 2008 to 2011, were included in the study. Patients were divided into two groups: with CV events (n=70) and without CV events (n=114). Traditional and non-traditional RF that predict CV events were analysed. Cardiovascular events were defined as the presence of myocardial infarction, invasive coronary artery therapy, cerebral vascular events, congestive heart failure, rhythm disturbances or cardiac death. Recipients were classified as having graft dysfunction if their Glomerular filtration rate (GFR) was < 60 ml/min per 1.73 m^2 body surface area, calculated with the CKD-EPI Creatinine, 2021 equation. Logistic regression analysis was used to determine the RF. Kaplan-Meier analysis assessing survival of patients with and without CV events was conducted.
Results: Overall, 70 (38%) of all recipients had CV events. Analysis of clinical-demographic data showed that patients with CV events had a higher mean age (60.37 years vs 48.61 years, p<0.001), a higher incidence of smoking (52.9 % vs 21.9%, p<0.001) and graft dysfunction was more common (85.7 % vs 72.8 %, p=0.03) than patients without CV events. In a multifactor analysis using logistic regression, significant CV risk factors were confirmed: age (OR:1.09; P<001); smoking (OR:5.80; P<0.001); proteinuria (OR:2.31; P=0.038 and time on dialysis (OR:1.02; P=0.040). The odds ratio showed that patients with graft dysfunction had a 2.24-fold higher risk of developing a CV event than those without graft dysfunction (OR=2.24; 95% CI, 1.02-4.92). Kaplan-Meier 120-month survival curves for patients were significantly lower in patients with CV events (70% vs. 90%; P<0.0001).
Conclusions: It can be concluded that KT recipients have a high incidence of CV events, which occurs in 38% of cases in our study. CV events affect the survival of KTR compared to patients without CV events. Detection of CV risk factors timely is of utmost importance in management of KT recipients.

P241 MISMATCHED HUMAN LEUCOCYTE ANTIGENS BETWEEN BLOOD DONORS AND WAITLISTED TRANSPLANT PATIENTS LEADS TO TRANSFUSION SPECIFIC HLA-B ANTIBODIES

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Background: HLA (human leucocyte antigens) sensitisation affects access to kidney transplantation; the median wait time for highly sensitised patients is twice that of unsensitised patients. Red cell transfusion provokes alloimmune anti-HLA antibodies and is a potentially modifiable source of HLA sensitisation. It has been shown to cause broad HLA sensitisation. Here we show it can cause transfusion specific antibodies (TSAs) and degree of mismatch can predicts the formation of antibodies.
Methods: We identified waitlisted kidney transplant candidates who received a blood transfusion. The corresponding blood donors were identified, contacted and retrospectively HLA typed (REC 18/WM/0161). Donors and recipients were typed to split specificity antigen level. We compared HLA antibodies, as determined by single antigen bead assays pre- and post-transfusion and identified the transfusion specific antibodies (TSA) against donor antigens.
Results: We identified 55 patients who received 111 typed blood transfusions (median 2, range 1-5). 17 patients (30.9%) had HLA antibodies prior to transfusion. Post-transfusion, 36 patients (65.5%) had at least one new HLA-antibody specificity; all 17 of the pre-sensitised patients and 19/38 (50.0%) without known prior sensitisation. 21 patients (38.1%) developed at least one TSA. The mean number of transfusion specific antibodies was 1.95 (± 1.43). Of the 41 TSAs which developed 11 (26.8%) targeted class II antigens. The most common locus targeted was HLA-B, with 9 patients (16%) developing 17 HLA-B antibodies. The mean total HLA-A, -B, -DR and -DQ mismatch was 5.87 (±1.26). The HLA mismatch at HLA-B was predictive of developing an HLA-B TSA, with a mean mismatch of 1.88 and 1.63 for TSA+ and TSA- patients respectively (p=0.026). Too few antibodies targeted other loci to assess the impact of mismatching.
Conclusions: We have shown that red cell transfusion increases HLA-sensitisation in waitlisted patients. Poorly matched transfusions result in many patients developing a TSA. Most TSAs target Class I HLA but a significant proportion target Class II. Class II antibodies are known to be more persistent so will impact listing. The degree of mismatch between blood donor and recipient predicts HLA-B antibody formation. The use of HLA matched red cells may help mitigate this effect.

P242 PROGESTERONE EFFECTS ON INTESTINAL CHANGES CAUSED BY ISCHEMIA AND REPERFUSION PROCESS

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Background: Intestinal transplantation is becoming the standard treatment in patients with nutritional impairment, and patient graft survival rates have improved over time. However, bowel transplantation is still associated with significant mortality and morbidity, which may be directly linked to the ischemia and reperfusion process Progesterone depresses the inflammatory response and reduces the free radicals development in the intestine. Thus, our aim was to evaluate the impact of treatment with progesterone on the intestinal ischemia and reperfusion (IR) process.
Methods: Male Wistar rats were divided in 3 groups (n= 7): Sham (SH) group, animals submitted only to surgical procedure; IR group, animals submitted to ischemia (30 min) and reperfusion (2h); P4 group, animals submitted to ischemia/reperfusion and treated with progesterone (P4) (2mg/Kg, i.v.) at the moment of flow reestablishment. The ischemia was induced by insertion of a 2-F balloon catheter in the descending aorta leading visceral ischemia. Intestinal transit, vascular permeability and serum inflammatory mediators (ELISA) were measured at the final of the experiment period.
Results: IR decreased intestinal transit compared to sham group (SH 71.5%±2.6; IR 46.04%±6.7 p=0.006), and the treatment reduced these alterations; (P4 62.1%±4.7; p= 0.057). In the analysis of vascular permeability, IR group showed higher values compared to other groups (SH 347.6ug/mg±104.8; IR 575.8ug/mg±157.3; P4 160.9ug/mg±;29,53 p=0,33). Moreover, IR increased systemic inflammatory mediators, such as TNF-α (SH 7.2pg/ml±1.8; IR 24.9pg/ml ±8.1; p=), IL-10 (SH 65.9pg/ml±3.3; IR 942.8pg/ml ±253.0) and IL-6 (SH 957.4 pg/ml±42.64; IR 22300 pg/ml ± 8903), and the treatment was able to reduce TNF-α (P4 8.9±2.2 pg/ml; p=0,03) and IL-10 (P4: 367.8pg/ml±92.7; p=0,03).
Conclusions: Progesterone treatment modulated intestinal transit and reduced the release of inflammatory mediators caused by visceral ischemia and reperfusion. Therefore, progesterone therapy could be an alternative to reduce complications after gut transplant. Financial Support: 2021/05673-0 Fundação de Amparo à Pesquisa do Estado de São Paulo-FAPESP

P243 PRE-TRANSPLANT KIDNEY ASSESSMENT DURING NORMOTHERMIC MACHINE PERFUSION USING NOVEL IMAGING TECHNIQUES

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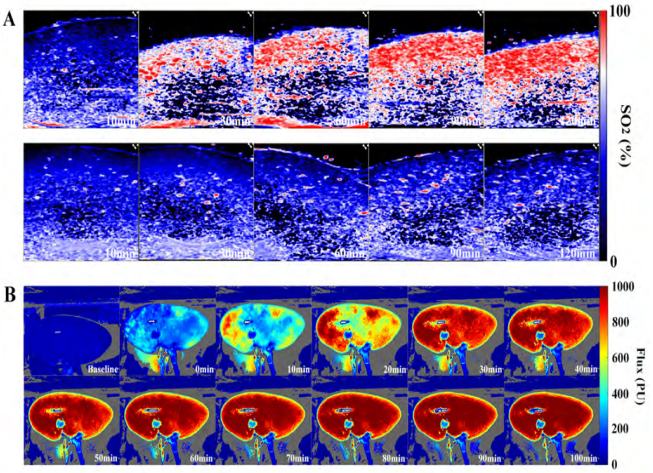
Background: Normothermic machine perfusion (NMP) provides a platform to assess donor organ quality prior to transplantation, which is significant when using marginal donor kidneys. As novel imaging techniques, photoacoustic imaging (PAI) can identify different tissue molecules and laser speckle contrast imaging (LSCI) can visualize the movement of particles. The aim of this study is to investigate the value of PAI and LSCI as kidney quality assessment tools during NMP.
Methods: Two independent studies using slaughterhouse porcine kidneys were conducted. In the 1st study, kidneys (n=16) were subjected to 30 minutes (n=8) and 75 minutes (n=8) warm ischemia time (WIT) respectively. Volumetric PAI of the renal cortex was acquired for each kidney during 120 minutes of NMP. The PAI data were used to quantify oxygen saturation (SO_2). In the 2nd study, all kidneys (n=10) were subjected to 30 minutes WIT. LSCI was used to measure one-sided microcirculation in the first 100 minutes of NMP, followed by measurement on both ventral and dorsal aspects after clamping one renal artery branch to induce ischemia.
Results: In the 1st study, kidneys with 30 minutes WIT showed significantly higher SO_2 (Figure 1A), blood flow, creatinine clearance and oxygen consumption compared to the kidneys with 75 minutes WIT. Renal cortical SO_2 had a positive correlation with renal blood flow (r=0.82, p<0.001) and oxygen consumption (r=0.73, p<0.001). In the 2nd study, the increase of renal cortical perfusion could be visualized with LSCI (Figure 1B). LSCI fluxes correlated linearly with renal blood flow (R^2=0.90, p<0.001). Kidneys had comparable creatinine clearance, fractional excretion of sodium and total sodium reabsorption after occlusion of the inferior renal artery branch as before, while the decrease in renal cortical perfusion could be visualized and quantified by LSCI.
Conclusions: PAI and LSCI are promising imaging techniques in real-time kidney perfusion measurement during NMP. PAI can be a valuable addition to evaluate renal metabolism and LSCI can visualize cortical microcirculation. The combination of using PAI and LSCI can help assess pre-transplant kidney quality.

Figure 1. A. Oxygen saturation of the kidneys with 30 minutes (top) and 75 minutes (bottom) WIT; B. Laser speckle contrast images of the kidney during 100 minutes of NMP.



P245 THE EXPERIENCES OF HEALTH CARE PROFESSIONALS APPROACHING FAMILIES FOR ORGAN DONATION CONSENT: A MIXED-METHOD SYSTEMATIC REVIEW

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Background: Healthcare professionals (HCPs) play an essential role in organ donation (OD) particularly when approaching families to discuss consent to OD. The percentage of families agreeing to deceased donation varies globally and therefore gaining insights in the complexities of approaching families is paramount. We conducted a mixed-method systematic review to synthesize the evidence reporting HCPs' experiences in approaching potential donor families for donation after brain or circulatory death.
Methods: Fourteen bibliographic databases were searched to identify studies describing HCP experiences when approaching potential donor families or associations between HCP experiences and consent rates. Independent reviewers extracted the data and assessed the methodological quality using the Mixed Methods Appraisal Tool. Data were analysed using parallel-results convergent synthesis design using thematic synthesis.
Results: We identified 12,698 unique references of which 86 studies met the inclusion criteria. The methodological quality of studies varied. Despite the common assumption that staff experiences can be improved by training and education, quantitative studies showed that consent rates did not increase significantly following OD training. HCP experiences were categorised according to broad themes including personal, organisational, patient, family, death and approach. HCP experiences were conceptualised as a paradox due to the challenges to negotiate the boundaries between life and death. Organisational and personal aspects shape the experiences of professionals broadly. The complexities of the family approach were evident in the variety of definitions of HCP experiences and experienced interactions between HCPs and the donor family, which may explain why there is no uniform approach across settings and countries.
Conclusions: The review highlights the challenges faced by professionals when negotiating policy and practice globally. Findings inform the development of recommendations for good practice and training to support staff involved in the OD process worldwide. This will require strategies of international collaboration and cooperation taking into account legal and sociocultural factors of countries.

P246 NORMOTHERMIC MACHINE PERFUSION ALTERS RENAL GENE EXPRESSION PATTERNS

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Background: Renal normothermic machine perfusion (NMP) is gaining interest because of its potential for viability assessment and graft repair before transplantation. During NMP, in vivo-like conditions are pursued. However, physiology during NMP is still incompletely understood, and it is likely that in vivo functional markers, such as creatinine clearance or fractional sodium excretion, are not appropriate for ex vivo viability assessment. Therefore, a better understanding of ex vivo physiology is warranted to further develop NMP as an assessment tool. We aimed to unravel ex vivo organ biology by analyzing the RNA profiles of kidneys in vivo and during NMP.
Methods: Thirty landrace pigs were anesthetized and prepared for a bilateral nephrectomy. During surgery, an in vivo biopsy was taken. One kidney was exposed to 75 minutes of warm ischemia (WI), while the contralateral kidney sustained no WI. Kidney grafts were cold preserved for 6 hours, followed by 6 hours of NMP. Cortical biopsies were taken at 0, 1, 2, 3, and 6 hours of NMP. RNA sequencing was performed in all biopsies and aligned to a reference genome. Sequencing results were analyzed using the Seurat pipeline in R. Clusterprofiler was used for functional analysis of identified gene clusters.
Results: A total of 27,626 genes were identified. Unsupervised clustering analysis revealed distinct clustering between the different time points and exposure to WI (Figure 1A). Only two significantly differentially expressed genes (DEG) were identified after cold preservation compared to in vivo (P adj < 0.05) (Figure 1B). However, during NMP, gene expression profiles changed considerably. Functional enrichment analysis of protein-coding genes revealed downregulation of genes involved in mitochondrial respiration and upregulation of inflammatory processes during NMP. Kidneys exposed to WI showed upregulation of the genes related to stress responses compared to the kidneys with no WI.
Conclusions: These results show that in vivo renal function significantly differs from function during NMP, emphasizing that the interpretations based on our in vivo reference frame should be carefully weighed. Additionally, the duration of NMP and the timing of viability assessment are of great importance, as the active physiological processes change over time.

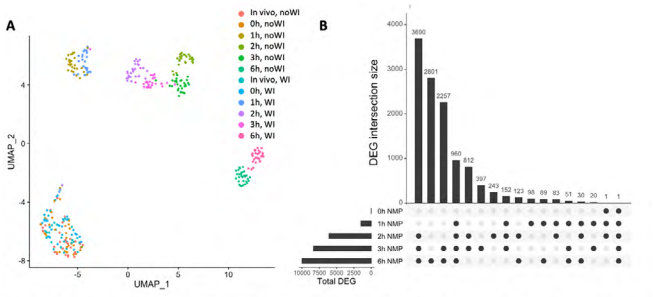

Figure 1. (A) UMAP of all samples. (B) Upset plot of DEG (P adj. < 0.05) of all timepoints compared to in vivo gene expression. Bars indicate overlapping DEG between timepoints. DEG: differentially expressed genes. WI: warm ischemia. NMP: normothermic machine perfusion.

P247 DEFINING THE STABILIZATION POINT OF KIDNEY FUNCTION FOLLOWING TRANSPLANTATION: AN OBSERVATIONAL COHORT STUDY

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Background: "Baseline kidney function", the change point between initial rapid improvement after kidney transplant and subsequent stabilization, is often used in clinical decision-making and clinical trials but is not well defined. We aimed to characterize the evolution of kidney transplant function in the first year after transplant and objectively define the "change point" of baseline function.
Methods: The retrospective cohort consisted of 921 recipients, who were alive with a functioning graft at 1 year after transplant. Only eGFR observations within the first year were included (N = 46 575 in total; median = 47 observations per transplant; IQR = 39–58 observations). Segmented regression models with one change point were used to estimate change point timing, eGFR value at change point, rate of change before and after change point for each transplant. Associations of the eGFR evolution with recipient/donor characteristics and graft failure rate were assessed with linear and Cox regression respectively.
Results: The change point occurred at an eGFR value of 45.2±16.4 mL/min/1.73m^2, at a median time of 10 days since transplant (IQR = 4.4–21.5 days). The initial increase in kidney function was steeper (+11.3 mL/min/1.73m^2/day ; P<0.001) and the change point occurred earlier (-8.4 days; P=0.002) in case of a living donor. Among cases with a deceased donor, the change point occurred later in case of donation after cardiac death (DCD), compared to brain death (DBD) (+4.9 days; P=0.007). While the eGFR value at change point was higher in case of a living donor (+10.7 mL/min/1.73m^2; P<0.001), the subsequent rate of change was lower compared to both DCD and DBD (-1.32 mL/min/1.73m^2/month; P<0.001). All aspects of the early evolution until the change point were associated with graft failure rate (beyond one year post-transplant). However, these associations with graft failure rate became insignificant when correcting for eGFR value at one year post-transplant.
Conclusions: This study indicates that donor characteristics importantly determine kidney function evolution and timing of the "change point" within the first year after transplant. Long-term outcome is less affected by the shape of the kidney function trajectory during the first year, and rather explained by the eGFR value reached at one year post-transplant.

P248 LONGITUDINAL PHENOTYPICAL CHARACTERIZATION OF SARS-COV-2 SPIKE-SPECIFIC T-CELL RESPONSES AFTER MRNA-1273 VACCINATION IN KIDNEY TRANSPLANT RECIPIENTS

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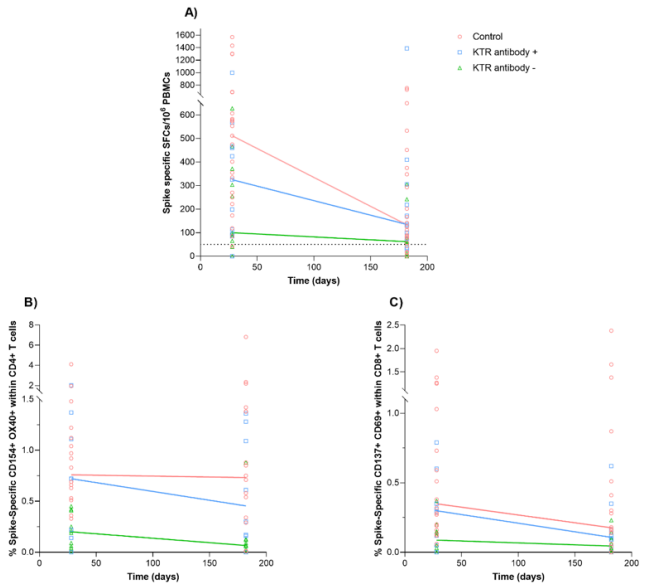
Background: Previous research indicates an inferior SARS-CoV-2 spike-specific T-cell response, following COVID-19 vaccination in kidney transplant recipients (KTR) compared to controls. Here, we perform an in-depth longitudinal phenotypical study of these T-cell responses in KTRs and controls.
Methods: For this study, we selected 21 KTR and 21 controls who mounted a positive T-cell response after second mRNA-1273 vaccination. Of the KTR, 11 also mounted a positive antibody response (KTR+), whereas 10 did not (KTR-). Peripheral blood mononuclear cells (PBMCs) were isolated 28 days and 6 months after second vaccination. Spike-specific IFN-γ producing T-cells were enumerated using an SARS-CoV-2 spike-specific IFN-γ ELIspot assay. SARS-CoV-2 spike-specific T-cells were phenotypically characterized using a flow cytometry based activation-induced markers (AIM) assay.
Results: Compared to controls, the number of IFN-γ producing T-cells was comparable in KTR+, and lower in KTR- 28 days after the second vaccination (532.5 (265.0 – 689.2) vs. 375.0 (91.2 – 492.1) and 100.0 (65.0 – 371.7) SFCs/10^6 PBMCs; p=0.18 and p=0.006, resp). The same accounted for percentages of CD4+ and CD8+ T-cells which were only lower in KTR- (CD4: 0.76% vs. 0.20%; p<0.001 and CD8: 0.35% vs. 0.09%; p=0.003). Interestingly, these CD4+ T-cells tended to be more often from the terminally differentiated effector memory (TEMRA) phenotype compared to controls (4.1 vs. 2.3% p=0.07). IFN-γ T-cell levels decayed less rapidly towards six months in KTR- compared to controls (-78.3 vs. -260.0 SFCs/10^6 PBMCs; p=0.50, p=0.08). The CD4+ T-cell percentages, however remained stable in controls and declined only in KTR, with an equal rate in KTR+ and KTR- (Figure 1).
Conclusions: In KTR who did not mount a positive antibody response after COVID-19 vaccination, a different T-cell phenotype was found compared to controls in addition to lower T-cell levels. Moreover, a decay of CD4+ T-cell percentage was observed 6 months after vaccination. This may indicate that even though a T-cell response is observed after COVID-19 vaccination in these patients, it may not be longstanding and effective to protect against severe COVID-19. These insights may help in the development of more efficient vaccination strategies in this vulnerable patient group.



P251 POST-LIVER TRANSPLANTATION RECURRENCE OF PRIMARY SCLEROSING CHOLANGITIS: ROLE OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Primary sclerosing cholangitis (PSC) represents 5% of the indications for liver transplantation (LT). Recurrence of PSC (rPSC) is reported in 8-27% of cases and it has a great impact on graft and patient survival.
Methods: The clinical data of 35 patients with PSC who underwent LT in our center in the last 20 years were retrospectively evaluated.
Results: 25 were male (71,4%) with a history of IBD before LT (67%). Tacrolimus + steroid was the most frequent immunosuppressive schedule (84.8%). Graft and patient survival at 5 years were respectively 73.6% and 88%. 5 patients (15.1%) underwent re-LT: 3 for rPSC, 2 for immunological damage (with an average and median time between first and second transplantation of respectively 37 and 31 months). A female patient transplanted for the first time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT. The time interval between 2nd and 3rd LT was much shorter than the time between the 1st and 2nd LT (2015-2019-2021). In order to modulate the patient's immune reactivity, within 3 months from the 3rd LT, stem cell mobilization (cyclophosphamide + G-CSF) was performed and CD34+ cells were harvested. The patient then underwent autologous hematopoietic stem cell transplantation (aHSCT), preceded by a myeloablative regimen (melphalan + rabbit antithymocyte globulin). In the immediate post-aHSCT, the patient experienced E. Coli-related sepsis. The full immunosuppressive regimen was reintroduced 18 days after aHSTC. Follow-up liver biopsies were done at 3 and 14 months after aHSCT: they excluded rPSC and showed a picture consistent with liver injury secondary to chemotherapy. Liver tests were maintained normal.
Conclusions: Re-LT is the only treatment option for aggressive rPSC. Our patient successfully underwent 3rd Re-LT combined with aHSCT with no evidence of rPSC at over 18 months follow-up: this may represent a successful approach as a preemptive strategy in selected cases of re-LT for rPSC.

P252 EXPLORING THE TRENDS IN SYSTEMATIC REVIEWS OF KIDNEY TRANSPLANTATION: A COMPREHENSIVE ANALYSIS OF THE EVIDENCE BASE OVER A DECADE

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Background: Systematic reviews (SRs) are considered the highest form of evidence for all types of clinical questions in evidence-based practice. The last decade has seen a significant increase in the number of published SRs in most areas of medicine, including kidney transplantation. For the first time in 2018, the number of SRs published in transplantation outstripped those from randomised controlled trials (RCTs). This raises some concerns of either duplication or increased use of non-RCT evidence. Lower quality SRs are less likely to generate meaningful recommendations for practice because of poor-quality underlying evidence. This review aims to analyse the trends and evaluate the strength and quality of evidence in SRs in kidney transplantation over a 10-year period.
Methods: Systematic reviews in kidney transplantation were identified from the Transplant Library, without language restriction. All full-text citations were exported to a custom Research Electronic Data Capture (REDCap) database prior to evaluation. The quality of evidence in all included reviews was assessed using a predesigned pro-forma and the AMSTAR-2 tool. Papers were screened and extracted by two blinded, independent reviewers and quality of evidence in all included reviews was assessed. All extracted data was exported onto Microsoft Excel and interpreted using descriptive analysis.
Results: We included 454 reviews, of which, only 3 were scored as 'high quality'. We found that 96.70% of SRs were identified as 'critically low quality', which increased in number over time(fig.1). We also found that the number of reviews comprising non-RCT data increased in the most recent 5 years. Only 14.12% of reviews had made a clear recommendation for practice.
Conclusions: This review highlights several concerning statistics that need to be addressed. In the last 10 years, only 3 out of 454 SRs in kidney transplantation were 'high quality'. The weaknesses identified in critical domains, alongside the increased use of non-RCT data and lack of conclusive recommendations undermines the confidence in the results of the reviews and purpose of publication. As these reviews are instrumental to clinical decision-making and patient care in kidney transplantation, we advocate for improved reporting quality among SRs in the field of kidney transplantation.

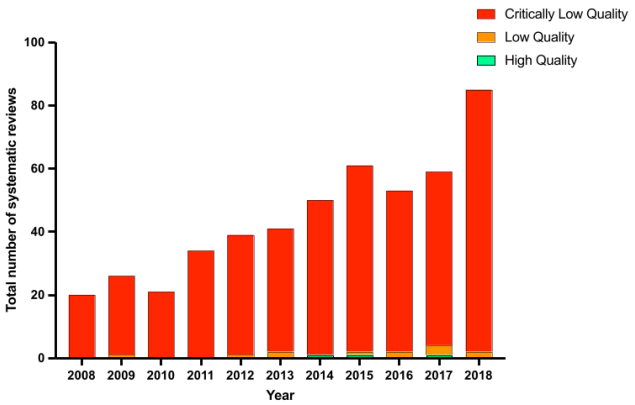

Figure 1: Trends in number and quality of systematic reviews over a 10-year period.

P253 HUMORAL AND CELLULAR RESPONSE AFTER THE 3RD TOZINAMERAN DOSE IS ACCOMPANIED WITH ACTIVATION OF CERTAIN LYMPHOCYTE SUBPOPULATIONS

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Background: Response to vaccination is a complex procedure, implicating humoral and cellular immunity. The aim of our study was to assess differences in cellular immunity between Renal Transplant Recipients (RTRs) classified as "responders" and "non-responders" to vaccination with Tozinameran.
Methods: Thirty-nine RTRs on stable immunosuppression, naïve to COVID-19 infection, who had not developed protective humoral immunity three weeks after the 2nd vaccine dose (T_0), were evaluated 48hrs before (T_1) and 3 weeks after (T_2) the 3rd dose. Nab levels >0.3AU/ml (chemiluminescence immunoassay) and/or enzyme-linked immunosorbent spot (ELISpot) values >30SFC/5×10^5 PBMCs were regarded as response. Results were correlated with cellular immunity. Concentrations of CD4+, activated CD4+, CD8+, activated CD8+ T-cells, CD3+CD16+CD56+ (NKT), activated NKT cells, CD3-CD16+CD56+ (NK) cells, CD19+, CD19+CD27- (Naïve), CD19+IgD+CD27- (Marginal), CD19+CD24+C-$D38^{high}$ (Transitional), CD19+CD27+$CD38^{high}$ (Plasmablasts) and CD19+CD27+ (Memory) B cells were measured with flow cytometry at T_1 and T_2.
Results: The number of responders significantly increased from T_1 [17/39, responders: Nab(-) - ELISpot(+)] to T_2 [34/39, responders: Nab(+) and/or ELISpot(+)] (x^2=16.2, p<0.0001). No difference was observed between responders and non-responders regarding age, renal function, calcineurin inhibitor levels, dialysis and transplantation vintage. Compared to non-responders, responders presented increased concentrations of: NK, activated CD8+ and NKT at T1 and of: total B cells, marginal and memory B-cells at T2 (table). A notable increase in naïve B-cells, as well as a significant drop in activated CD4+ and activated NKT cell numbers from T1 to T2 [56.3(69) vs 1123.6(751)/μL, p<0.001, 10.38(12) vs 5.71(7)/μL, p: 0.007 and 2.6(3) vs 1.28(3), p: 0.028 respectively] was evident only in the group of patients that were regarded as responders at T2.
Conclusions: The 3rd Tozinameran dose substantially improved RTRs' immune response, inducing a prominent stimulation of the B lymphocyte compartment.

Table

Cellular Subpopulation	Time Spot	cells/μL MED(IQR)		p
		Responders	Non-Responders	
Activated CD8+	T_1	23.6(29)	9.49(10)	0.04
Activated NKT cells	T_1	4.77(8)	1.73(2)	0.001
NK cells	T_1	198.91(161)	104.45(103)	0.02
B-cells	T_2	87.63(101)	26.86(42)	0.01
Marginal B-cells	T_2	10.03(13)	1.12(5.9)	0.04
Memory B-cells	T_2	28.31(42)	10.57(19)	0.04

P254 HEMOCHROMATOSIS IN KIDNEY TRANSPLANT RECIPIENTS: CASE SERIES

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Background: The diagnosis of hemochromatosis is based on transferrin saturation and ferritin levels. However, inflammation may also increase ferritin levels. Therefore, imaging studies should be used in the diagnosis, since hepatic iron accumulation is not homogeneous, which makes liver biopsy unreliable. Magnetic resonance imaging (MRI) has been developed to detect iron overload in the liver and heart. Iron overload may be due to a hereditary iron metabolism disorder or to factors such as iron administration, and blood transfusions. The type of immunosuppression may be the potential trigger in kidney transplant recipients. Since the need for iron administration and blood transfusion decreases in kidney transplant patients (KTRs), ferritin and iron accumulation are expected to reduce. However, ferritin levels may increase rapidly and lead to multi-organ damage.
Methods: The data of 20 consecutive KTRs, who had undergone phlebotomy or had a ferritin value greater than 1000 ng/ml, were reviewed retrospectively. We demonstrated the iron accumulation in KTRs with cardiac MRI, liver MRI and/or liver biopsy. Serum ferritin and transferrin saturation (TSAT) values were recorded in the sixth month after the transplantation and on the day of last follow up. Normal cardiac and elevated liver iron content was accepted as less than 0.5 mg/g dry weight and higher than 3.2 mg/g dry weight, respectively.
Results: We found 14 patients with iron accumulation confirmed by imaging and/or pathology findings. T2* weighted axial images of the upper part of the abdomen demonstrated signal loss in the liver of nine patients. The liver pathology findings of six patients, the bone marrow of two patients and the spleen of one patient were consistent with hemochromatosis. The five patients' genetic studies showed no hemochromatosis gene mutation. Nine patients underwent intermittent phlebotomy, and three patients who underwent phlebotomy were receiving iron chelators simultaneously. Transferrin saturation and ferritin values of patients, including some patients who underwent phlebotomy, were increasing. The follow-up period after the transplantation was 162±72 months.
Conclusions: KTRs with high serum ferritin and/or who need phlebotomy for high serum iron parameters should be screened with imaging studies for hemochromato sis.

P255 PORCINE PRECISION-CUT LIVER SLICES AS AN ACCOMPANYING MODEL TO STUDY PERFUSATE COMPOSITION DURING LONG-TERM LIVER NORMOTHERMIC PERFUSION

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Background: Long-term normothermic machine (NMP) perfusion may open the opportunity for *ex vivo* regeneration of marginal organs and help to overcome organ shortage. Thus, perfusion protocols need to be adapted for extended perfusion durations. One important point to consider is that perfusate electrolyte levels may exceed physiological levels during isolated liver perfusion since filtration is lacking. To this end, we developed a precision-cut liver slice (PCLS) model to evaluate the cellular effects of changing perfusate composition.
Methods: 8 mm punch biopsies were taken of cold preserved porcine livers prior they were applied to NMP. PCLS (300 μM) were generated using a Leica 1200S vibratome and cultivated for 7 days in 24-well plates on a rocking platform in conditioned DMEM media containing defined concentrations of Na^+ (160 or 165 mmol/L), K^+ (7 or 15 mmol/L) and urea (200 or 400 mg/dL). To assess tissue viability and functionality MTS assay was performed and albumin production was assessed. LDH secretion into culture media was analyzed to evaluate cell damage.

Results: Viable and metabolically active PCLS could be generated and cultivated for 7 days. Viability was maintained irrespectively of the utilized media with no significant differences compared to the control group and compared to viability after slicing. Albumin production was observed for all conditions with no significant differences, confirming the results of the MTS assay. However, due to the slicing process LDH release into the supernatant was observed. In the course of cultivation, LDH levels remained stable for all conditions. No significant differences between conditioned media and control were found, indicating elevated electrolytes or urea cause no further damage to liver tissue.
Conclusions: PCLS can be utilized to study long-term Na^+, K^+ and urea levels above the physiological range do not cause damage to PCLS. Thus, elevated perfusate levels of those analytes may not lead to tissue injury during long-term machine perfusion.

P256 ATYPICAL HAEMOLYTIC UREMIC SYNDROME (AHUS) RECURRENCE AFTER KIDNEY TRANSPLANTATION IN PATIENTS WITH ECULIZUMAB PROPHYLAXIS

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Background: The outcome of kidney transplantation in patients with aHUS before the use of eculizumab was poor and it was conditioned to the appearance of recurrence of the disease. Nowadays, this outcome has changed with the use of eculizumab. The aim of this study is to know the incidence of aHUS recurrence after kidney transplantation in patients with eculizumab prophylaxis
Methods: We studied all patients with aHUS and that had received a kidney transplantation from 1981.Recurrence was defined as the appearance of hemolytic anemia (low levels of Hemoglobin, thrombocytopenia, increase of LDH and haptoglobin no detected) and a deterioration of renal function. When a deterioration of renal function was detected, a biopsy was performed in all patients. Biopsy of surveillance was done at first week and at six months after kidney transplantation only in patients with eculizumab. We compared the incidence of recurrence between patients with and without eculizumab and we analyzed the risk factors for this recurrence
Results: We studied 46 kidney transplantation (mean age 39±14.8 years old) to 33 patients (13 with eculizumab) from 1981 to 2023, 33 were first kidney transplantation and 13 second, third or fourth kidney transplantation. Eculizumab was used from 2016 and dose and mode of administration was made as data sheet. After a follow up of 69.6±84 moths, 14 patients showed recurrence of aHUS, all of them didn´t receive eculizumab (p=0.003). Recurrence was associated with: mean age 32.5±11.2 vs 42.5±15.3 years old; p=0.03, CMV infection (83.3% vs 33.3%; p=0.04) and the time to start dialysis from diagnosis of aHUS 1.1±0.5 vs 9.7±23 months (p=0.04). We didn´t find relationship with variants of complement proteins, cold ischemia time, immunosuppressive agents, acute rejection and others. The probability of recurrence was 24.1 at 6th month and 38.6% at first year. We withdraw eculizumab in four patients, in two cases due to lost allograft (chronic rejection at five years and thrombosis at first month) and two in patients without variant of complement at eight months after kidney transplantation. We didn´t observed aHUS recurrence although the follow up was 3 and 15 months respectively.
Conclusions: We didn´t find aHUS recurrence in kidney transplant recipients when prophylaxis with eculizumab was performed.

P257 HUMAN LIVER TRANSPLANTATION: EVALUATION OF IMMUNE T CELLS WITH TISSUE REPAIR FUNCTIONS

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Background: The immune system plays a crucial role in several “domestic” processes, including repair, which consists of two successive phases: inflammation and its resolution characterized by new tissue formation and/or remodeling. Sterile inflammation in organ transplantation is an important feature of ischemia-reperfusion (IR) injury. Although immune cells have been shown to play an important role in IR injury, their potential role in ensuring tissue repair and the return to homeostatic conditions is not yet well-documented. Here, we analyzed the influence of human liver transplantation (LT) on the relative proportion and activation of blood T cells known for their regulatory and repair functions (i.e., T regulatory cells (Treg), and innate T cells (ITC)).
Methods: The study was conducted from a prospective biological collection of 20 LT recipients. Peripheral mononuclear cells (PBMC) were isolated from blood collected at different times: prior to surgery (D0), at the end (EoT) of LT, one day (D1) and seven days (D7) after LT, and stored prior to multiparametric spectral flow cytometry analysis.
Results: Analysis of PBMC showed a D7 post-LT increase in the relative proportion of Treg within T cells, compared to D0. This late phenomenon was not found when considering the other conventional T cell subsets and ITC. Moreover, D7 post-LT increase of Treg was accompanied by an activation status, as testified by their upregulation of CD69 surface expression, compared to D0. Interestingly, D7 post-LT increase of Treg correlated with the release at EoT of interleukin-33 (IL-33), an alarmin/cytokine known to drive expansion of Treg. Considering ITC, relative proportions of invariant natural killer T cells (iNKT), γδ-T cells and mucosal-associated invariant cells (MAIT) were found to have increased between D0 and EoT, prior to decreasing up until D7 post-LT. Remarkably, the early cell activation observed between D0 and EoT for 30 and 10% of MAIT and γδ-T cells, respectively, was maintained until D7 post-LT.
Conclusions: Our preliminary data reveal a late/maintained activation state of blood Treg and ITC after LT, suggesting their contribution to inflammation resolution and tissue repair. Current liver IR studies using IL-33-deficient mice are under investigation to directly test the role of IL-33 in this phenomenon.

P258 TAILORED IMMUNOSUPPRESSION WITH LCPT EXTENDED RELEASE TACROLIMUS BASED ON NFAT-REGULATED GENE EXPRESSION

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Background: There is a narrow therapeutic window for immunosuppression (IS) with calcineurin (CNI) inhibitors. The immunosuppressive effect of CNIs differs between individuals. Therefore, the drugs` trough levels do not reflect IS and should be replaced by pharmacodynamic monitoring. Since nuclear factor of activated T-cells (NFAT)-depending gene expression correlates with cyclosporine induced IS, this study was designed to evaluate the effect of LCP extended release tacrolimus (Tac) on NFAT regulated residual gene expression (RGE).
Methods: Gene expressions of interleukin-2, interferon-γ and granulocyte-macrophage colony-stimulating factor and three reference genes were measured with droplet digital polymerase chain reaction (ddPCR) in whole blood samples at day 2, 7, 14, month 1 and 6 until 1 year after LT in 23 patients transplanted between February 2019 and June 2020. The RGE after Tac intake was calculated as $c_{peak}/c_0 x100$, where c_0 is the adjusted number of transcripts at the Tac predose level and c_{peak} is the number of transcripts at peak level. IS consisted of LCPT extended-release Tac introduced directly after LT, mycophenolic acid, and a corticosteroid-taper for 3 months.
Results: Tac peak levels and NFAT-RGE showed a strong inverse correlation (r=-0,8). Our descriptive analysis shows that although patients show a Tac trough level within the targeted therapeutic window, low RGE can result in a higher risk for infection. Mean individual trough effect of Tac on the 3 target genes with all timepoints pooled was 33% (26-56%) in patients without infection and 81% (53-95%) in patients with infection (p<0.011), mean individual peak effect was 48% (44-64%) in patients without infection and 91% (90-94%) in patients with infection (p<0.001).
Conclusions: Tailored IS monitored with NFAT-RGE is promising to decrease infectious complications by optimization of the IS level in LT recipients on LCP extended release Tac.

P260 TRACER METABOLOMICS DURING NORMOTHERMIC KIDNEY PERFUSION AS A NON-INVASIVE TOOL TO UNRAVEL WHOLE ORGAN KIDNEY METABOLISM

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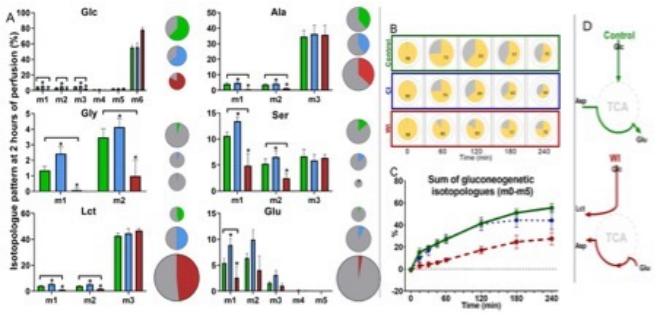
Background: A metabolic collapse at reperfusion, impairing the kidney's energy metabolism, was recently proposed as mechanism behind delayed graft function. More specifically, a potential Krebs cycle defect was identified. Since perfusate/tissue metabolite abundances can result from different underlying biochemical pathways, we further elucidate the complex biochemical processes on a whole organ level by applying tracer metabolomics during isolated normothermic kidney perfusion.
Methods: Pig kidneys exposed to no, 22h of cold or 1h of warm ischemia were perfused with a red cell based perfusate for 4 hours. Key nutrients (glucose, glutamine and glutamate) were completely replaced by their fully labelled 13C isotopes/tracers (13C-glucose (n=3); 13C-glutamine (n=1); 13C-glutamate (n=1)). Perfusate was sampled longitudinally (baseline, 15 min, 30 min, 45 min, 1h, then hourly) and tissue biopsies were snap frozen at the end of perfusion. Glucose, lactate, amino acids, Krebs cycle intermediates and their respective isotopologue forms (based on the number of labelled atoms per metabolite) were measured by Liquid Chromatography Mass Spectrometry. Changes in both the relative abundances of metabolites as well as the contribution of 13C-isotopes to the pool of the respective metabolite (fractional contribution) and isotopologue percentages were determined.
Results: The isolated kidney incorporated 13C-atoms from glucose into amino acids (alanine, glycine, serine, and glutamate) and lactate, released back into the perfusate. Differences between ischemic conditions at 2h of perfusion were seen for m1 and m2 isotopologues of serine and glycine. Furthermore, the kidney's gluconeogenic capacity was impaired in ischemic kidneys. Additional analyses of tissue Krebs cycle intermediates from glucose, glutamine and glutamate labelling experiments showed a truncated Krebs cycle in healthy kidneys displaying an active aspartate-glutamate cycle, while ischemia reverses this towards the glutamate-aspartate cycle.
Conclusions: Combining tracer metabolomics and normothermic organ perfusion is a powerful non-invasive tool to understand how perturbations like ischemia change underlying biochemical processes.



P261 ISCHEMIA-INDUCED METABOLIC PATTERNS PREDICT KIDNEY FUNCTION DURING PIG NORMOTHERMIC PERFUSION

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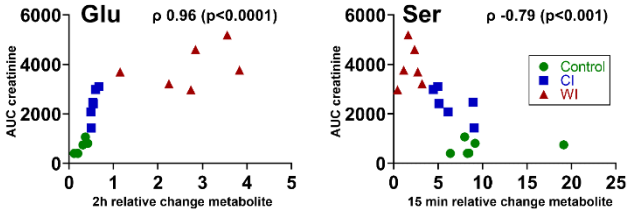
Background: Objective tools to predict post-transplant kidney function are urgently needed. As oxygen deprivation during ischemia will cause metabolic changes, we hypothesized that amino acid profiles during normothermic kidney perfusion would correlate with kidney function.
Methods: Pig kidneys were exposed to no, 22h of cold or 1h of warm ischemia and then reperfused with a blood based perfusate for 4 hours (n=6 per group). Perfusate was sampled longitudinally (baseline, 15 min, 30 min, 45 min, 1h, then hourly). Perfusate glucose, lactate, and 18 amino acids were measured by Liquid Chromatography Mass Spectrometry (LC-MS). To compare measurements between ischemic conditions, ANOVA testing with post-hoc Tuckey was performed. To assess the association between changes in metabolites and kidney function during perfusion (measured by clearance of an added bolus of creatinine), Spearman's correlations were calculated.
Results: We found that at 2h of perfusion, abundances of 17 amino acids were significantly different between groups. Glutamate, asparagine, phenylalanine, tyrosine, tryptophane, lysine, threonine, serine, (iso)leucine and valine could differentiate all three groups. Glutamate, glucose and methionine discriminated kidneys with warm ischemic injury from those with cold ischemic or no injury while arginine discriminated between healthy and ischemic kidneys. Furthermore, the correlation of creatinine clearance over 4h of perfusion with the fold changes of metabolite levels between 15 min and 2h of perfusion showed that glutamate, phenylalanine, tryptophane and tyrosine were strongly and significantly correlated with creatinine clearance. Of these, glutamate provided the highest correlation (Spearman's ρ 0.95). We also focused on the very early stages of perfusion, the wash out phase. We evaluated the association of the fold change of a metabolite between the start of perfusion and 15 min after the start of perfusion. These analyses showed that asparagine and serine were predictive of creatinine clearance over 4h of perfusion (Spearman's ρ -0.81 and 0.70 respectively).
Conclusions: Amino acid changes over time during normothermic kidney perfusion show a unique nutritional behavior with the potential to predict future kidney function.



P262 THE LONG PATHWAY TOWARDS CLINICAL OPERATIONAL TOLERANCE IN LIVER TRANSPLANTATION: THE BRUSSELS APPROACH FOR ACTIVE IMMUNOSUPPRESSION MINIMISATION

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Background: Clinical operational tolerance (COT), defined as the absence of immunosuppressive treatment (IS) without graft immunological damage, was initially observed in non-compliant liver transplant (LTx) recipients or in recipients with (de-novo) malignancy or uncontrollable infection. Several clinical trials failed however to establish a protocol for IS withdrawal in clinical practice out of these conditions. Here we describe a clinical approach to actively minimize and eventually complete IS withdrawal in LTx recipients over time.
Methods: Patients who achieved tacrolimus (TAC) 1mg/day monotherapy regimen with liver tests (LTs) up to 1.5 normal values, no previous immunological events and with normal liver biopsies were scheduled for a progressive and slow IS reduction approach using 1mg steps. LTs were monitored after each IS reduction and, if undisturbed, future checks were performed as standard of care. If alterations happened, LTs were repeated, and in the absence of normalization, initial IS regimen was resumed. Liver biopsies were performed per protocol at 7 days, 6, 12months, and then every 5years post-LTx, or when clinically indicated.
Results: During the period 01/01/1994-31/12/2017, 866 adults received a LTx. The 1mg/day TAC regimen was achieved in 164 (19%) recipients, all included in the stepwise IS reduction approach. Patients' demographics and IS reduction dynamics are displayed in Table 1. At the end of follow-up on 07/31/2022, IS was further reduced in 110 (67.1%) recipients as follows: in 50: 5-6mg/week, in 24: 3-4mg/week, in 17: 1-2mg/week; and 19 patients (11.6%) reached COT status. No demographics differences were observed between these 4 groups. Reduction had not yet been attempted in 38 patients (1mg/day recently started), while in 16 (9.8%) the strategy failed; however, LTs normalized after resumption of the previous IS regimen. Histology from recipients on progressive reduction or complete withdrawal did not show increase of fibrosis or evolution towards chronic rejection.
Conclusions: These findings indicate that active minimization and even withdrawal of IS are feasible in clinical practice in very selected LTx patients under close biological/histological surveillance. Further studies would validate these results.

Table 1: Demographics and clinical characteristics of liver recipients

Variables	Total population n = 164 (100%)
Gender (male)	111 (68%)
Indication to Liver transplantation	
Alcoholic Cirrhosis	75 (45.9%)
Viral Cirrhosis B and C	52 (32%)
Cryptogenic Cirrhosis	7
Polycystic disease	3
Hemangioendothelioma	6
Others	21
Presence of HCC	55 (33.7%)
Child Score	A=59, B=45, C=60
Meld Score	13±9.9
Graft type (Cadaveric/Living donor)	151/13
Age at LTx (years)	51.0±9.1
Age at Start of IS withdrawal (years)	56.6 ± 7.1
Tacrolimus trough levels at start of spacing protocol (ng/ml)	3.12 ± 0.55
Number of reduction steps per patient	5.2
Interval between two reduction steps (months)	12.1±7.2
Time from IS reduction start to 1-2mg/week (months)	42.7±13.7
Time from IS reduction start to No IS treatment (months)	48.1±14.5
Follow-up (months)	122.5±55.4

P263 SAFETY AND BENEFIT OF A SMALL INCISION FOR DONOR HEPATECTOMY IN LIVING-DONOR LIVER TRANSPLANTATION

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Background: Living-donor liver transplantation is still the mainstream in Japan, therefore, safety and reduction of the surgical burden on donors are the top priority in the transplantation. The aim of this study was to evaluate the donor hepatectomy with a small incision compared to the hepatectomy with a conventional procedure.
Methods: Data from 325 living donors who underwent hepatectomy between January 1990 and December 2022 were retrospectively reviewed. Patients were categorized into two groups based on the skin incision: T-group, the inverted T-shaped incision until May 2019 (n = 294); M-group, the middle incision in the upper abdomen since June 2019 (n = 31). The short-term postoperative outcomes were compared.
Results: The donor age in the M-group was significantly higher than that in the T- group (45.5 vs. 34.8yo, P < 0.01). The ratio of left-hemi-liver graft and the ratio of the remnant liver volume to the total liver volume in the M-group were lower (59.4 vs. 98.6%, P < 0.01; 66.1 vs. 69.6%, P = 0.024, respectively). The operation time and the blood loss in the M-group were significantly shorter and lesser (308 vs. 481min, P < 0.01; 300 vs. 480ml, P < 0.01, respectively). No significant difference was observed between the two groups in the incidence of overall or severe postoperative complications (Clavien-Dindo grade ≥ IIIa) (32.3 vs. 40.8%, P = NS; 6.5 vs. 11.9%, P = NS, respectively). In contrast, the postoperative hospital stay in the M-group was shorter than that in the T-group (11.5 vs. 20.0 days, P < 0.01). There was no need for reoperation, and no patients died or had critical sequelae within one year after surgery in both groups.
Conclusions: Donor hepatectomy with a small incision can be safely performed and has benefits with less invasion than the conventional procedure.

P265 INVESTIGATION OF STUDIES ON PHYSICAL ACTIVITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Insufficient physical activity increases the risk of all-cause mortality and cardiovascular disease among kidney transplant recipients. The aim of this review is to examine the published studies on physical activity in kidney transplant recipients.
Methods: In this study, all databases (ClinicalKey, Cochrane, Ebsco, Ovid, Proquest, Science Direct, Scopus, Springer, Turkey Citation Index, Ulakbim, Wiley Online Library, Web of Science etc.) The studies published using the keywords “Physical Activity” “Kidney Transplant Recipients” were reviewed.
Results: As a result of the examination, a total of 70 publications were reached. When repeated publications were removed, 67 articles were reached. The publications were made between 2007-2022. The most publications belonged to the year 2021 (n=10). When analyzed by research type, two publications were research protocols, twelve were interventional, eight were cross-sectional, four were cohorts; five were longitudinal, thirteen were descriptive, seven were prospective, four were qualitative research articles, and twelve were review articles. The level of physical activity was low in kidney transplant recipients. It was determined that the subjects of weight gain, nutrition, cardiopulmonary functions, fluid intake, graft function, quality of life and self-efficacy were studied together with physical activity. Interventional studies were conducted for three, six and 12 months. Studies have shown that interventions increase physical activity levels after three months, and more research is needed for long-term results.
Conclusions: As a result of the examinations, it was found that the physical activity level was low in kidney transplant recipients; When analyzed according to research types, interventional studies are limited; It was determined that randomized controlled studies are needed to improve physical activity levels.

P266 FIRST CLINICAL EXPERIENCE WITH TIXAGEVIMAB AND CILGAVIMAB IN LUNG TRANSPLANT RECIPIENTS DURING OMICRON WAVE

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Background: Evusheld™(tixagevimab and cilgavimab, formerly AZD7442), a long-acting antibody combination is an approved prevention therapy for COVID-19 apart from vaccines. The efficiency of Evusheld in lung transplant recipients and the in vivo neutralization potency against Omicron variant strains is not yet known.
Methods: We analyzed lung transplant recipients who underwent Evusheld immunization between 04/2022-10/2022. All consecutive patients receiving a primary lung transplantation and consented to the injection were included in this retrospective single-center analysis. The dose for prevention of symptomatic disease caused by SARS-CoV-2 was 150mg of tixagevimab and 150mg of cilgavimab, administrated as separate sequential intramuscular injections.
Results: Of the 203 LTRs (53% males and 47% females, with a median age of 57 years) who received prophylactic injections of Evusheld™, 30 (14.7%) developed COVID-19 infection (median of 58,5 days after vaccine). With the exception of four patients, all LTRs were symptomatic. Hospitalization with oxygen support was necessary in two cases, admission to an intensive care unit was not required, respectively. Fifteen patients developed mild, nine patients moderate symptoms including fever, cough and headaches. Two patients reported long-COVID symptoms. The development of symptoms was not in correlation with the COVID-19 antibody status, with the immunosuppressive regimen (including induction therapy) or with the transplant date or diagnosis. The Torque Teno Virus load of infected patients were with a median of 2.39log09 in the upper threshold of the norm.
Conclusions: Evusheld was generally well-tolerated in our cohort. The results validate the original PROVENT phase III study regarding the clinical effectiveness of Evusheld prophylaxis for immunocompromised patients (lung transplant recipients), notably demonstrating effectiveness during the Omicron wave as an appropriate option to prevent COVID-19.

P268 HISTOLOGICAL SCREENING FOR BK POLYOMAVIRUS NEPHROPATHY FOLLOWING VIRAL REPLICATION IN PLASMA: AN OBSERVATIONAL COHORT STUDY

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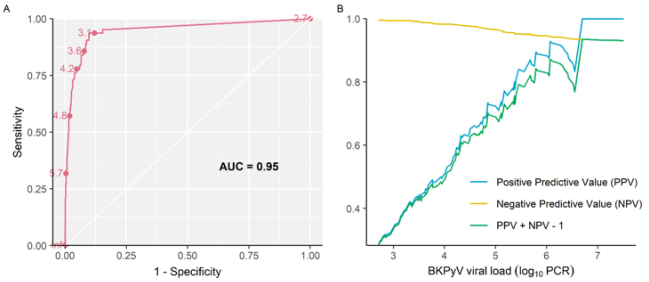
Background: Systematic screening for BK polyomavirus-DNAemia (BKPyV-DNAemia) has been advocated to aid prevention and treatment of polyomavirus associated nephropathy (PyVAN), an important cause of kidney graft failure. The added value of performing a biopsy at time of BKPyV-DNAemia, to distinguish presumptive PyVAN (negative SV40 immunohistochemistry) and proven PyVAN (positive SV40) has not been established.
Methods: We studied an unselected cohort of transplantations (N = 950), performed between 2008-2017. The diagnostic performance of BK viral load in plasma for positive SV40 staining in a contemporaneous biopsy was assessed. Using Cox regression we investigated associations of recipient/donor characteristics and treatment with rates of the following events: first occurrences of BKPyV-DNAemia and positive SV40 staining, BKPyV-DNAemia resolution and graft failure. Associations of BKPyV-DNAemia resolution and graft failure with histological scores at time of first BKPyV-DNAemia were assessed.
Results: BKPyV-DNAemia was detected in 250 (26.3%) transplant recipients, and positive SV40 in 91 cases (9.6%). Among 210 patients with a concurrent biopsy at time of first BKPyV-DNAemia, 60 (28.6%) biopsies were SV40 positive. Plasma viral load showed high diagnostic value for concurrent SV40 positivity (ROC-AUC 0.951, 95%CI 0.920 - 0.977, Figure 1A) and intrarenal BKPyV load (*pvl* score) (0.979, 95%CI 0.969 - 0.989). SV40 positivity is highly unlikely when plasma viral load is below 4 $\log_{10}$ copies/ml (negative predictive value 0.989, 95%CI 0.979 - 0.994, Figure 1B). In SV40 positive patients, higher plasma and intrarenal BKPyV load were associated with slower viral clearance from the blood (Hazard Ratio [HR] 0.712, 95%CI 0.604 - 0.839, and HR 0.268, 95%CI 0.116 - 0.621, respectively), whereas the dichotomy positivity/negativity of SV40 did not predict viral clearance.
Conclusions: Although intrarenal BKPyV load offers some prognostic value for viral clearance on top of plasma viral load, the latter provides good guidance on when a biopsy is unnecessary to exclude PyVAN. Our study supports the current guidelines that a biopsy is not required for the primary management of patients with BKPyV-DNAemia, and that the difference between presumptive and proven PyVAN is of limited clinical value.

Figure 1: Accuracy metrics for BK polyomavirus (BKPyV) viral load as predictor for SV40 positivity



P269 PERI-OPERATIVE KINETICS OF PLASMA MITOCHONDRIAL DNA LEVELS DURING LIVING DONOR KIDNEY TRANSPLANTATION

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Background: During ischemia and reperfusion injury (IRI), mitochondria may release mitochondrial DNA (mtDNA). mtDNA can serve as a propagator of further injury during and after kidney transplantation. Aim of this study was to measure the perioperative plasma kinetics of mtDNA during living donor kidney transplantation (LDKT) and the potential of plasma mtDNA levels as markers of graft outcome parameters.
Methods: This is a post-hoc analysis of plasma samples of the Volatile Anaesthetic Protection of Renal Transplants-1 (VAPOR-1) study. All donor-recipient couples of the Volatile Anaesthetic Protection of Renal Transplants-1 (VAPOR-1) trial were included (n=57). Systemic venous, systemic arterial and renal venous samples were taken at multiple timepoints in the peri-operative period. Real-time PCR analysis was used to measure 3 mtDNA genes: displacement loop (D-loop), NADH ubiquinone oxidoreductase subunits 1 and 6 (ND1 and ND6).
Results: Levels of mtDNA genes changed over time and differed between sample origin. Donor mtDNA levels were significantly lower compared to recipients at pre-transplantation (all P<0.001). Systemic venous D-loop levels significantly increased from pre-transplantation till day 9 post transplantation (P<0.05). Systemic arterial mtDNA genes all significantly increased at 2 hours post transplantation (all P<0.001). Renal venous mtDNA levels at 30 sec after reperfusion were significantly higher compared to later timepoints (P<0.05). No association to graft outcome parameters was found after correction for multiple testing. Several donor, recipient and transplant characteristics had a significant effect of the dynamics of mtDNA over time.
Conclusions: These results demonstrate mtDNA release during the LDKT procedure. Furthermore, mtDNA release differed over time. In addition, different concentrations of mtDNA were measured in different sample origin, demonstrating the importance of timing and sample origin to study the diagnostic potential of mtDNA.

P270 COVID-19 INFECTION IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS AFTER IMMUNIZATION WITH THE BNT162B2 COVID-19 MRNA VACCINE

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Background: Evidence from adult studies has shown that immunocompromised renal transplant recipients (RTR) belong to a high risk group for complicated COVID-19 infection. Data on the clinical course of the disease in the pediatric population especially after vaccination are limited.
Methods: We retrospectively analyzed the incidence and clinical course of PCR confirmed SARS-CoV-2 infection in a cohort of 20 (13 males/7 females) pediatric RTR. In the vaccinated patients we measured spike protein of SARS-CoV-2 IgG antibody using chemiluminescent microparticle immunoassay (Architect/Alinity,Abbott). IgG results ≥50 AU/ml were considered positive.
Results: 17/20(85%) RTR were vaccinated with the BNT162b2 Covid-19 mRNA vaccine and 3/20(15%) declined vaccination. 13 patients received 2 vaccine doses and 4 patients 3 doses. 11/17 (65%) patients had positive antibody titer (mean 2209,26 AU/ml) and 6/17(35%) patients had negative antibody titer. 14 patients developed COVID-19 disease; 11/17(65%) vaccinated patients (mean time post vaccination: 6 months) and 3/3(100%) of the unvaccinated patients. The mean post vaccination antibody titer of the infected RTR was 1741,22 AU/ml versus 3067,33 AU/ml in the not infected group (p=0.53). After approval of remdesivir for treatment of COVID-19 infection, 5 patients received remdesivir as per our local protocol for immunocompromised patients. The mean symptom duration was 3 days (range 1-7 days) in the vaccinated patients, 2.6 (range 2-3 days) in the unvaccinated patients and 4.2 (range 3-7 days) in the patients that received remdesivir. None of our patients developed pneumonia nor oxygen requirements. The major symptom was rhinitis in 11/14(78%) patients while fever >38 ℃ had 6/14(42%), low grade pyrexia <38 ℃ 3/14(21%), cough 5/14(36%), diarrheas 2/14(14%), headache 2/14(14%) and myalgias 2/14(14%). We observed a transient creatinine increase in 4/11(36%) vaccinated and 1/3(33%) of unvaccinated patients. None developed acute rejection, however 2 patients developed graft rejection, both 6 months after COVID-19 infection.
Conclusions: The incidence of COVID-19 infection in pediatric renal transplant recipients is high after vaccination, however our data indicate that the risk for severe disease is very low.

P272 VALGANCICLOVIR VS LETERMOVIR PROPHYLAXIS AND RISK OF CYTOMEGALOVIRUS DNAEMIA IN A RANDOMIZED PHASE 3 TRIAL

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Background: Valganciclovir (VGCV), indicated for cytomegalovirus (CMV) prophylaxis in adult donor CMV-seropositive/recipient CMV-seronegative [D+/R-] kidney transplant recipients (KTRs), is limited by myelosuppression and need for dose adjustment for creatinine clearance (CrCl) <60 mL/min. Letermovir (LET) is non-myelotoxic and needs no dose adjustment for CrCl. This large, randomized Phase 3 non-inferiority study (NCT03443869) demonstrated that CMV prophylaxis with LET was non-inferior to VGCV in adult D+/R- KTRs and significantly safer as measured by rate of leukopenia or neutropenia (IDWeek 2022). A post-hoc analysis was conducted to understand the impact of renal function on CMV DNAemia and CMV disease (CMV end-organ disease or syndrome confirmed by an adjudication committee) during prophylaxis.
Methods: Adult KTRs were randomized (1:1) within 7 days post-KT to receive LET daily at the approved dose with acyclovir (400 mg twice daily) vs VGCV (900 mg daily; adjusted for CrCl) through Week 28 (~200 days). CrCl was calculated by Cockcroft-Gault equation at each visit; doses of VGCV were adjusted if needed according to the manufacturer. CMV DNA was obtained at each visit through Week 28 post-transplant (Roche COBAS® AmpliPrep/COBAS TaqMan® [CAP/CTM] assay; LLOQ 137 IU/mL).
Results: 586 D+/R-KTRs were randomized and received ≥1 dose of prophylaxis. The rate of quantifiable CMV DNAemia through Week 28 post-KT was 2.1% with LET vs 8.8% with VGCV. The rate of CMV disease through Week 28 post-KT was 0% with LET and 1.7% with VGCV. The proportions of LET- and VGCV-prophylaxed KTRs with CrCl <60 mL/min were 68% and 70% at week 1 and 37% and 38% at Week 28, respectively. Figure 1 shows CrCl over time by treatment arm. Dose adjustments of LET occurred in 0% of LET-prophylaxed KTRs, and dose adjustments of VGCV occurred in 63% of VGCV-prophylaxed KTRs, of whom 27% had >10 adjustments. The proportion of KTRs with quantifiable CMV DNAemia or CMV disease by CrCl quartile (Table 1) was higher in patients receiving VGCV prophylaxis with low CrCl. No association was observed for KTRs receiving LET.
Conclusions: In D+/R- KTRs, LET dosing independent of renal function avoids the burden of dose adjustments for renal function and is associated with a reduced risk of CMV DNAemia and CMV disease during prophylaxis compared with VGCV.

Figure 1. Creatinine Clearance Over Time

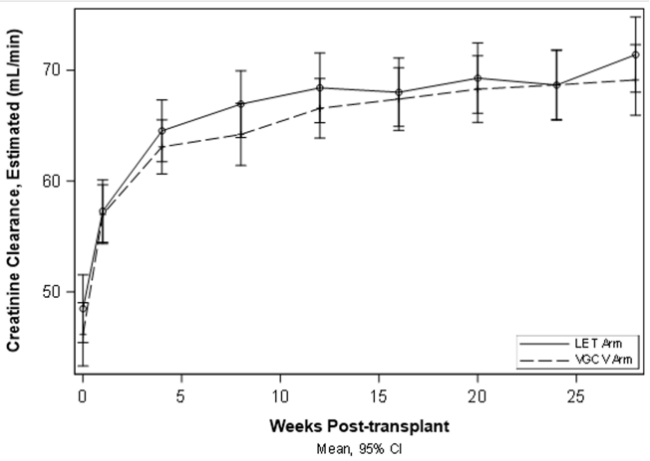

Table 1. Proportion of KTRs with quantifiable CMV DNAemia or CMV disease by CrCl quartile

CrCl Quartile at Week 28, mL/min	LET arm Failures	VGCV arm Failures	LET Failures quartiles 1&2 vs 3&4	VGCV Failures quartiles 1&2 vs 3&4
Quantifiable CMV DNA through Week 28 by Week 28 CrCl Quartile*				
1 (0–≤52)	2	9	2 (1.7%) of 117	17 (13.1%) of 130
2 (>52–≤67)	0	8		
3 (>67–≤85)	2	1	3 (2.6%) of 116	5 (4.3%) of 117
4 (>85)	1	4		
CMV Disease through Week 28 by Week 28 CrCl Quartile*				
1 (>0–≤52)	0	3	0 (0.0%) of 117	4 (3.1%) of 130
2 (>52–≤67)	0	1		
3 (>67–≤85)	0	0	0 (0.0%) of 116	0 (0.0%) of 117
4 (>85)	0	0		

*Participants without a CrCl at Week 28 are not included

P273 A NEW KIDNEY OFFERING SCHEME IN THE UK - 3 YEAR REVIEW

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Background: On 11th September 2019 a new kidney offering scheme (NKOS) was introduced in the UK to reflect the changing donor pool which had led to a higher rate of offer declines and an increasing use of DCD donors. The scheme was designed to meet several key objectives identified through reviewing the past Kidney Allocation Scheme introduced in April 2006, comparing alternative schemes across the world, looking at the philosophies in allocation, and understanding whether improvements could be made in histocompatibility and immunogenetics

Methods: The 2019 NKOS allocates all kidneys from both DBD and DCD donors and gives absolute priority to difficult to match and long waiting patients, and then a points score defines priorities for offering. The points score includes donor-recipient risk index combinations, waiting time from earliest of dialysis or activation on the list, tissue match and age combined, location, match-ability, total mismatch, and blood group match.

Results: There were 5139 kidney-only transplants performed during the first three years of the new scheme. Of these, 3226 were from DBD donors and 1913 from DCD donors. There has been a significant benefit to difficult to match patients with 19% of transplant recipients being highly sensitised compared to 12% in the previous scheme. Older patients and long waiting recipients have also benefited. The introduction of longevity matching has contributed to a reduction in declines due to donor related reasons. No statistical difference is reported in 3-month patient survival following transplant compared to the previous scheme, but improvements in graft survival have been shown (p=0.0002).

Conclusions: The scheme was designed to increase access to transplant for difficult to match and ethnic minority patients, better kidney longevity matching and improved equity of access across different patient groups. Initial analysis reveals that the scheme is meeting these objectives.

P274 LONGITUDINAL DYNAMICS OF SARS-COV-2 SPIKE-SPECIFIC ANTIBODY RESPONSES IN PATIENTS ON WAITING LIST AND AFTER LUNG TRANSPLANTATION

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Background: Patients with end-stage lung diseases on the MHH waiting list for lung transplantation (LTx) have been vaccinated against SARS-CoV-2 spike protein with usually 3 doses of the mRNA vaccine. They are supposed to develop robust antibody and T cell responses when immunized prior to LTx without the influence of immunosuppression. We hypothesized the induction of high spike-specific IgG levels protected against SARS-CoV-2 infection and severe COVID-19. To gain information about the humoral response in waitlist patients (WL-LTx) vaccinated prior to LTx, we compared spike S1-, RBD- and S2-domain- specific IgG levels in WL-LTx patients pre vs. post LTx.

Methods: Plasma obtained pre- (n=70) and post-LTx (n=28) of WL-LTx patients was analyzed by Luminex-based multiplex assays. Threshold for positivity was set separately for each spike domain based on the median MFI +2σ in healthy, unexposed pre-pandemic controls. Patients with previous known SARS-CoV-2-infection were excluded.

Results: 95.7% of WL-LTx patients had seroconverted for either RBD-, S1- or S2-specific IgG pre-LTx and 92.86% were positive post-LTx. S1-, S2- and RBD-specific IgG MFI values did not significantly differ between pre- vs. post-LTx. Subanalysis of matched plasma samples (n=25) revealed that 52% of WL-LTx patients showed a higher IgG response pre- than post-LTx for all three spike protein domains and 28% showed even elevated antibody levels post-LTx. Lastly, S2-specific IgG MFI values were significantly elevated compared to RBD-specific IgG MFI values, both pre- (S2 vs. RBD $p<0.0001$) and post-LTx (S2 vs. RBD $p=0.0225$).

Conclusions: The majority of WL-LTx patients mounted high SARS-CoV-2 spike-specific IgG responses following vaccination pre LTx. Based on the more efficient antibody production against the S2 domain compared to RBD- and S1-domains, S2-specific IgG responses should be included also in the general evaluation of humoral immune responses to SARS-CoV-2. WL-LTx patients exhibited superior antibody responses to vaccination compared to LTx-recipients first vaccinated after LTx. Pre-transplant responses were maintained in some patients following transplant. Collectively, these results support patients, both on the waiting list and after LTx, benefitting from additional booster vaccinations after transplantation.

P275 PATIENTS REFERRED TO RETRANSPLANTATION MAY BENEFIT FROM MAINTAINING CALCINEURIN INHIBITOR AFTER KIDNEY TRANSPLANT FAILURE

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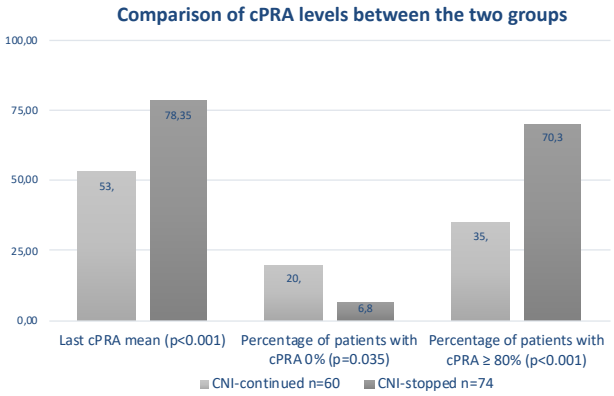
Background: Managing immunosuppression after kidney transplant failure remains controversial. Continuous balancing between sensitization and risk of infections remains challenging. Our aim was to evaluate the benefits and harms of continuing immunosuppression when aiming for re-transplantation.
Methods: We evaluated retrospectively all patients wait-listed for retransplantation after kidney transplant failure between 2006 and 2022 in our institution. From 2015 the institutional policy recommended to continue immunosuppression if aiming for retransplantation. The outcomes studied were calculated PRA (cPRA) at the time of retransplantation, time on waiting list until retransplantation, the rate of infection-related hospitalizations, and delayed graft function of the repeat transplant. For comparison, the patients were classified in two groups based on whether calcineurin inhibitor had been continued (CNI-continued) or withdrawn (CNI-stopped) before retransplantation or end of the follow-up.
Results: Altogether 110 of 134 cases analyzed proceeded to retransplantation. CNI was continued in 60 patients and withdrawn in 74 patients. In the CNI-continued group there were more non-sensitized (PRA 0%) patients (20% vs 6.8% p=0.04), fewer highly sensitized (PRA ≥ 80%) patients (35% vs 70,3%, p < 0.001) and a lower mean cPRA compared to CNI-stopped group (Figure 1). Mean transplant waiting time was shorter in the CNI-continued group (557 vs. 893 days, p <0.001). There were 0.93 infection-related hospitalizations per 1000 patient-days in the CNI-continued group compared to 1.68 in the CNI-stopped group (p<0.01). In the CNI-continued group, 60% had no hospitalizations due to infection compared to 24% in CNI-stopped (p<0.001). Delayed graft function of the retransplant was more common in the CNI-stopped than in the CNI-continued group (50% vs 26%, respectively, p = 0.02).
Conclusions: Continuation of calcineurin inhibitor seems beneficial among patients referred to retransplantation after kidney graft failure, as it was associated with lower sensitization, shorter waiting time, and lower risk of delayed graft function, whereas the risk of infection-related hospitalizations was not increased.

Figure 1. Comparison of the last PRA levels measured before the re-transplantation or at the end of the follow up.



P277 THE PROSPECTIVE EFFECT OF LIVING AND DECEASED RELATED DONOR TRANSPLANTATIONS IN PATIENTS' IMMUNE PROFILE

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Background: Phenotypic changes in lymphocytes have been described following renal transplantation (RT), including both CD4 and CD8 subpopulations.
Aim: Prospectively assess of T lymphocyte phenotypic alterations, after RT and compare differences between deceased (DR) and living (LR) donor recipients.
Methods: One hundred six RTRs were included in the study, 78/106 (74%) DR, age 52.5(15)yrs and 28/106 (26%) LD, 35(21)yrs. Lymphocytes, CD4, CD8, CD4CD28null, CD8CD28null, CD16+CD56+ (NK) and CD4+CD25+FoXP3+ (Tregs) were evaluated at peripheral blood, by flow cytometry, at certain time points: RT and 3, 6, 12 months (T0, T3, T6, T12, respectively).
Results: During follow up, at T3, T6, T12, eGFR was 61(23.6), 62.2(31.1), 63.5(23.9)ml/min/1.73m2, , p=NS and 59.1(24.8), 61(25.3), 62(22.7), p=NS, in DR and LR group, respectively. eGFR showed no significant difference between DR and LR at any time point. At any time point, T0, T3, T6, T12, lymphocytes were significantly increased in DR compared to LR groups, p=0.001, p<0.0001, p=0.002, p<0.0001, similarly CD4, p=0.001, p<0.0001, p=0.001, p<0.0001, and CD8 cells, p=0.002, p<0.0001, p=0.005, p=0.006, respectively. Tregs were increased at T0, T3, T6, not at T12, p<0.0001, p<0.0001, p=0.001, p=0.1, respectively. At this point, Tregs were increased in RTRs with eGFR>50ml/min/1.73m2, 20.3(9.3) vs. 27.2(18.6), p=0.03. CD4CD28null, CD8CD28null cells did not change during follow up, and there was no difference between two groups at any time point.
Conclusions: Immune profile, was improved in both groups, DR and LR, however a significantly better effect managed in LR, although elimination of CD28 molecule could not be restored. Interestingly, Tregs were associated only by renal function one year following RT.

	DR				
Cells/μL	**T0**	**T3**	**T6**	**T12**	**p**
Lymphocytes	1100(300)	1308(800)	1600(918)	1500(800)	p<0.001
CD4 cells	414(249)	600(607)	729(615)	588(417)	p<0.001
CD8 cells	266(163)	390(223)	455(275)	450(289)	p=0.002
NK cells	198(125)	125(131)	142(149)	149(158)	p=0.001
Tregs	20(13)	24(23)	27(25)	20(16)	p=0.001
	LR				
Lymphocytes	1350(750)	2250(1300)	2150(1275)	2250(1123)	p<0.001
CD4 cells	582(424)	994(817)	880(635)	863(442)	p<0.001
CD8 cells	388(189)	630(341)	623(614)	639(558)	p<0.001
NK cells	210(270)	170(218)	145(213)	166(244)	p=0.002
Tregs	36(27)	52(27)	35(44)	24(22)	p=0.02

P278 LONG TERM SURVIVAL OF THE HEPATOCELLULAR CARCINOMA WITH OR WITHOUT LIVER TRANSPLANTATION

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Background: Hepatocellular carcinoma (HCC), which is frequently diagnosed at late stages, 5-year survival rate of less than 12%. The gold standard treatment is liver transplantation (LT) or surgical resection. Various local regional treatment strategies (transarterial chemoembolization (TACE), radiofrequency ablation (RFA), and radioembolization (TARE)) can be performed to the treatment of tumors inappropirate for surgical resection and LT. We evaluated the differences between the outcomes of the treatment protocols.
Methods: All 636 HCC patients diagnoses were pathologically confirmed. As a result of examinations, we determined the treatment protocol (LT, surgical resection, locoregional treatment methods). Systemic chemotherapy treatment was given to HCC patients with distant organ metastases. During follow-up period, patients had routine laboratory tests, alpha-fetoprotein tests and ultrasonography examinations every 3 months and computed tomography or magnetic resonance scans done every 6 months.
Results: Between November 1988 and February 2023, 965 patients were diagnosed with hepatocellular carcinoma. As a treatment protocol, locoregional therapy (TACE, RFA, TARE) was performed to 652 patients, systemic chemotherapy (sorafenib) was given to 156 patients, LT was performed to 107 patients, and surgical resection was performed to 50 patients. The mean survival of all LT recipients, who diagnosed HCC was 137.45. months. One year, 5 years and 10 years survival rates were 90.2%, 71.7% and 61.4% repectively. The mean survival time of 50 HCC patients who underwent surgical resection was 156.6 months. One year, 5 years and 10 years survival rates of these patients were 86%, 75% and 57% repectively. Locoregional treatment was performed to 652 patients. The mean survival time was 27.9 months. One year, 5 years and 10 years survival rates of these patients were 33%, 48% and 18% repectively.
Conclusions: Appropriate treatment methods must be selected with detailed evaluation in experienced centers in HCC patients. In patients who cannot undergo surgical resection or liver transplantation, in the absence of distant organ metastases, locoregional treatments can provide longer survival times than those reported in the literature.

P279 TARGETED DELETION OF HYPOXIA INDUCIBLE TRANSCRIPTION FACTOR-1A GENE IN CD4+ T CELLS IMPROVES VASCULARIZED COMPOSITE ALLOTRANSPLANTATION OUTCOME

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Background: This study aims to determine the impact of the deletion of the HIF-1α gene in CD4$^+$ T cells on the immune response and allograft outcome after VCA. Both regulatory T cells (Tregs) and effector T cells (Teff) play a role in the acceptance of the allograft and the deletion of the HIF-1α gene influences the differentiation and function of various T cell populations. The study will investigate how the deletion of HIF-1α gene affects the immune response and allograft outcome.
Methods: In this study, mice with a deletion of the HIF-1α gene in CD4$^+$ T cells were created using the Cre-lox-P system. The immune response was evaluated in an in vivo model of vascularized composite allotransplantation. The assessment included measures of Tregs and Teff cell activation, inflammatory cytokine levels, and allograft acceptance.
Results: The results show that the recipient with HIF-1α deficiency in CD4$^+$ showed longer allograft survival than wild-type recipient under the same immunosuppressive regimen of either CTLA4Ig and Rapamycin or anti-CD154 and CTLA4Ig. These effects can be at least partially elucidated by reduced alloreactive T cells, lower levels of pro-inflammatory cytokines (such as IL-6 and TNF-α), and a significantly increased Helios$^+$ Tregs population with improved suppressive capacity.
Conclusions: The findings of the study suggest that manipulating the differentiation of CD4$^+$ T cells through the HIF-1α pathway could be a promising strategy to enhance the outcome of allotransplantation. This approach holds the potential to positively impact allograft survival and the immune response, leading to improved transplant outcomes.

P280 EFFECTS OF COLONIZATION WITH MULTIDRUG-RESISTANT BACTERIA ON PNEUMONIA ETIOLOGY IN THE FIRST YEAR AFTER KIDNEY AND HEART TRANSPLANTATION

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Background: Our aim was to analyze if previous colonization with multidrug resistant (MDR) bacteria has effects on etiology of pneumonia in kidney (KTx) and heart (HTx) transplant recipients during the first year after transplantation.
Methods: Our retrospective study enrolled KTx and HTx recipients transplanted between January 2019 and December 2020 with 12 months follow-up. Pneumonias were identified according to American Society of Transplantation Infectious Diseases Community of Practice guidelines. Surveillance cultures including nasal, throat and rectal swab, and urine culture were used.
Results: Our study included 106 KTx and 30 HTx recipients with bacterial pneumonia occurence of 6.6% (7/106) and 13.3% (4/30), respectively (Table 1). Surveillance cultures detected colonization with MDR bacteria in 40,6% (43/106) of KTx and 53,3% (16/30) of HTx recipients. The most frequent MDR isolate in KTx was extended-spectrum beta-lactamase-producing (ESBL) *Klebsiella pneumoniae* (18/53, 34.0%) and vancomycin-resistant enterococci (VRE) (8/53, 15.0%), and in HTx recipients MDR *Pseudomonas aeruginosa* (7/25, 28.0%), VRE (5/25, 20.0%) and *K. pneumoniae* ESBL (5/25, 20.0%). In five patients etiological pathogens were detected and those were Gram-negative bacilli (GNB). In KTx recipients with pneumonia (N=7), there were no MDR bacteria as proven etiological pathogen. In all Htx recipients with pneumonia (N=4), GNB were MDR and in 75% (3/4) of HTx recipients they were present as previous colonization in surveillance cultures.
Conclusions: GNB are responsible for the majority of bacterial pneumonias in our patient population. MDR GNB were more frequent etiological pathogens in HTx recipients majority of whom were previously colonized with the same bacteria. Despite small number of HTx recipients with pneumonia included, understanding the current epidemiology in different SOT recipients may help to better prevent and treat these infections.

Table 1. Characteristics of kidney and heart transplant recipients

Characteristic	Kidney	Heart
Transplantations	106	30
Median age at transplantation, y (range)	53,5 (8-77)	55,5 (5-67)
Gender (male) (%)	77 (72.6)	22 (83.3)
Bacterial pneumonia, n (%)	7 (6.6)	4 (13.3)
Time of pneumonia onset, n (%)		
0-1 month	0	2 (50.0)
>1-6 months	5 (71.4)	1 (25.0)
>6-12 months	2 (28.6)	1 (25.0)

P281 DELAYED REGULATORY T CELL THERAPY FOLLOWING ALEMTUZUMAB INDUCTION

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Background: In the ONE study, phase 1 trials of Treg therapy showed feasibility and safety in kidney transplantation. The goal of the TWO study is to expand on this and demonstrate further safety and efficacy of Treg therapy using a modified protocol of delayed Treg infusion following lymphodepletion with alemtuzumab induction to promote a Treg-skewed immune phenotype.
Methods: This was designed as a prospective single centre randomised controlled trial to explore delayed Treg therapy in living donor kidney transplant recipients. Patients were randomised to receive either 5-10x10^6 autologous polyclonal Tregs per kg at week 28 post transplantation, or standard immunosuppression. Both groups received alemtuzumab induction and initial immunosuppression with tacrolimus and mycophenolate mofetil. Primary outcomes were rejection and patient survival. Trial recruitment was paused in March 2020 due to the COVID-19 pandemic. Alemtuzumab induction was discontinued due to the uncertainty around safety of alemtuzumab in the context of COVID infection and the protocol was modified. Here we report data from the original protocol.
Results: We present here the outcomes of the cohort of 9 patients who underwent alemtuzumab induction under the original TWO study protocol. Two patients withdrew due to temporary suspension of the living donor transplant programme during the pandemic, and on resumption alemtuzumab could not be used. Seven patients completed the trial following alemtuzumab induction. Post-transplant patient and graft survival was 100%. Acute rejection free survival was 100% in the Treg arm compared to 75% in the control arm at 18 months post-transplant. Alemtuzumab resulted in prolonged depletion of T cells, with only 2/7 patients returning to pre induction CD4+ T cell levels at the 18-month visit. A trend towards transient increases in Treg numbers at weeks one and two post infusion were observed in patients receiving Treg therapy. Increases in naïve and transitional B cells were also observed in the Treg groups, similar to previous reports in operational tolerance.
Conclusions: Autologous Treg therapy is feasible and safe and can be delayed following lymphodepleting induction immunosuppression.

P282 A DEEP DIVE ON REAL-WORLD IMMUNOSUPRESSIVE THERAPY PATTERNS FOR RENAL TRANSPLANT PATIENTS IN FRANCE: 10 YEAR FOLLOW-UP DATA FROM THE OISTER STUDY

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Background: Immunosuppressive (IS) therapy modification is often required to maximize long-term patient and graft survival for kidney transplant recipients. Real-world data on IS strategies are limited. This analysis aims to describe real-world patterns of IS use and survival outcomes among renal transplant patients in France from OISTER, a long-term observational study.
Methods: A retrospective cohort of 29,709 adult patients receiving a renal graft and subsequent treatment with ≥1 IS therapy between 2009 and 2019 was identified from the French National Health Data System (SNDS). Patients were followed from first kidney transplant up to first event of interest (i.e., death, graft loss) or last observation available.
Results: Calcineurin inhibitors (CNI) were the most common first-line IS therapy (96.1% of patients, Table 1), while mammalian target of rapamycin inhibitors (mTORi) (1.2%) and belatacept (0.5%) initiations remained marginal. In subsequent lines of therapy, CNI use remained dominant, whereas the use of mTORi, belatacept and combination IS regimens increased (Table 1). Nearly 25% of patients on first-line IS had treatment modifications (8% in 2nd line, and >2% in 3rd line). During the study period, belatacept was unavailable until 2012 and since 2017, belatacept initiations were limited by supply issues. The 1-month, 1-year and 5-year patient survival rate were estimated at 99.1%, 96.8%, and 89.0%, respectively. Unsurprisingly, older age at transplantation negatively impacted 5-year patient survival; 73.1% in patients aged ≥70 years vs. 97.8% in 18-29 years. The 5-year graft survival rate was comparable across age groups (range: 84.2-87.3%), although decreased slightly in higher age groups (82.3 % in 60 years and 80.6% in ≥70 years).
Conclusions: This study provides a wide picture of IS therapies used for kidney transplant maintenance nationwide. The observed therapeutic strategies are aligned with French and international recommendations. In clinical practice, patient and graft survival at 5 years in renal transplant patients was excellent, most patients were alive with a functional graft. Graft survival remained comparable irrespective of age at transplantation, underlying that there was no discrimination with regard to the quality of the graft transplanted.

Table 1. Distribution of IS treatments by line, from 2009 – 2019; kidney transplant patients receiving IS (except antimetabolites and corticosteroids)

IS therapy	1st line (n=29,709) n (%)	2nd line (n=6970) n (%)	3rd line (n=2371) n (%)	4th line (n=498) n (%)
Tacrolimus	23,883 (80.4%)	1389 (19.9%)	1405 (59.3%)	122 (24.5%)
Cyclosporine	4678 (15.7%)	1423 (20.4%)	216 (9.1%)	99 (19.9%)
Tacrolimus + mTORi	568 (1.9%)	1620 (23.2%)	119 (5.0%)	72 (14.5%)
mTORi	353 (1.2%)	1491 (21.4%)	415 (17.5%)	88 (17.7%)
Belatacept ± tacrolimus	137 (0.5%)	887 (12.7%)	133 (5.6%)	97 (19.5%)
Cyclosporine + mTORi	90 (0.3%)	160 (2.3%)	83 (3.5%)	20 (4.0%)

IS - immunosuppressive; mTORi - mammalian target of rapamycin inhibitor
Note: 1st line refers to initial treatment after renal transplantation, and 2nd line to 4th line refer to subsequent treatment modifications.

P283 TOWARDS CREATING A FRAMEWORK FOR ENVIRONMENTAL SUSTAINABILITY IN KIDNEY TRANSPLANTATION SERVICES

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Background: Kidney transplantation (KTx) offers a longer life expectancy and improved quality of life in comparison to dialysis. Cost-effectiveness analyses have also proven its superiority for the health economy.
Methods: PubMed and EMBASE literature search using keywords “kidney transplantation”, “carbon footprint”, “sustainability”.
Results: There is no published work in the field of environmental sustainability in KTx. Relevant literature was identified for general surgical services and applied to transplantation. We believe that a series of actions can help identify and reduce the environmental impact of transplant services. Assuming its environmental superiority to dialysis, maximising KTx rate would be an important action. That could be achieved through living organ donation, systematic use of machine perfusion for extended criteria deceased donors and individualised immune risk stratification protocols. These measures aim towards implementing enhanced recovery protocols and two vital steps can be taken towards assessing their value. The first is a detailed audit of the carbon footprint of these novel approaches and secondly their impact in reducing length of hospital stay and if that correlates with a reduction in carbon footprint. Another key element is delivering proportionate and targeted post-operative care based on non-invasive techniques and reducing physical outpatient follow-up, using telemedicine (summary of proposals in Table1).
Conclusions: There is gap in quantifying KTx services environmental impact and an urgent need to develop strategies working to that purpose within in the framework of the multidisciplinary transplant team. Introducing novel modalities can lead to donor pool expansion and improved organ utilisation rates, transforming transplant services in green hubs.

Measures to “green up” kidney transplantation
Promote KTx instead of dialysis
Accept pre-emptive living donor KTx as the treatment of choice of kidney failure
Increase the deceased donor pool by employing machine perfusion
Implement enhanced recovery post-transplant protocols
Utilise stratified protocols for dealing with immunological risk
Non-invasive and remote follow-up

P284 FACTORS ASSOCIATED WITH GROWTH IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE, SINGLE-CENTER COHORT STUDY

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Background: Catch-up growth after pediatric kidney transplantation (kTx) is usually insufficient to reach normal adult height. Moreover, the incidence of overweight and obesity increases post kidney transplantation (KT). We aimed to describe growth parameters and predictive factors in children post KT.
Methods: We retrospectively reviewed the records of 28 children who underwent KT in our center between 2002-2022. Height (hSDS) and body mass index (BMISDS) z-scores at various time points and possible predictors were assessed
Results: Median age at KT was 11.2 years (5.3-14), 20 were male, mean time on dialysis was 5.95 years. KT from a living donor (LRD) was performed in 18 patients. Mean follow-up time was 4.88 (1-10) years. rhGH was administered pre-KT in 15/28 patients and in 3 post KT. Following the first year post KT, steroid free, alternate day and daily steroid regimes were adopted for 9, 11 and 8 patients, respectively. Mean hSDS at the time of KT, one year after and at last visit were -1.76, -1.87, and -1.77 (p>0.05). Mean BMISDS at the respective time points were 0.13, 0.65 and 0.05 respectively (p>0.05). At last visit, 29% and 17% of children showed moderate and severe height deficit. hSDS at last visit was associated with preoperative hSDS, whereas difference between hSDS pre and last visit post KT (ΔhSDS) was associated with the type of KT [mean ΔhSDS for LRD and DDT -1.45 (95%CI -1.87, -1.03) and -2.66 (95%CI -3.4, -1.93) respectively, p=0.002] and steroid regime [mean ΔhSDS for daily and alternate day steroid treatment -0.39 (95%CI -0.77, -0.003) and 0.55 (95%CI -0.07, 1.17) respectively, p=0.037]. There was no association between ΔhSDS and rejection episodes or rhGH administration pre-KT. At the time of KT and at last visit 25% and 10.7% were overweight, respectively, whereas only 1 patient was obese preoperatively but none at last visit. The overall incidence of overweight and obesity had reduced at last visit compared to pre-KT (p=0.01).
Conclusions: Linear growth post KT remained limited, resulting in short stature in nearly half of children. Strategies to improve height post pediatric KT could include height optimization pre-KT, steroid withdrawal/avoidance protocols, and LRD KT.

P285 SHORT-TERM PREDICTIVE MODELS FOR POST-KIDNEY TRANSPLANT DIABETES MELLITUS USING MACHINE LEARNING APPROACH: PRELIMINARY DATA

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Background: Post-transplant diabetes mellitus (PTDM) increases morbidity and mortality of transplant recipients. This study aims to develop a predictive model for PTDM from Korean Organ Transplant Registry cohort data and further build a platform preventing PTDM.
Methods: A prospective cohort study was conducted on KOTRY data of 6455 kidney transplant patients. The data consisted of a total of 110 variables (23 binary, 9 categorical, 78 continuous) including demographic and clinical data. Patients were classified by the occurrence of diabetes 6 months post transplantation. The total study population was divided into training set (n=5809, 90%) and test set (n=646, 10%). Machine learning was applied in finding the model with optimized accuracy. Four machine learning methods (Logistic Regression, XGBoost, CatBoost, Lightgbm) were constructed to analyze the data. Performances of algorithm were calculated by AUC (area under the receiver operating characteristic curve) score. Significance of each feature was determined using SHAP method.
Results: Out of 6455 patients, 2569 (40%) showed the incidence of PTDM within 6 months. 9% were patients with newly developed diabetes, and 31% were patients who had pre-transplant diabetes. Four machine learning methods (Logistic Regression, XGBoost, CatBoost, Lightgbm) developed prediction models using the training set. The 6 months prediction AUC scores in the test set were 0.92, 0.91, 0.92, and 0.91, respectively. Categorical features were especially more associated with PTDM. The significance of modifiable features was in the order of pretransplant HbA1c, fasting serum glucose, and body mass index.
Conclusions: We developed a prediction model for PTDM within 6 months after kidney transplantation based on biological cohort data of patients. We found that PTDM was most successfully predicted by using CatBoost model among 4 machine learning models. HbA1c, fasting serum glucose, and body mass index were proved to be the most significant modifiable features in predicting PTDM.

P286 SILICONE DEPOSITIONS, AN UNUSUAL FINDING IN THE EXPLANTED AND NEWLY TRANSPLANTED LUNGS

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Background: Chronic pulmonary silicone microembolism is a rare cause of interstitial lung disease (ILD) that can reoccur in the transplanted lungs.
Case report: A 45-year-old woman underwent a bilateral lung transplantation because of progressive unclassifiable ILD despite treatment with corticosteroids, IV cyclophosphamide and rituximab. The initial pathology of the explanted diseased lungs was consistent with severe pulmonary fibrosis with a non-classifiable pattern of interstitial fibrosis. Review of pre- and post-transplant chest imaging noted ruptured old PIP silicone breast implants that were never removed, raising concerns as to whether her ILD was related to continued leaking from these implants. Numerous small vacuoles were seen in the explanted lungs, particularly in the alveolar/acinar areas as well as one in a branch of the pulmonary artery. These vacuoles contained material suspected to be silicone, suggesting repeated haematogenous spread of silicone from the breast implants to the lungs, resulting in progressive lung inflammation and fibrosis. Subsequently, a surveillance bronchoscopy with transbronchial biopsies performed six months post-transplant also revealed the presence of silicone emboli in the transplanted lungs. As such, there was clear evidence of ongoing silicone microembolisation from her breast implants to the recently transplanted lungs, and the bilateral breast implants were therefore removed. Fortunately, her post-transplant lung function trajectory has remained stable so far and chest imaging shows no abnormalities.
Conclusion: Cases of chronic pulmonary silicone microembolism due to leakage from breast implants or silicone injections have been described, although this is an uncommon finding. However, in case of a possible implant rupture and unexplained ILD and/or histology findings, systemic leakage and haematogenous spread to the lungs and other organs should always be considered.

P287 CHARACTERISATION OF GRAFT INFILTRATES FOLLOWING REGULATORY T CELL THERAPY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: In the Phase 1 ONE study, adoptive Treg therapy was found to be safe and feasible in clinical practice. The TWO study is a Phase 2b randomised controlled trial of Treg therapy in living donor kidney transplant recipients which seeks to further expand on the safety data and explore the efficacy of this novel treatment strategy.
Methods: In this study we assessed graft infiltrates in patients receiving Treg therapy, using the Nanostring GeoMx digital spatial profiling platform. Protocol biopsies were retrieved from patients 9 months post-transplantation in patients who received Tregs 5 days post-transplant as an alternative to induction immunosuppression. These were compared to graft infiltrates in control patients with biopsy-proven rejection, or protocol biopsies from control patients not receiving cell therapy. Multiplexed protein expression was assessed on regions of interest identified using CD3, CD4 and FOXP3 immunofluorescence.
Results: Spatial profiling demonstrated unique differences between the infiltrates seen in the cellular therapy group and the control group which experienced rejection. Cellular therapy infiltrates showed relative increases in CD20, BCL-2, and FOXP3. Furthermore, the cellular therapy group demonstrated reduced relative expression of Ki67, CD68, CD163, IL-6, CD14 and IDO-1. FOXP3 infiltrates expressed known markers of Tregs.
Conclusions: The dense focal infiltrates seen in the cellular therapy group appeared to express an overall signature of immune regulation, in contrast to those in rejecting transplants. Defining the characteristics of these infiltrates is important in understanding how treatment with cell therapy alters tissue rejection responses.

P288 DE NOVO EXTRAMEMBRANOUS GLOMERULONEPHRITIS AND ANTIBODY-MEDIATED REJECTION AFTER RENAL TRANSPLANTATION: TWO SIDES OF THE SAME COIN?

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Background: Antibody-mediated rejection (AMR), the first cause of late graft loss, results from the generation of donor-specific antibodies (DSA). De novo GEM affects graft podocyte cells in patients whose cause of end-stage renal failure is not GEM. In this work we test the hypothesis that de novo GEM is a particular form of AMR with podocyte expression.
Methods: We retrospectively identified the 57 cases of de novo GEM diagnosed in France between January 2000 and January 2021 that were compared with 56 case of recurrence of primary GEM on the graft. Analyses of renal graft biopsies and of sera collected on the day-of-transplant and at GEM diagnosis were centralized.
Results: De novo GEM were diagnosed later and had a more severe impact on graft survival than recurrence (Log rank p respectively: 0,009 and 0,0007). Compared to patients with recurrence, those with de novo GEM had characteristics associated with alloimmunization with more female, past transfusion, and cyclosporine rather than tacrolimus. Furthermore, analysis of graft biopsies found more microvascular inflammation (glomerulitis and/or peritubular capillaritis, associated with AMR in Banff) in the de novo GEM group. Finally, although there was a trend for a higher proportion of patients with anti-HLA DSA at diagnosis in the de novo GEM (20%) vs recurrence (13%) group, this difference was not significant (p=0.51). Rather than ruling out our hypothesis, this result could indicate that the humoral alloimmune response that drives de novo GEM is directed against minor (non-HLA) polymorphic antigens. Ongoing analyses of biopsies by laser microdissection/mass spectrometry should allow validating this hypothesis.
Conclusions: De novo GEM is a rare complication of kidney transplantation that detrimentally impact on graft survival. Several clues indirectly suggest that this entity might represent a particular form of AMR directed against minor histocompatibility antigen expressed on podocyte surface.

P289 CHEMOTAXIS DIVERTS THE CYTOTOXIC RESPONSE OF ALLOREACTIVE T CELLS, CONFERRING PROTECTION TO THE VASCULAR ENDOTHELIUM DURING TCMR

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Conclusions: De novo GEM is a rare complication of kidney transplantation that detrimentally impact on graft survival. Several clues indirectly suggest that this entity might represent a particular form of AMR directed against minor histocompatibility antigen expressed on podocyte surface.

P290 ALPHA-1 ANTITRYPSIN DEFICIENCY IS UNDERDIAGNOSED IN CIRRHOTIC LIVER TRANSPLANT PATIENTS: A RETROSPECTIVE MULTICENTER STUDY

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Background: Alpha-1 antitrypsin deficiency (AATD) is one of the most common genetic diseases in Europe. Although it is responsible for liver fibrosis, AATD is not always diagnosed, even in patients who are candidates for liver transplantation (LT). The aims of this study was to determine when the diagnosis was made for patients transplanted for AATD, to describe their clinical characteristics and the outcome on the transplant waiting list.
Methods: We performed a multicenter retrospective study between May 2019 and June 2021 in 9 French and Canadian centers by including all liver transplant patients with AATD. The selection of patients was made on the explant analysis with PAS+, diastase-resistant inclusions within hepatocytes. A control group (n=305) to study the evolution on the transplant waiting list was selected from an existing monocentric cohort of liver transplant patients for decompensated cirrhosis.
Results: We included 58 liver transplant patients with AATD between 1996 and 2020, with a mean age of 55.6 ± 9.9 years at LT, mostly men (78%). Indication of LT was AATD in only 31% of cases whereas excessive alcohol consumption, NASH, cryptogenic cirrhosis represented 43%, 14% and 12% of patients respectively. The diagnosis of AATD was made before LT in only 40% of cases, after LT in 15% of cases. For 45% of patients, the diagnosis was never confirmed before the retrospective analysis. Only 46% of patients in the cohort had confirmation of AATD by phenotyping or genotyping before or after LT. Only 60% of patients had a pre-LT serum AAT assay, which was significantly lower in homozygous versus heterozygous patients (0.36 vs. 0.82 mg/ml, $p < 0.01$). Moreover, 25% of the patients had non-specific pulmonary symptoms and 8% had pulmonary emphysema. Compared to the control group, patients transplanted for AATD had a higher MELD score at listing for transplant (21.9 vs 14.2, $p<0.001$) and a shorter waiting time on the transplant waiting list (4.7 months vs 8.3 months, $p<0.001$).
Conclusions: Our study demonstrates that AATD is largely under-diagnosed in the context of LT. Regarding the development of curative treatments, systematic phenotype/genotype screening of patients on waiting list could be suggested as well as raising awareness of transplant physician to achieve better management of the patients and their relatives.

P291 STATE OF KNOWLEDGE OF ALPHA 1 ANTI-TRYPSIN DEFICIENCY AMONG PRACTITIONERS SPECIALIZED IN LIVER TRANSPLANTATION IN FRANCE: A NATIONAL SURVEY

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Background: Alpha-1 antitrypsin deficiency (AATD) is one of the most common genetic diseases in Europe with a prevalence of heterozygosity of 1.6%. Although it is also responsible for liver damage leading to end stage liver diseases, AATD is not always diagnosed, even in the most severe patients who are candidates for liver transplantation (LT). Considering the recent advances in potential treatment and the understanding of AATD involvement in progression of liver diseases, we aimed to investigate the level of knowledge on AATD and the current practices of liver transplant physicians in France.
Methods: A practice survey of 22 multiple-choice questions in the form of a questionnaire created and distributed via GoogleForm was sent by e-mail to the members of the French think tank in LT, GREF2.
Results: Adherence to the survey was 54%, including 89% hepatologists, 7.5% liver surgeons and 3.5% anesthesiologists. 81% of practitioners rated their level of knowledge as very low, low, or average, and only 22% answered the question of disease prevalence correctly. Half of the responders had >15 years of experience in high-volume LT centers. Only 57% of practitioners routinely performed AATD screening before LT. AAT dosage was used in 97% of cases for the screening but 47% knew that it is decreased by hepatocellular insufficiency and 20% by pregnancy. Only 47% knew that heterozygosity status could be a cofactor of liver disease progression. Furthermore, 62% of practitioners with < 5 years of experience considered their level of knowledge to be low but systematically screened before LT in 75% of cases compared to 44% for practitioners with between 5 and 15 years of experience and 61% for practitioners with > 15 years.
Conclusions: AATD is a poorly known disease among LT practitioners in France. A better knowledge of screening methods, diagnosis and treatment of the disease would allow a better management of the patients and their relatives.

P292 THE ROLE OFADIPOCYTOKINES IN DEVELOPMENT OF NEW ONSET DIABETES AFTER LIVER TRANSPLANTATION

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Background: The development of new-onset diabetes after transplantation (NODAT) has the greatest negative impact on long-term survival after liver transplantation (LT). The pathogenesis of NODAT is most likely similar to that of type 2 diabetes mellitus, with insulin resistance (IR) and beta-cell dysfunction being the main driving factors. Adiponectin and leptin dysregulation are associated with the occurrence of IR and diabetes in the general population, but their role in LT patients remains unclear.
Methods: The study included patients undergoing LT without prior glucose intolerance or overt diabetes. Metabolic parameters (including adiponectin and leptin concentrations) were assessed before and 3, 6, and 12 months after LT to determine the incidence and risk factors for NODAT.
Results: The study involved 152 people, of whom 29 (19.1%) developed NODAT. Patients with alcoholic liver disease had a higher incidence of NODAT with 19 (26%) compared to 10 (12.7%) patients in the rest of the population (p=0.041). NODAT occurrence was not associated with higher mortality, increased rates of acute graft rejection, infectious or cardiovascular complications. Risk factors for the occurrence of NODAT included BMI before LT (OR 1.1, 95% CI: 1.02-1.22), BMI 12 months after LT (OR: 1.15, 95% CI: 1.01-1.31), and beta cell function 3 months (OR 0.98, 95% CI: 0.97-0.99), 6 months (OR 0.99, 95% CI 0.97-1.00) and 12 months (OR 0.98, 95% CI 0.97-1.00) after LT. Adiponectin and leptin levels before or after LT were not associated with the development of NODAT. However, elevated leptin concentrations were found to be a risk factor for the development of IR in cirrhotic patients. A leptin increase of 1 µmol/L increased the odds ratio for the occurrence of IR by 1.25-fold (CI: 1.08-1.45).
Conclusions: NODAT was a common complication in the first year after LT, but no association between NODAT and adverse events was found. The levels of adiponectin and leptin did not affect the occurrence of NODAT in the first year after LT. This may be because beta cell dysfunction, rather than IR, is the main pathophysiological mechanism for the occurrence of NODAT in the early period. Further studies are needed to determine whether adiponectin and leptin play a role in the occurrence of NODAT in the long-term course after LT.

P294 CORRELATION OF DD-CFDNA AND REJECTION PHENOTYPES IN A BRAZILIAN PATIENT POPULATION

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Background: Donor derived cell free DNA (dd-cfDNA) is a validated marker for detection of allograft rejection in kidney transplant recipients. Here we investigate how dd-cfDNA correlates with different rejection archetypes in a Brazilian patient population.
Methods: In this single center study we selected patients with dd-cfDNA samples obtained prior to biopsy. Histological interpretation served as the gold standard to assess percent dd-cfDNA (dd-cfDNA%) test performance in patients assigned to categories of rejection (TCMR and ABMR/Mixed) or non-rejection. dd-cfDNA% was measured using the Prospera™ test.
Results: The study included 482 unique patient samples. The median age of patients was 44 (range 19-76) years, 64% (309/482) were male and median time since transplant was 1.4 (range 15-23) years. Rejection was found in 63 samples (23 ABMR/Mixed and 40 TCMR). Receiver operator curve analysis produced an area under the curve (AUC) of 0.89 for distinguishing ABMR/Mixed from non-rejection and 0.71 for TCMR vs non-rejection. Incorporating estimated quantity of dd-cfDNA into the analysis correctly identified two additional TCMR cases (16 high-risk for rejection cases (dd-cfDNA%≥1%) with TCMR increased to 18). When other injuries such as infection and recurrent disease were excluded from the non-rejectors AUCs rose to 0.91 and 0.76 respectively. Stratified analysis indicated that patients with chronic TCMR and high dd-cfDNA% (≥1%) had more graft loss (high dd-cfDNA% 3/6; low dd-cfDNA% 2/11), were more often DSA positive (high dd-cfDNA% 3/6, low dd-cfDNA% 1/11) and had higher median change in serum creatinine 6 months after biopsy (high dd-cfDNA% +10%, low dd-cfDNA% -7%). For patients with sustained poor graft function, logistic regression analysis indicated an interaction between age and dd-cfDNA% (p=0.02). Using an optimal dd-cfDNA% threshold, this model showed improved performance for detecting rejection (sensitivity 89%, specificity 89%, positive predictive value 47%, negative predictive value 99%).
Conclusions: In this single center study of patients with clinically indicated biopsies, dd-cfDNA% showed a strong association with rejection. Our results provide an early basis for future studies looking at how dd-cfDNA can help risk stratify difficult to interpret patient populations.

Table. dd-cfDNA test performance (AUC) in detecting rejection and comparison of median dd-cfDNA% for rejection subtypes vs non-rejection.

Rejection subtype	AUC	Rejection Median dd-cfDNA% (IQR)	Non-rejection median dd-cfDNA% (IQR)	P-value (rejection vs non-rejection)
ABMR/mixed	0.89	3.1% (1.2-7.0%)	0.31% (0.17-0.53%)	P < 0.001
TCMR	0.71	0.54% (0.39-1.1%)	0.31% (0.17-0.53%)	P < 0.001

P296 THE IMPACT OF POSTREPERFUSION SYNDROME ON RECIPIENT MORTALITY AND GRAFT FAILURE IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Post-reperfusion syndrome (PRS) during liver transplantation (LT) is known to be related to higher morbidity and mortality after surgery. However, most of the studies that investigated effect of PRS on prognosis could not control various pharmacological interventions immediately before or after reperfusion. Furthermore, they are mainly based on deceased donor LT (DDLT), and thus the effect of PRS on prognosis in the living donor LT (LDLT) is unclear. By utilizing our institution's standard protocol in LDLT and minimizing prophylactic use of pharmacological interventions before or after reperfusion, we aimed to investigate the effect of PRS on graft failure and post-transplant mortality in LDLT.
Methods: With approval of IRB, medical records of adult recipients (age ≥ 19 years) who received LDLT between April 2010 and December 2019 at Samsung Medical Center were retrospectively reviewed. Primary outcome was the effect of PRS on mortality and graft failure. Secondary outcome was the effect of PRS on other postoperative outcomes including the lengths of ICU and hospital stay, rejection.
Results: A total of 399 patients were enrolled. The incidence of PRS was 35.3%. To reduce confounding variables, patients were divided to two groups, No PRS group and PRS group, and then matched at a 1:1 ratio with the factors that are known to be associated with prognosis. Before matching, only the length of ICU stay showed significantly longer in PRS group than no PRS group (P<0.001). After matching, 120 paired sets of patients were generated and all postoperative outcomes including death, graft failure, and the lengths of ICU and hospital stay did not show significant difference. Cox regression analysis on postoperative mortality and graft failure showed that PRS was not a risk factor.
Conclusions: In this study, PRS did not affect mortality and graft-failure in LDLT. Only the length of ICU stay showed statistical difference before matching.

P299 CHARACTERIZING ADHERENCE PROFILES BASED ON C0 MONITORING IN KIDNEY TRANSPLANT PATIENTS: ILLUSION OR REALITY?

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Background: Many authors claim the relationship between adherence and immunosuppressive drug concentrations, and trough level monitoring has been proposed as a tool to characterize patients' adherence. Our objective was to explore the relationship between exposure to calcineurin inhibitors (CNIs) and adherence over time in kidney transplant patients followed-up for up to three years after transplantation.
Methods: Adherence was repeatedly estimated with the 4-Item Morisky-Green-Levine Medication Adherence Scale (MMAS) in 712 kidney transplant recipients followed-up in the EPIGREN and EPHEGREN cohorts between 2007 and 2017. Non-adherence was defined for a MMAS score >0. Adherence time-profiles were explored by mixed effect modeling with latent process and latent classes. The relationship between drug exposure and adherence was explored by comparing the proportion of subtherapeutic trough concentrations (C_0) between patients with: (i) adherent vs. non-adherent time-profiles; (ii) simultaneous MMAS-score >0 vs. =0. The inter-patient coefficient of variation (CV) of C_0 was calculated for cyclosporine and tacrolimus in patients with adherent and non-adherent profiles.
Results: Two profiles of adherence over time were characterized: the first subgroup of patients (85%) displayed a good and stable adherence, while patients of the second subgroup (15%) displayed a poorer adherence, worsening over time. The proportion of subtherapeutic C_0 was comparable between groups for both cyclosporine and tacrolimus. No patient was found to simultaneously have subtherapeutic C_0 and a MMAS score >0. The intra-patient CV of C_0 was not associated with adherence for either molecules (non-adherent vs. adherent patients: 42.8 vs. 49.5% for tacrolimus and 52.9 vs. 51.6% for cyclosporine).
Conclusions: No relationship was found between exposure to CNIs and adherence over time. The TDM of CNIs can allow identifying episodes of non-adherence in patients who display very low C_0, but is of limited interest to characterize adherence profiles. The characterization of adherence profiles is relevant only when TDM is associated with patient interviews.

P300 EVALUATION OF POST REPERFUSION BASELINE BIOPSIES FOR KIDNEY TRANSPLANT OUTCOME

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Background: In times of increasing graft shortage the identification of risk factors for a prognostically poor kidney transplant outcome is of high clinical relevance. A biopsy of the kidney transplant in the setting of transplantation could provide information about its quality. However, the relevance of this baseline biopsy and its predictive value for transplant success is controversially debated.
Methods: To determine the predictive value of histologic findings in post reperfusion kidney transplant biopsies, we evaluated the degree of glomerulosclerosis, interstitial fibrosis and tubular atrophy (IF/TA), arteriosclerosis (AS) and acute tubular injury (ATI) in 338 biopsy specimens collected from 2006 to 2016 after deceased (n=243) and living donation (n=95). All baseline biopsies were scored by a blinded renal pathologist. Survival analysis was performed using multivariate Cox regression analysis and binary regression analysis to investigate an association with delayed graft function (DGF).
Results: Mean follow-up time was 4.1 years. DGF was reported in 108 (32%) cases. As expected, ATI and arteriosclerosis were significantly associated with DGF (for ATI >25%, Odds ratio (OR): 3.79, 95% confidence interval (CI): 1.12-12.87, p = 0.033; for moderate AS, OR: 2.11, CI: 1.02-4.36, p = 0.043). Survival analysis revealed IF/TA as the only histologic lesion being associated with death-censored graft failure over the entire observation period, determined by multivariate Cox regression analysis in three different models adjusted for known clinical risk factors as e.g., donor age, donor history of hypertension, cold ischemia time and terminal serum creatinine >1.5mg/dl (Hazard ratio: 1.04, CI: 1.00-1.08, p = 0.032). The median survival of kidney transplants with IF/TA > 0% was 8.3 compared to 9.8 years to those without evidence of IF/TA. None of the histologic lesions had a significant effect on one-year graft survival.
Conclusions: ATI as histological hallmark of ischemia-reperfusion damage and the extend of arteriosclerosis were associated with DGF. IF/TA provides independent information on graft survival but cannot be used alone as a prognostic tool given the still acceptable survival time. The inclusion of histologic markers in a combined tool with clinical features may be promising.

P301 A LENGTHENED EUTHANASIA ELIMINATES THE BURDEN OF ORGAN DONATION RELATED PREMORTEM INQUIRIES AND IN HOSPITAL PERFORMED EUTHANASIA

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Background: Organdonation after euthanasia (ODE), has been performed since 2012 in the Netherlands. ODE exposes the euthanasia donor (ED) to a non-familiar environment in the last moments of life. Decoupling of euthanasia and organ donation (OD) has been shown to be feasible in ODE starting from home. Preparations for ODE with premortem inquiries may also be experienced as burdensome. We describe a modified ODE to reduce the ODE related physical and mental burden.
Methods: A patient with a neurodegenerative disease suffered from aggravating symptoms. She lived her life mainly solitarily at night and isolated. She requested for euthanasia and had a sincere wish to donate her organs. Assessments were performed and euthanasia was consented. There were no objections for OD in her medical history. She explicitly preferred not to have any exposure to hospital surroundings and medical professionals in the preparation and performance of ODE.
Results: To facilitate her wish to donate, she consented to come to the hospital, would be deeply sedated in a private room as start of the euthanasia, and thereafter general anesthesia (GA) was provided to maintain sleep and secure vital functions, immediately followed by additional testing (laboratory, CT scanning, echocardiography, bronchoscopy). Allocation was to be awaited in the next hours. After allocation and settlement of the OD procurement team, last acts of euthanasia resulted in a respiratory arrest, 14 minutes later followed by a circulatory arrest, and declaration of death after 5 minutes 'no touch'. The functional warm ischemia time (WIT) was 19 minutes. The body was immediately transported to the operation room. OD procurement followed successfully.
Conclusions: A further decoupling of OD and euthanasia in ODE is feasible. The OD related burden is transferred from the ODE patient to medical professionals, especially to the euthanasia provider, who must attend at the ED from beginning of euthanasia till death declaration. From the perspective of the ED this may result in a significant reduction of moral-ethical and logistical distress. GA followed by last acts of euthanasia might also hasten death, reducing the functional WIT without doing harm to the ED. ODE patients should be informed about the alternative pathways of ODE, decoupling euthanasia and postmortal OD.

P302 PREGNANCY OUTCOMES AFTER LIVER AND KIDNEY TRANSPLANTATION

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Background: Thanks to advances in surgical techiques and immunosuppression, patient and graft survival after organ transplantation have increased significantly. Most of the female patients who had liver and kidney transplants in childhood want to become pregnant when they reach reproductive age. Among this patients, concerns regarding adverse immunosuppression effect on the fetus and consequence of pregnancy of allograft function represent significant sources of anxiety. We retrospectively analyzed pregnancy outcomes after liver and kidney transplantation at our transplant center.
Methods: Since November 3, 1975 we have performed 3404 kidney transplantations (KT) and 720 liver transplantations (LT) at Baskent University. Among KT recipients 394 were pediatric and 348 of LT patients were pediatric (age <18 years old). On March 15, 1990, Dr. Haberal performed partial LT in children, a first in Turkey, Europe and the region. Mean age of the pediatric KT recipients was 13.8 ± 6.7 (range 1.5-18 years) and of the pediatric LT recipients was 7.44 years (range 4 months – 17 years). Of 394 pediatric kidney transplant patients 177 were female and 156 of 348 pediatric LT patients were female. All of KT and LT's were living related kidney transplant and all recipients were relatives with their donors.
Results: In total, 28 kidney and liver transplant recipients became pregnant. Of these patients, 10 were LT recipients and 18 were KT recipients. The mean age at which the patients gave birth was 30 years (range 24-38 years). The mean time between the organ transplantation and delivery of the patients was 10.63 years (range 2-22 years). Recipient patients were immunosuppressed with tacrolimus or cyclosporine together with prednisone during pregnancy. The mean delivery time of the babies was 35.5 weeks (range 24-39 weeks). One patient delivered vaginally, and the other patients delivered by cesarean section. Except for 1 baby, all of the other babies were born healthy. One baby died at 24 weeks due to placenta previa. No significant complications or organ rejection occurred during or after delivery in any of the mothers.
Conclusions: Liver and kidney transplant female recipients can have a safe pregnancy and give birth to healthy children if they are followed up and treated in experienced centers.

P303 UROLOGIC COMPLICATIONS AFTER KIDNEY TRANSPLANTATIONS AND THEIR MANAGEMENT

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Background: Urologic complications are most common surgical complications encountered after kidney transplant, causing significant morbidity and mortality. Rates of urologic complications after kidney transplant range between 2% and 12.5%. In parallel with the evoluation of minimally invasive percutaneous techniques and acquired experience, there has been a major shift from surgery to interventional radiologic procedures in the management of these complications. In these study we aimed to evaluate our urologic complications and their management retrospectively.
Methods: Between November 1975 and January 2023 our transplant team has performed 3404 kidney transplant. From 1975 to 1983, we performed ureteroneocystostomies using the modified Politano-Leadbetter technique. From 1983, we began using the extravesical Lich-Gregoir techique in combination with temporary ureteral stenting in 1141 patients. Then, in September 2003, we began using corner-saving technique. We analyzed types of urologic complications, mean time to diagnose from kidney transplant, management of complications and their long term results.
Results: Urologic complications occurred in 96 (2.8%) kidney transplant recipients. Forty six (1.3%) of these patients had urine leakage, 36 (1%) had urinary obstruction due to ureteral stricture, 6 (0.1%) had distal ureter necrosis, 4 (0.1%) had urine leakage and obstruction and 2 (0.05%) developed renal calculi in the late postoperative period. Twenty-four out of 96 required reoperation for urologic complications. The remaining 22 patients were treated conservatively in our interventional radiology department with excellent results. Our interventional treatment methods are percutaneous nephrostomy with a double J stent, percutaneous nepfroureterostomy, ballon dilatation or double J stent only.
Conclusions: Urologic complications are most common complications after kidney transplant. Early diagnosis by experienced personnel and use of interventional radiology can greatly reduce the need for surgical treatment. Thanks the early diagnose and treatment graft kidney functions can be successfully preserved.

P304 PREVALENCE OF POST-COVID-19 CONDITION IN PATIENTS WITH CHRONIC KIDNEY DISEASE, ON DIALYSIS AND LIVING WITH A KIDNEY TRANSPLANT

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Background: The prevalence of post-COVID-19 condition (PCC) is estimated to be 13% in healthy individuals. We analyzed the prevalence and disease burden of PCC in patients with chronic kidney disease (CKD) G4/5, dialysis patients and kidney transplant recipients (KTR).
Methods: Patients participated in the RECOVAC study, in which SARS-CoV-2 antibodies were measured in CKD G4/5, dialysis patients and KTR after the second and third COVID-19 vaccination in the Netherlands. A questionnaire was sent to 4868 participants one year after initial vaccination asking for the presence of long-lasting symptoms after diagnosis in COVID-19 positive patients, or since the start of the pandemic in COVID-19 negative patients. PCC was defined according to the WHO clinical case definition. Blood samples at one month after the second and third vaccination were analysed with anti-RBD IgG ELISA. COVID-19 diagnosis was assessed by questionnaire or positive anti-nucleocapsid IgG antibodies. Logistic regression analysis was used to compare the presence of one or more long-lasting symptoms between COVID-19 positive and negative patients. In COVID-19 positive patients, we likewise identified predictors of PCC by backward selection and estimated the association between log-transformed antibody levels and PCC.
Results: 2747 patients were included, of which 222 patients with CKD G4/5, 390 dialysis patients and 2135 KTR. PCC was present in 25%, 16%, and 21% of CKD G4/5 patients, dialysis patients and KTR with high or very high symptom burden in 57%, 61% and 71%, respectively. In COVID-19 negative patients, long-lasting symptoms were present in 15%, 13% and 18%, respectively. COVID-19 positive patients (n= 1004) were at higher odds of having one or more long-lasting symptoms compared with COVID-19 negative patients (n=1743) (OR: 1.33 [1.09-1.61], p=.005). Predictors of PCC were chronic lung disease (adjusted OR 2.04 [1.18-3.50], p=.01) and hospital/ICU admission (adjusted OR 5.03 [3.22-7.86], p<.001). Log anti-RBD IgG antibody level was negatively associated with PCC (adjusted OR: 0.79 [0.66-0.94], p=.008).
Conclusions: Patients with CKD G4/5, dialysis patients and KTR are at risk for PCC with a high symptom burden, especially if antibody levels after COVID-19 vaccination are low.

P305 EFFECT OF A NATIONWIDE INTERVENTION TO REDUCE HEPATECTOMY TIMES IN DUTCH ORGAN PROCUREMENT TEAMS

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Background: Donor hepatectomy time > 60 minutes is associated with poorer transplantation outcomes. The Dutch organ procurement committee executed a nationwide audit to evaluate hepatectomy times of procedures performed from December 2017 until February 2018. Liver procurements exceeded the 60-minute threshold in more than 50% of cases. Subsequently, a nationwide improvement program ("intervention") was enrolled to reduce hepatectomy time, ideally below 40 minutes. Aim of this study was to determine whether this intervention successfully reduced hepatectomy time.
Methods: A nationwide, retrospective database study of organ procurement procedures, both DBD and DCD was conducted. All procedures from January 2013 until October 2022 were included. Donor hepatectomy time was defined as time between start of abdominal flush and hepatectomy. The intervention period, from March 2018 till June 2018, was excluded from analysis. We compared hepatectomy times before and after intervention, of procurement teams who were affiliated to a liver transplant center (n=3) with those not affiliated to a liver transplant center (n=2).
Results: In total 1749 liver procurements were analyzed, of which 876 before and 873 after intervention. Median hepatectomy time significantly decreased from 50 (39-63) to 35 (28-43) minutes, p<0.01 for affiliated procurement teams and from 67 (52-84) to 34 (28-42), p<0.01 for non-affiliated procurement teams. Before intervention 24.1% of the hepatectomies in the Netherlands were performed within 40 minutes. This increased to 69.5% after the intervention (p<0.01). Before intervention, simultaneous procurement of thoracic organs was significantly associated with increased hepatectomy time (B=0.31 95% CI: 0.24-0.38, p<0.001), while this was not the case after intervention (B=0.03 95% CI: -0.35-0.10 p=0.37). There was no significant difference in preventable surgical damage before or after the intervention (p=0.27).
Conclusions: The nationwide audit and the subsequent intervention resulted in a significant decrease in hepatectomy times for all procurement teams. Therefore, we recommend implementing such procurement analysis in all ET countries. Monitoring and intervention, if needed, will assure the same procurement standards, and increase donor liver quality.

P306 THE COST-EFFECTIVENESS OF PROPHYLAXIS IN CYTOMEGALOVIRUS SEROPOSITIVE (CMV R+) KIDNEY TRANSPLANT RECIPIENTS OVER THE FIRST YEAR POST-TRANSPLANTATION

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Background: The medico-economic benefits of prophylaxis over preemptive strategy in cytomegalovirus (CMV) seropositive kidney transplant recipients (R^+) are still debated. This study aimed to evaluate the cost-effectiveness and cost-utility of oral ganciclovir prophylaxis vs. preemptive strategy on CMV-infection-free survival over the first year post-transplantation.
Methods: Clinical, biological and economic data were collected from 188 CMV R^+ kidney transplant recipients: 101 patients benefited from prophylaxis and 87 from preemptive strategy. The impact of the strategy on CMV infection free survival was explored using a time-dependent Cox proportional hazard model (using R software). Costs were calculated from the hospital perspective and quality-adjusted life years (QALYs) were determined using the EQ5D. Incremental cost effectiveness and cost utility ratios (ICER and ICUR) were estimated in euros by nonparametric bootstrapping for each case of infection avoided and for each QALY gained over 1 year.
Results: Prophylaxis significantly decreased the risk of CMV-infection over the first year post-transplantation (HR=0.22, CI95%=[0.12-0.37], p<0.01). Compared with the preemptive strategy, prophylaxis allowed resources saving (€-1155 per patient), and was more effective (0.42 infection avoided per patient), resulting in an ICER = €-2769 per infection avoided. Prophylaxis was superior to the preemptive strategy, with a net gain of 0.046 QALY per patient and costs saving of €1422 for 1 QALY gained.
Conclusions: In this study, the most cost-effective strategy for the management of CMV infections in R+ kidney transplant recipients was prophylaxis, despite the high cost of ganciclovir. Prophylaxis had a positive effect on quality of life at reasonable costs and resulted in net savings. Further studies comparing prophylaxis and preemptive strategies should be conducted to confirm the medico economic superiority of prophylaxis in CMV R+ kidney transplant recipients.

P307 RENAL TRANSPLANTATION IN HYPERSENSITIZED PATIENTS. DESENSITIZATION VS. PATHI

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Background: Higher sensitized patients suffer from greater difficulties to access kidney transplantation. We have designed the present study to analyse and compare two methods that facilitate access to transplantation for these patients: HLA-desensitization in living-donor kidney transplantation and PATHI (Spanish allocation system for high sensitized patients)
Methods: Sensitized patients undergoing renal transplantation were studied ccording to two different action protocols: pre-transplant desensitization with a living donor and the national PATHI program (cPRA>98%). We analysed time on waiting list, the degree of cPRA and the prognosis: patient and graft survival, acute rejection and infectious complications.
Results: 51 patients are studied (27 desensitized and 24 PATHI). The time on the list was longer in PATHI (115 +- 79 vs 87+-87, p=0.24), higher number of incompatibilities in desensitization group (3.6 +-1.1 and 2.8+-1.6) and longer follow-up in desensitization group (78+-56 vs 34+-27 months, p 0.001). Delayed graft function 14.8% in desensitized patients and 66.7% in PATHI (p 0.001). The incidence of acute rejection at one year was 16.3% in desensitization and 13.4% in PATHI (p 0.95) with ABMR in 2 patients in desensitization and 4 in PATHI. Graft survival at 1 and 3 years was 88.3% in desensitization and 90% in PATHI p 0.75. Patient survival of 96.3% and 91.7% at one year and 3 years in desensitization vs 94.4% at one year and 3 years in PATHI, p 0.69. The incidence of CMV at one year was 30.2% in desensitization vs 21.9% in PATHI p=0.45. The incidence of BK at one year was 0% in desensitization vs 10.5% in PATHI, p = 0.001.
Conclusions: The time on the waiting list is longer in PATHI and the number of incompatibilities is higher in desensitization group. Follow-up is longer in desensitization, so the results in the medium-long term must be interpreted with caution. We did not find significant differences in survival, higher frequency of rejection mediated by tests in PATHI without statistically significant difference. Higher CMV in desensitization without statistical significance and higher incidence of BK in PATHI.

P308 KIDNEY TRANSPLANTATION IN JEHOVAH'S WITNESSES: ETHICAL IMPLICATIONS, MANAGEMENT PROPOSAL AND REVIEW OF LITERATURE

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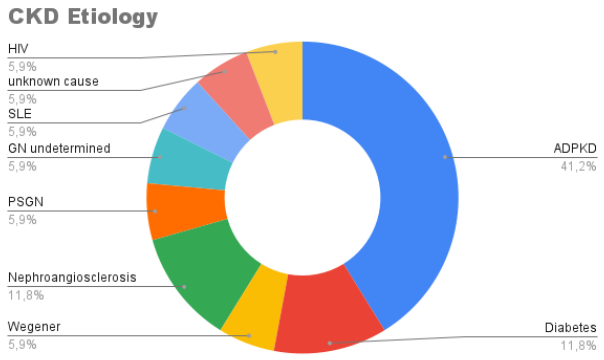
Background: For Jehovah's Witnesses (JW) religious principles organ transplant is permitted but blood transfusions are proscribed: blood is a symbol of life and only God can give or take life. JW represents a challenge for the surgeon: even if often not necessary, there is no proof that transfusions can be avoided systematically and safely. Especially for non-lifesaving organs, doubts remain on the wisdom to engage in such a complicated procedure. Moreover, denial of transfusions may be considered an additional risk factor for premature graft loss and might discourage transplant physicians from enrolling JW in their waiting lists. Aim of this study is to describe a single center experience and analyze the issues still present on surgical decision-making.
Methods: From 2013 to 2022, 17 JW received a Kidney Transplant (KTx) at our institution. Grafts procured from deceased donors were allocated to JW on the basis of regionally allocation rules. Living donations were performed too. To secure JW needs, various techniques have been developed for reducing the extent of bleeding and recovering the blood loss intraoperatively. Systematic review of the literature was carried out, analyzing publications from 1990 to 2023.
Results: We have established an operating protocol focused on the patient's cardiovascular system, verifying the ability to deal with transient states of anemia by satisfying the oxygen demands of peripheral tissues. Continuous circuit blood salvage and reinfusion was employed during surgery as were recombinant erythropoietin and intravenous iron during the posttransplant period. About literature review, of 536 articles found, only 18 items were included after the text analysis.
Conclusions: Most JW can safely receive a KTx without increasing the risk of graft failure. Ethical debate is still open on the risk of reduced chance of graft survival, which may be seen as a violation of the rights of non–JW recipients who might accept any therapy to save the organ. It is unfair to deny transplant listing to a JW right up front. More effort is needed to establish international protocols allowing careful selection of candidates and perioperative management optimization. Donor safety is undoubtedly of the utmost concern. A comprehensive approach to bloodless surgery is a necessity for a successful outcome.



Demographic Categories	Frequency (n)	Percentage (%)
Sex Male Female	 8 9	 43 57
Deceased donor DBD DCD	14 12 2	82 70 12
Living donor	3	18
Typology Single Tx Double Tx	 16 1	 94 6
Median age at KTx	57 years (37-74)	
Median in-hospital-stay	16 days (8-28)	
Complications according to Clavien-Dindo Classification	1 grade I 2 grade II 2 grade IIIb	6 12 12
Overall patients survival	16/17	94
Overall graft survival	17/17	100%

P309 SHORT- AND INTERMEDIATE-TERM OUTCOMES OF LIVING KIDNEY DONATION: FROM THE STAND-POINTOF DONOR

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Background: Kidney transplant is the best available therapeutic modality for patients enduring end stage renal disease (ESRD). From the perspective of kidney graft recipient, kidney transplant therapy is economical, extends better quality of life and maximizes survival. The objective of the present research study was to investigate the short- and intermediate-term outcomes of living kidney donation in donors with regard to kidney function and post kidney transplant complications at a single center in Pakistan.
Methods: The present study recruited healthy kidney donors who underwent nephroureterectomy at the Renal Transplant Unit, Dow University Hospital, Karachi, Pakistan. In order to ascertain the outcomes, early post kidney transplant complications and kidney functions were evaluated at last follow up. The average duration of follow up was 1.1 ± 0.7 years.
Results: A total of 86 living related kidney donors participated during the period of 1 year. Of them, 52 (60.5%) were males, while 34 (39.5%) were females. The mean age of the living donors was 35.3 ± 11.0 years. Most of the donors were siblings (n = 45, 52.3%). Left nephrectomy was performed in 65 donors (75.6%) and right nephrectomy in 21 donors (24.4%). The mean postoperative hospital stay was 7.99 ± 0.87 days. No deaths were evidenced during or after the kidney donation. However, a total of 15 donors (17.4%) were found to have one or more surgical complications. In addition, hypertension (HTN) and diabetes mellitus (DM) was diagnosed in 10 (11.6%) and 3 (3.5%) living donors, respectively. Creatinine clearance was > 90 mL/min in 47 (54.7%), 60 to 90 mL/min in 34 (39.5%), and ≤ 60 mL/min in 5 donors (5.8%).
Conclusions: Living kidney donation continues to exist as a standard therapeutic option for ESRD patients and harbors a minor risk. Post-operative complications can be reduced with vigilant selection of donors and appropriate post-surgical management

P310 COMPARISON OF PERFUSATE COMPOSITION DURING NORMOTHERMIC LIVER PERFUSION - TRANSPLANTED VERSUS NON-TRANSPLANTED LIVERS

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Background: An increase in perfusate components during normothermic machine perfusion (NMP) could be indicative for the synthesis capability of the graft and extent of preservation injury. Our aim was to compare perfusate composition of transplanted (tx) with not transplanted livers (non-tx).
Methods: During NMP of 27 livers, blood gas analysis (BGA) of perfusate and bile was performed, as well as perfusate analysis for factor XIII activity (FXIII), fibrinogen, bilirubin, sodium, alkaline phosphatase (AP), alanine-aminotransferase (ALT), aspartate-aminotransferase (AST), gamma-glutamate transferase (gGT) and lactate dehydrogenase (LDH). Viability assessment was based on lactate clearance, perfusate and bile glucose, perfusate and bile pH, and bile production.
Results: In total 31 livers underwent NMP, 20 were transplanted following viability assessment while 11 livers did not meet the criteria for transplantation. The two groups did not differ significantly in donor age (p= 0.06) and BMI (p=0.197), but WIT was significantly longer (p=0.016) and gGT was higher (p=0.005) in the non-tx group. Perfusate sodium (30 minutes, p=0.001; 60 minutes, p=0.05) and bicarbonate (60 minutes, p=0.011) levels were lower in non-tx livers. The pH was higher in tx livers at 0 (p=0.012), 30 (p=0.001), and 60 (p=0.024) minutes. Non-tx livers presented with higher FXIII activity at 5 min (p=0.041), 60 min (p=0.07), 120 min (p=0.084), and 240 min (p=0.069). FXIII act was increasing in non-tx livers but remained stable in tx livers. Bilirubin (5 min, p=0.02), AP (5 min, p=0.027; 60 min, p=0.049), AST (5 min, p=0.02; 60 min, p= 0.04; 120 min, p=0.008; 240 min, p=0.014), ALT (120 min, p=0.009; 240 min, p=0.043), gGT (5min, 0.002; 60 min, p=0.013), LDH (5 min, p=0.05; 60 min, p=0.011; 120 min, p=0.009) was significantly higher in non-tx livers. Fibrinogen levels trended higher in tx livers (not significantly) and were increasing over the course of the perfusion in both groups.
Conclusions: Damage markers in perfusate confirmed the decisions during viability assessment. Interestingly, FXIII in perfusate was higher in non-tx livers and presented with different dynamics. Fibrinogen was increasing over the course in all livers, tx livers presented with higher fibrinogen levels, which might indicate a higher regenerative capacity.

P311 CLINICAL OUTCOMES OF DISTINCT INDUCTION THERAPIES IN LOW IMMUNOLOGICAL RISK KIDNEY TRANSPLANTS FROM CONTROLLED DONORS AFTER CIRCULATORY DEATH (CDCD)

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Background: The convenience of the use and type of T-cell depletion Induction immunosuppression in kidney transplants (KT) from cDCD donors is not well-established yet. We aimed at characterizing main clinical outcomes in a large consecutive cohort of KT patients from cDCD according to different induction immunosuppressive therapies.
Methods: From 2015 to 2021 we performed 302 KT from cDCD and we considered recipients of a single KT with cPRA 0%. Induction immunosuppression was based on Thymoglobulin (rATG) from 2015 until 2019 and Grafalon thereafter. During this time period there were recipients treated with Basiliximab to avoid longer cold-ischemia time (CIT). Maintenance immunosuppression was based on tacrolimus, MMF and steroids. Valganciclovir prophylaxis was employed for high-risk recipients (D+/R-) and for KT receiving T-cell depletion therapy. We evaluated donors and recipient characteristics, transplant-related variables, and major clinical outcomes.
Results: Main baseline, clinical, demographic and immunological, donor/recipient characteristics were not different between groups (table 1). Post-transplant lymphocyte kinetics showed a significantly lower cellular depletion and faster recovery among Grafalon-treated patients as compared to rATG. After adjusting for donor KDPI and functional warm and CIT, treatment with Grafalon was associated with lower risk of DGF (OR: 0.39; 95%CI: 0.16-0.97; p=0.043) and Thymoglobulin (OR: 0.52; 95%CI: 0.24-1.14; p=0.101). Furthermore, when adjusting for DGF and HLA mismatches, treatment with both Grafalon (OR: 0.14; 95%CI: 0.04-0.57; p=0.006) and rATG (OR: 0.37; 95%CI: 0.14-0.95; p=0.04) were associated with a lower risk of rejection. Notably, incidence of CMV and BK virus infection was not significantly different between groups. However, when adjusting for CMV serological risk (D+/R-), patients treated with Grafalon showed a trend to a lower risk of late-onset CMV infection than rATG and basiliximab (OR: 0.48; 95%CI: 0.22-1.02; p=0.059). One-year patient and graft survival were not -different between the three groups.
Conclusions: In our cohort, grafalon is associated with less lymphocyte depletion, maintaining an excellent safety profile in term of the incidence of AR and viral opportunistic infections such as CMV.

Table 1. Clinical, demographic and immunological, donor/recipient characteristics on different groups.

Variables	Thymoglobulin N= 121	Grafalon N= 63	Basiliximab N= 48	*p-value*
Mean doses (mg/kg)	3.8 ±1.0	7.5 ± 2.9	n.a.	*n.a.*
Donor Age (years)	63 (53-73)	62 (55-73)	62 (56-75)	*0,863*
Donor sex (male, n (%))	79 (64)	38 (61)	31(68)	*0,808*
Donor weight, kg	75 (68-89)	78 (70-86)	80 (65-89)	*0,745*
Donor terminal Creatinine (mg/dL)	0,7 (0,4-0,9)	0,7 (0,5-0,9)	0,7 (0,5-0,9)	*0,390*
Donor KDPI, %	**80** ± 22	**79** ± 22	**80** ± 21	***0,989***
Functional warm ischemia time (min)	20 (16-24)	21 (17-25)	19 (16-23)	*0,171*
Recipient Age (years)	65 (54-71)	67 (58-73)	61 (52-71)	*0,230*
Recipient sex (male, n (%))	78 (64)	44 (71)	31 (67)	*0,627*
Recipient BMI (kg/m²)	26 (23-30)	26 (23-30)	27 (24-29)	*0,990*
RRT modality HD/PD/Preemptive, n	80/38/6	45/12/5	30/14/2	*0,488*
Diabetes mellitus, n (%)	40 (32)	27(44)	11(24)	*0,091*
Previous non-skin cancer, n (%)	19 (15)	8 (13)	8 (17)	*0,827*
Cardiovascular disease n, (%)	38 (31%)	23 (37%)	14 (31%)	*0,879*
CMV D+/R-, n (%)	**10 (8,3)**	**6 (9,5)**	**5 (10,4)**	***0,905***
HLA A/B/DR mm	5(4-5)	5 (4-5)	4 (4-5)	*0,156*
Cold ischemia time (hours)	10 (7-14)	12 (9-17)	11 (9-15)	*0,013*
DGF, n (%)	33 (28)	12 (19)	19 (41)	***0,038***
Delayed tacrolimus after transplant (days)	2 (1-3)	2 (1-2)	1(1-2)	***0,006***
Acute rejection, yes (%)	13 (10,7)	3 (4,7)	10 (20,8)	***0.028***
Timing AR (months)	2,4 (0,7–7,2)	8,2 (1,6–34,9)	1,0 (0,4–2,3)	*0,067*
Type of AR (TCMR grade I/TCMR grade II/ABMR)	5/4/4	1/1/1	3/4/2	*0,396*
CMV cumulative incidence (%)	49	38	56	*0,151*
Timing CMV replication (months)	4,3 (1,3–5,9)	5,1 (2,5–,4)	2,1 (1,1–2,9)	***0,001***
Tissue-invasive disease/viral syndrome/asymptomatic viremia	3/6/50	2/4/18	1/1/25	*0,334*
BK virus cumulative incidence (%)	13,2	11,1	18,6	*0,694*
Timing BK replication (months)	2,4 (1,8–6,8)	3,5 (1,3–5,9)	2,5 (1,7–3,7)	*0,943*
BK maximal viral load (log)	3,3 ± 6,8	2,1 ± 4,1	3,2 ± 6,1	***0,001***
BKVAN/BK viremia/no BK	4/12/105	1/6/56	0/8/40	*0,469*
Lymphocytes at 15 days (cells/mm³)	511 ± 386	914 ± 513	1656 ± 906	***<0,001***
Lymphocytes at 1 month (cells/mm³)	655 ± 427	1095 ± 562[a]	1567± 920[a,b]	***< 0,001***
Lymphocytes at 6 months (cells/mm³)	1064 ± 641	1592 ±813[a]	1968 ± 860 [a,b]	***< 0001***
1-year patient survival (%)	90	90	85	*0,716*
1-year death-censored graft survival (%)	93	96	95	*0,597*

P312 GPBAR-1/CAMP/PKA SIGNALLING MITIGATES THE MACROPHAGE-MEDIATED ACUTE CHOLESTATIC LIVER INJURY VIA ANTAGONIZING NLRP3-ASC INFLAMMASOME

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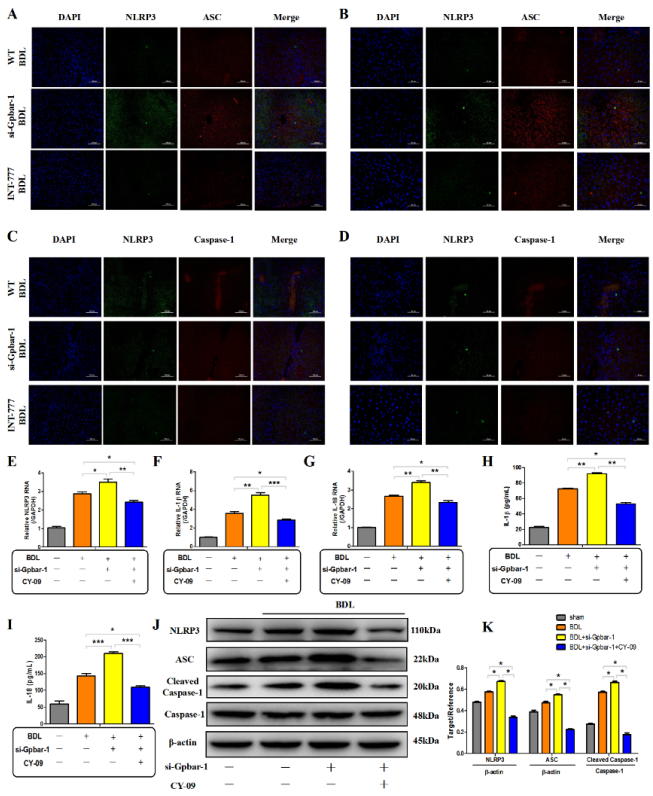
Background: ACLI is an acute liver disease related to bile duct obstruction leading to liver inflammation response and apoptosis. Gpbar-1 is a cell surface receptor that is involved in the regulation of multiple metabolic pathways. However, the function of Gpbar-1 in the context of innate immune activation in ACLI remains unclear.
Methods: The liver tissues and blood samples from Twenty ACLI patients and twenty healthy subjects were collected and subjected to biochemical test, HE staining, western blot and immunohistochemistry assay to vertify liver damage and expression of Gpbar-1. WT and si-Gpbar-1 mice with ACLI induced by BDL were used in vivo, and primary KCs with or without Gpbar-1-siRNA were used in vitro. We used animal and cell experiments to vertify macrophage-mediated ACLI and the regulatory mechanism between Gpbar-1 and NLRP3/ASC inflammasome.
Results: In this study, Gpbar-1 knockdown significantly exacerbated BDL-induced acute hepatic damage, inflammatory reaction and liver apoptosis compared with WT mice in vivo. The KCs with knockdown of Gpbar-1 were more susceptible to lipopolysaccharide (LPS) stimulation than normal KCs. Gpbar-1 activation by its ligand suppressed LPS-induced pro-inflammatory response in WT but not Gpbar-1-knockdown KCs. Notably, expression of NLRP3-ASC inflammasome was effectively enhanced by Gpbar-1 deficiency. Furthermore, Gpbar-1 directly increases intracellular cAMP levels and phosphorylation of PKA, thus disrupting the NLRP3-ASC inflammasome. The pro-inflammatory nature of Gpbar-1 deficiency was almost neutralized by NLRP3 inhibitor CY-09 in KCs. M1 polarization in vitro was accelerated under LPS-stimulated Gpbar-1-knockdown KCs. From a therapeutic viewpoint, the administration of KCs with Gpbar-1 deficiency aggravated BDL-induced ACLI, which was effectively rescued by inhibition of NLRP3-ASC inflammasome.
Conclusions: Our studies reveal that Gpbar-1 plays a crucial role as a novel regulator of immune-mediated ACLI by inhibiting NLRP3-ASC inflammasome, with therapeutic implications for the management of human ACLI.



P313 T LYMPHOCYTE SUBSETS IN LONG-TERM KIDNEY TRANSPLANT SURVIVORS

Asimina Fylaktou[1], Efstratios Kasimatis*[2], Grigorios Myserlis[3], Aliki Xochelli[1], Erasmia Sampani[2], Margarita Samali[1], Apostolia Zolota[2], Vasilki Nikolaidou[1], Maria Stangou[2], Georgios Tsoulfas[2;4], Aikaterini Papagianni[2]

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Background: Kidney transplant recipients who have survived more than 20 years with a functioning graft are considered long-term survivors after kidney transplantation. However, mortality with functioning graft is increased in these patients due to cardiovascular diseases and cancer in particular. CD28null T lymphocytes (CD3CD28null) are associated with cardiovascular diseases and T regulatory lymphocytes (Tregs), while crucial in the induction of tolerance, may also inhibit antitumor immune responses. In this study, we investigated T lymphocyte subsets in long-term kidney survivors.
Methods: Flow cytometry analysis was performed on 31 long-term kidney recipients who retained graft function for more than 20 years. Specific T lymphocyte subtypes studied were CD4CD28null, CD8CD28null, and CD4CD25FoxP3 (Tregs). We performed the same analysis on 31 kidney recipients one year after kidney transplantation, matched for age and eGFR, who served as a control group.
Results: Long-term kidney recipients (53±10 years old) maintained graft function for a median of 25 years, while their estimated GFR was 53.2±20.3 ml/min/1.73m^2. In comparison with one-year kidney recipients, long-term patients had increased CD4 T lymphocytes, both in percentage [51.5(17.4) vs 42.9(18.8) %, p=0.013) and absolute cell number [1200(801) vs 535(329) cells/μl, p<0.001]. The CD3CD28null cells/μl were increased [402(441) vs 236(344), p=0.049] while Tregs almost doubled [41(49) vs 21(15), p<0.001] in long-term patients.
Conclusions: In long-term kidney survivors, alterations observed in T cell subpopulations may render these patients more susceptible to specific common risk factors for morbidity and mortality, independent of their graft function.

P314 SHORT-TERM EFFECTS OF LOSARTAN TREATMENT IN ELDERLY PATIENTS AFTER KIDNEY TRANSPLANTATION – AN INTERIM ANALYSIS OF CELART STUDY

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Background: Globally, the number of people aged 60 years and older in the society is increasing. The population of patients with end-stage renal disease and after renal transplantation (RTx) is also ageing. It is known that older kidney transplant recipients (KTRs) have reduced overall survival and graft survival compared to younger recipients. The aim of the study was to evaluate the short-term influence of losartan on cardiovascular (CV) risk and allograft injury biomarkers and the safety of the therapy in elderly KTRs.
Methods: An interim analysis of a prospective, open, multicentre, controlled clinical trial CELART (*Cardiovascular Effects of Losartan After Renal Transplantation*) was performed. 135 patients after RTx were enrolled to the trial to either losartan (L 50-100mg) or standard hypotensive (ST) group to reach target blood pressure <140/90mmHg. 44 patient (32.6%) from the cohort was 60 years or older (25M/19F). 30 (68.2%) and 14 (31.8%) patients were allocated to ST and L group. After 6 months of the treatment albuminuria, eGFR, haemoglobin, potassium and creatinine concentrations were evaluated, as well as CV risk biomarker: serum concentration of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) and the intrarenal fibrosis biomarkers: urine excretion of transforming-growth-factor β-1 (TGFβ-1) and procollagen-type-III-amino-terminal propeptide (PIIINP).
Results: The groups did not differ with respect to age, gender, time after transplantation, comorbidities (age adjusted Charlson Comorbidity Index), graft function and albuminuria. After 6 months of treatment patients in both groups reached the target BP. There was no difference in changes of eGFR, creatinine, haemoglobin, potassium concentration, albuminuria, urine excretion of TGFβ-1 between groups. There was however a significant decrease in urine excretion of PIIINP (p<0.05) and serum concentration of NT-proBNP (p<0.05) in L group.
Conclusions: In short-term observation losartan shows no effect on graft function and no significant adverse reactions in elderly patients after RTx. Instead, it induced a decrease in graft fibrosis excretion biomarker and serum CV biomarker, which may have an impact on the long-term survival of elderly KTRs.

P316 QUESTIONNAIRE FOR EXPLORING QUALITY OF LIFE FOLLOWING LIVER TRANSPLANTATION IN ROMANIAN PATIENTS

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Background: A positive effect of liver transplantation (LT) on health-related quality of life (HRQOL) has been well documented in various studies using generic and liver specific instruments. However, this is the first Romanian study analysing QOL after LT. Our aim was to evaluate different aspects of QOL after LT with a QOLI (quality of life inventory) questionnaire adapted in Romanian language.
Methods: We have applied the questionnaire to the LT recipients and calculated the scores (T score) and the QOL graded as low (T score <42) and high (T score >58); the following data were noted: time since LT, recipient age/gender, etiology of liver disease and different long term complications requiring hospitalization and medical interventions.
Results: There were 64 patients that responded to QOLI questionnaire (50% males), median age at the moment of evaluation 57.5 years and the median T score was 57. There was no difference between times since LT in patients with low vs high QOL after LT. Presence of cured HCV or HCC before LT did not influence also QOL. A higher proportion of post-LT complications (biliary/cardiovascular/renal) (59.4%) were present in the group of patients with low QOL compared to patients (6.7%) with high QOL (p<0.0001); however, type of post-LT complication did not influence the low QOL. There was no correlation between the type of immunosuppression taken by the patient (single or multiple number of drugs/day) and QOL.
Conclusions: Presence of any type of post-transplant complications was the single factor that determined a low QOL following LT in our cohort.

P319 PLACENTAL CHORIONIC PLATE MESENCHYMAL STEM CELLS FOR THE TREATMENT OF DECOMPENSATED LIVER CIRRHOSIS: THE RESULTS OF A PILOT CLINICAL CASE SERIES

Denis Efimov*[1], Ekaterina Petrovskaya[1], Irina Romanova[1], Natalyia Dedyulya[1], Ekaterina Nazarova[1], Evgeniya Primakova[1], Ala Symanovich[1], Dzianis Sadouski[1], Leanid Kirkovsky[1], Sergey Korotkov[1], Aliaksei Shcherba[1], Svetlana Krivenko[1], Oleg Rummo[1]

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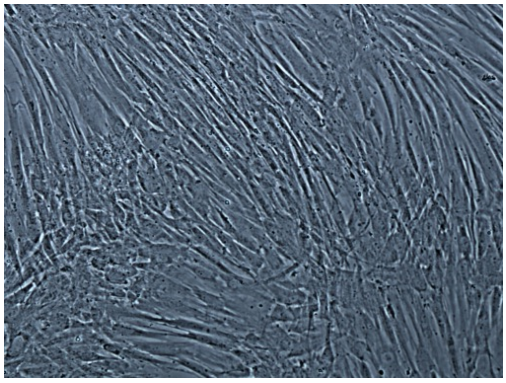
Background: Extraembryonic mesenchymal stem cells (MSC) possess multipotency and remarkable immunomodulatory features with robust and constitutive anti-inflammatory and anti-fibrotic properties, making them suitable for the treatment strategy of different acute and chronic liver disorders. The aim of this study was to evaluate the safety and the therapeutic potential of systemic intravenous chorionic plate MSC (CP MSC) infusion for the treatment of decompensated liver cirrhosis.
Methods: MSC were obtained from the placenta of a healthy woman in labour who signed an informed consent and was delivered by caesarean section. The chorionic plate as a source of MSC was chosen based on the high differentiation potential of this cell population (differentiated in adipogenic, chondrogenic and osteogenic directions), as well as on the basis of more significant secretion of hepatocyte growth factor in relation to MSC from other tissues of the placenta (>100 000 pg/ml vs 11 427 [3378; 19182] for CP MSC vs other placental MSC. We report an experience of 5 prospective clinical cases (age – 39 [37; 42]; MELD score – 24 [22; 25]) of intravenous systemic CP MSC infusion (~2mln/kg, see table) in decompensated liver cirrhosis patients. Inclusion criteria: age under 18, total bilirubin >100 mmol/l, Child C liver cirrhosis, inpatient treatment demand.
Results: Systemic administration of CP MSC did not cause side effects, was not associated with complications of administration or worsening of the clinical picture. There was one lethal outcome on the eighth day after administration due to profuse esophageal varices bleeding. In 4 patients, stabilization of the course of liver failure was observed, which made it possible to continue treatment at the outpatient stage, one patient subsequently underwent liver transplantation (2 months after), 1 patient is awaiting liver transplantation.
Conclusions: In selected patients systemic CP MSC infusion may stabilize the decompensation of liver cirrhosis. To make it evident, the future clinical trials are required.

Patient	Cell count, ×106	Passage	Viability, %	Criopreservation (yes/no)
K.	178,1	2	99	no
M.	138,0	2	97	no
L.	145,9	3	96	yes
P.	174,5	3	99	yes
H.	141,78	3	99	yes



P320 HIGH OXALIC ACID CONCENTRATION AND LOW RESIDUAL DIURESIS NEGATIVELY INFLUENCE KIDNEY TRANSPLANT OUTCOMES

Gideon Post Hospers*[1], Wesley Visser[1], Jeroen Verhoeven[1], Mirjam Laging[1], Sara Baart[1], Ingrid Mertens Zur Borg[1], Dennis Hesselink[1], Anneke van Egmond[1], Michiel Betjes[1], Madelon van Agteren[1], David Severs[1], Robert Zietse[1], Jacqueline van de Wetering[1], Chris Ramakers[1], Michel Vos[2], Ido Kema[2], Marcia Kho[1], Marlies Reinders[1], Joke Roodnat[1]

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Background: High plasma oxalic acid concentration may cause oxalic acid deposition and kidney function decline with a considerable recurrence risk after transplantation. Oxalic acid and its precursor glyoxylic are nephrotoxic agents. Kidney insufficiency itself can cause high oxalic acid concentrations through decreased excretion. We studied the influence of oxalic acid concentration and related factors on outcomes after kidney transplantation.
Methods: Patients who received a kidney transplant between September 2018 and January 2022 participated in our study. Oxalic acid and its precursors glyoxylic acid, and glyceric acid concentrations were determined in pre transplant blood samples. Twenty recipient, donor or transplant related variables and data on (patient-reported) residual diuresis were collected. Follow-up was until December 31st 2022.
Results: 496 patients were included. Oxalic acid and glyoxylic acid concentrations were above normal concentration in 98.8% respectively 100% of patients. One-third of patients had residual diuresis <500 ml, and one-third >1500 ml per day respectively. There was a significant, mediocre correlation between oxalic acid and residual diuresis (p <0.001; r= -0.529). 157 patients had delayed graft function (DGF). Multivariable binary logistic regression analysis showed that the prevalence of DGF was lower in living donor recipients. Prevalence of DGF was higher in recipients with lower residual diuresis (in ml/day), higher BMI, and higher glyoxylic acid concentration (table 1). There were 53 graft failures and 44 deaths. Multivariable Cox analysis showed that lower residual diuresis, higher donor age and higher oxalic acid concentration had a significant and negative influence on graft failure censored for death (figure 1). There was no interaction between oxalic acid and residual diuresis.
Conclusions: Oxalic acid and its precursors accumulate in pre transplant patients. High levels negatively influence the prevalence of DGF, graft failure and patient mortality. Oxalic acid concentrations are correlated with residual diuresis. Residual diuresis is an important and independent predictor of DGF and graft failure censored for death. Improvement of these parameters or preemptive transplantation might have a positive effect on kidney transplant outcome.

	B	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Donor type (living)		<0.001			
DBD	1.900	<0.001	6.688	2.780	16.089
DCD	3.406	<0.001	30.149	13.380	67.931
Renal replacement therapie (none)		<0.001			
Haemodialysis	3.221	<0.001	25.051	5.255	119.423
Peritoneal dialysis	2.130	0.009	8.416	1.717	41.242
Recipient BMI	0.090	0.001	1.094	1.040	1.152
Residual diuresis (ml per day)	-0.001	0.005	0.999	0.999	1.000
Glyoxylic acid (µmol/L)	0.100	0.028	1.105	1.011	1.208
Glycollic acid (µmol/L)	-0.091	0.054	0.913	0.832	1.002
Constant	-7.159	0.000	0.001		

Table 1: Binary logistic regression analysis on delayed graft function

	B	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
Residual diureses (ml/day)	-0.001	<0.001	0.999	0.999	1.000
Donor age	0.038	0.002	1.039	1.014	1.065
Oxalic acid (µmol/L)	0.007	0.030	1.007	1.001	1.014
Donor type (living)	0.699	0.046	2.012	1.012	4.000

figure 1: Multivariable Cox Proportional Hazards analysis on graft failure censored for death

P321 PREGNANCY AFTER KIDNEY TRANSPLANTATION- IMPACT OF FUNCTIONAL RENAL RESERVE ON ALLOGRAFT OUTCOME AND MATERNAL HEALTH

Rebecca Kaatz[1], Elisabetta Latartara2[2], Friederike Bachmann[2], Nils Lachmann[3], Bianca Zukunft[1], Kaiyin Wu[4], Danilo Schmidt[1], Fabian Halleck[1], Peter Nickel[1], Kai-Uwe Eckardt[1], Klemens Budde[1], Stefan Verlohren[2], Mira Choi*[1]

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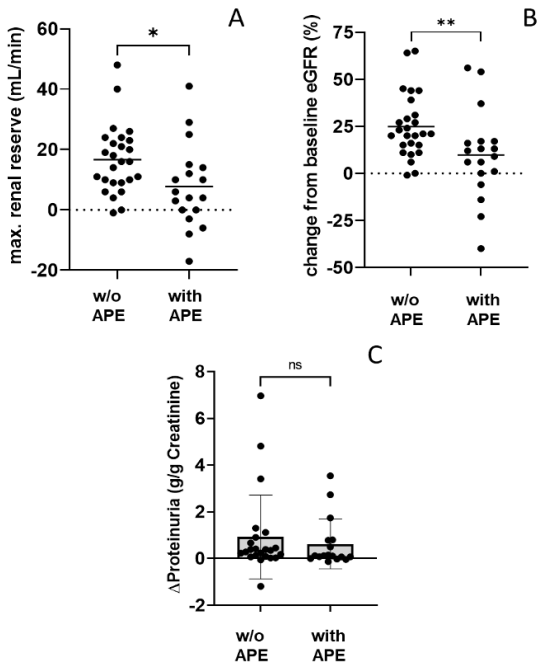
Background: Women of childbearing age show increased fertility after kidney transplantation. Of concern, preeclampsia, preterm delivery, and allograft dysfunction contribute to maternal and perinatal morbidity and mortality. Patients after KTX have an underlying chronic kidney disease and it can be difficult to discriminate whether the cause of deterioration of allograft function is related to pregnancy.
Methods: We performed a retrospective single-center study, including 40 women with post-transplant pregnancies after single or combined pancreas-kidney transplantation between 2003 and 2019. We took into account recent changes regarding the definition of preeclampsia as new onset of hypertension and proteinuria or new onset of hypertension and/or significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation. Outcomes of kidney function up to 24 months after end of pregnancy were compared with a matched-pair cohort of 40 transplanted patients without pregnancies to address the question if changes in allograft function depict the consequence of pregnancy itself rather than non-pregnancy-related risk factors.
Results: With a maternal survival rate of 100%, 39 out of 46 pregnancies ended up with a live-born baby. eGFR slopes to the end of 24 months follow up showed mean eGFR declines in both groups (-5.4±14.3 mL/min in pregnant versus -7.6±14.1 mL/min in controls). We identified 18 women with adverse pregnancy events (APE), defined as preeclampsia with severe end organ dysfunction. An impaired hyperfiltration during pregnancy was a significant risk contributor for both, APE (Figure) and deterioration of kidney function (p<0.01). In addition, a declining renal allograft function in the year before pregnancy was a negative predictor of worsening allograft function after 24 months follow up. No increased frequency of de novo donor-specific antibodies after delivery could be detected.
Conclusions: Overall, pregnancies in women after kidney transplantation showed good allograft and maternal outcomes. The use of biomarkers such as sFlt-1 and PlGF need to be explored in future studies.

Impact of hyperfiltration during pregnancy. Maximal renal reserve (A), change from baseline eGFR (B), change of proteinuria (C).*= p<0.05,**= p<0.01, ns=not significant.



P322 COMPARISON BETWEEN INTERNAL ILIAC ARTERY AND EXTERNAL ILIAC ARTERY FOR RENAL ARTERY ANASTOMOSIS IN KIDNEY TRANSPLANTATION

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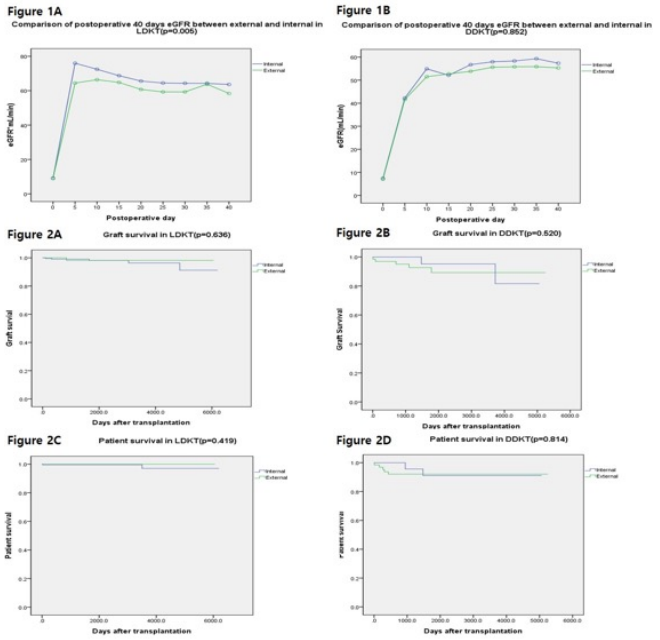
Background: The most common way to anastomose donor's single renal artery (DSRA) to recipients is using the internal iliac artery (IIA) or external iliac artery (EIA) in kidney transplantation (KT). One study showed no significant difference in long-term outcomes between the two groups in 38 deceased donor kidney transplant recipients. However, this study had some limitations. The number of patients was small, and living donor KT was not included. Therefore, we attempted to compare the outcomes of two groups using IIA and EIA in deceased and living donor KT.
Methods: 381 patients with DSRA who underwent KT at Seoul National University Bundang hospital from 2005 to 2021 were investigated retrospectively. Among 381 patients with DSRA, 288 patients underwent living donor kidney transplantation (LDKT) and 93 patients received deceased donor kidney transplantation (DDKT). In 212 cases of 288 LDKTs, the donor's renal artery was anastomosed end-to-end fashion to the recipient's IIA, and in 76 cases, the EIA was anastomosed end-to-side fashion. In 27 cases of 93 DDKTs, the donor's renal artery was anastomosed end-to-end to the recipient's IIA, and in 66 cases, the EIA was connected end-to-side. To compare the short-term result between the IIA and EIA groups, the estimated glomerular filtration rate (GFR) was collected for the first 40 days after surgery, and for the long-term result, graft survival and patient survival for 15 years of the two groups were compared.
Results: Baseline characteristics showed differences in the follow-up period, age, and prevalence of diabetes mellitus (p=0.011, p<0.001, p=0.002, respectively) (Table 1). The post-operative 40-day GFR of the IIA group was higher than the EIA group in the LDKT (p=0.005). On the other hand, there was no difference in GFR between the two groups in the case of DDKT (p=0.852) (Figure 1). There were no differences between two groups in graft survival and patient survival in both LDKT (p=0.636, 0.419) and DDKT (p=0.520, 0.814) (Figure 2).
Conclusions: Our study showed no difference in graft survival and patient survival between the two groups when the DSRA was anastomosed to the recipient's IIA or EIA in LDKT and DDKT. Therefore, it is desirable to select an appropriate reconstruction method according to the anatomy of donor and recipient in KT.

Table 1

Patients' Characteristics

	Internal (n=212)	External (n=76)	p-value
Length of follow-up, years, mean (±SD)	6.1 (±4.1)	5.0 (±3.8)	0.011
Age, mean (±SD)	52.8 (±12.1)	60.1 (±10.9)	< 0.001
Sex, n (%)			0.06
Male	135 (56.5)	94 (66.2)	
Female	104 (43.5)	48 (33.8)	
BMI, kg/m², mean (±SD)	23.9 (±3.9)	24.2 (±4.2)	0.355
Pre-transplant dialysis, n (%)	152 (63.6)	98 (69)	0.282
HTN, n (%)	181 (75.7)	117 (82.4)	0.128
DM, n (%)	62 (25.9)	58 (40.8)	0.002
ABOi, n (%)	56 (48.9)	22 (15.5)	0.063



P323 SHORT-TERM HEPATITIS B IMMUNOGLOBULIN (HBIG) COMBINED WITH ENTECAVIR IN PREVENTING HBV RECURRENCE IN LIVER TRANSPLANTATION

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Background: The combination of nucleoside analogs (NAs) and long-term hepatitis B immunoglobulin (HBIG) is considered to be the standard regimen for preventing hepatitis B virus (HBV) recurrence following liver transplantation (LT). However, the long-term usage of HBIG causes many side effects. The aim of this study was to evaluate the effect of NAs entecavir combined with short-term HBIG in preventing HBV recurrence following LT.
Methods: This retrospective study assessed the effect a combination of entecavir and short-term HBIG in prophylaxis of HBV recurrence among 56 LT recipients who had undergone the procedure due to HBV-associated liver disease at our center between December 2017 and December 2021. All patients received entecavir treatment combined with HBIG for the prevention of hepatitis B recurrence, and HBIG treatment was withdrawn within one month. The patients were followed up to determine levels of HBsAg, HBsAb, HBV-DNA and the recurrence rate of HBV.
Results: Only one patient appeared positive for HBsAg at 2 months post-LT. The overall HBV recurrence rate was 1.8%. The HBsAb titers of all patients gradually decreased over time, with a median of 376.6 IU/L at 1-month post-LT and a median of 13.47 IU/L at 12 months post-LT. During the follow-up period, the HBsAb titer of the preoperative HBV-DNA positive patients remained at a lower level than that of HBV-DNA negative patients.
Conclusions: Entecavir combined with short-term HBIG can exert a good effect for the prevention of HBV reinfection post-LT.

P324 ASSESSMENT OF COGNITIVE IMPAIRMENT IN KIDNEY TRANSPLANTATION AND ITS RELATED RISK FACTORS

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Background: Association of cognitive impairment with chronic kidney disease especially in Enstage-renal-Disease has been reported over the last decade. Data about cognitive function in transplanted patients is rare. Individuals after kidney transplantation are more likely to be affected by cognitive impairment than age-matched comparison groups. The goal of our study is to examine the extent of cognitive impairment after kidney transplantation and to derive a distinct profile of cognitive function using standard neurocognitive tests, as this is important for developing management strategies.
Methods: Participants completed standardized neurocognitive assessment and were then classified as having no, mild, moderate or severe cognitive impairment based on an established algorithm. For statistical analyses, we compared two groups (no vs. any impairment) using χ^2-tests for dichotomous variables, and unpaired (between groups) as well as paired (between domains) t-tests for continuous variables.
Results: 59 patients (43 men, 16 women, mean age 55±13 yrs) took part in the study. 26 (44%) of the patients had no, 9 (15%) a mild, 15 (25%) a moderate and 9 (15%) a severe cognitive impairment. There was no difference between groups in duration on dialysis before transplantation ($t(57) = -0.82$, $p = .208$) or in time since transplantation ($t(57) = -1.04$, $p = .150$). The group with cognitive impairment performed significantly worse in the cognitive flexibility domain than in the other domains (comparison with verbal memory t(32) = 2.93, p = .015; with attention t(32) = 3.69, p <.010).
Conclusion: The prevalence of cognitive impairment is common in non-demented patients after kidney transplantation and appears to be intermediate between dialysis patients and the normal population. The duration of dialysis before transplantation has no influence on cognitive performance.Creating a neurocognitive profile is helpful and important, as the therapy for the treatment of cognitive impairment is based on the cause of the disease, based on the reduction of vascular risk factors (consistent antihypertensive therapy, optimal adjustment of any existing diabetes, etc.) and seems to be of crucial importance and priority.

P326 BELATACEPT IN RENAL TRANSPLANTATION: A REAL-WORLD PHARMACOKINETIC STUDY

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Background: Belatacept, a CTLA4-Ig, inhibits T-cell activation by blocking the CD28-CD80/86 costimulatory pathway. It is increasinglyused following a switch from calcineurin inhibitor (CNI)-to a belatacept-based regimen, especially in the context of overt CNI toxicity. Therapeutic drug monitoring usually guides the benefit-risk assessment of long-term immunosuppression. However, belatacept concentration is not available in clinical routine, and extensive real-world pharmacokinetic data are lacking. We aimed to provide data about the inter-variability and intra-variability of belatacept concentrations in kidney transplant recipients (KTR), after conversion from a CNI- to a belatacept-based regimen.
Methods: All KTR with a signed consent, who were given maintenance belatacept doses at the outpatient transplant clinic of Necker Hospital (Paris, France), between March and June 2022, were enrolled. Plasma belatacept concentrations were measured by a quantitative liquid chromatography tandem mass spectrometry method (MabXmise kit, Promise Proteomics, France).
Results: A total of 252 trough concentrations of belatacept, from 108 KTR (45% women, 25-85 years old) were measured. They all displayed a stable graft function, and received belatacept as maintenance regimen (5mg/kg every 4 weeks) for at least 3 months, in order to assess steady-state belatacept concentrations. Notably, belatacept trough concentrations greatly varied from 1.4 to 24.8 µg/L, with a mean (±SD) concentration of 8.4±3.9 µg/L. The mean inter-individual variability was 46%. Belatacept concentrations were assessed at 3 consecutive time points in 37 KTR. The mean intra-patient variability was only 17%.
Conclusions: Despite standardized dosing, based on bodyweight, our study unveiled a high variability of belatacept exposure between patients under maintenance regimen. This finding strongly supports the use of belatacept moni-

toring to evaluate in an individualized manner the immunosuppressive burden of patients and the low intra-patient variability further reinforce the validity of the measurement. Further studies are needed to evaluate whether belatacept therapeutic drug monitoring, as assessed in a broad population, would correlate with clinical events, such as rates of infections, malignancies, or rejections.

P329 X-RAY ANALYSIS OF DONOR LUNGS IN EX-VIVO LUNG PERFUSION SYSTEM (EVLP). A PILOT STUDY WITH ASSESSMENT OF THE BRIXIA SCORE TO PREDICT TRANSPLANTABILITY

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Background: Ex-vivo lung perfusion (EVLP) is a safe and effective technique for lung evaluation and reconditioning of marginal donor lungs (DLs). The assessment of the DLs during EVLP is crucial for the transplantability decision making. There is a limited number of studies regarding the radiographic analysis of DLs within EVLP. Furthermore, there are only few X-Ray grading scores available. The Brixia score is a proven radiological score for the severity grading of lung abnormalities with confirmed predictive power of the clinical outcome that was successfully used in pneumonia patients during the Covid19 pandemic. It was the aim of our study to evaluate the X-Ray findings of DLs within EVLP and investigate the prognostic potential of this score regarding transplantability and clinical outcome.
Methods: This is a retrospective observational pilot study. Between 2016 and 2022, n=30 LuTx with EVLP DLs were performed. X-Rays with the best radiographic quality and exposure of the last eleven consecutive EVLP-DLs were chosen and blindly evaluated regarding the severity of interstitial and alveolar infiltrates. The Brixia score was assessed. Furthermore, the clinical outcome (transplantability, severe primary graft dysfunction PGD, survival, ICU and hospital stay) and EVLP parameters (delta pO_2) of these were analyzed and compared to the Brixia score for each case.
Results: A range of Brixia score values from 4 to 18 was determined. Eight DLs were transplanted (mean delta pO_2 394 mmHg, mean Brixia score 6,5) while three were rejected (mean delta pO_2 213 mmHg, mean Brixia score 6). The two EVLP–DLs cases with the higher Brixia score were transplanted after EVLP. Postoperative PGD Grade 3 at 72 hours was recorded in one case without correlation to the Brixia score (Brixia score 4). Interestingly, the case with the highest Brixia score had the highest pCO_2 value as well, and was transplanted with good clinical outcome. All patients survived to hospital discharge with a mean ICU and hospital stay of 9 and 30 days respectively.
Conclusions: In this pilot study the Brixia score did not predict transplantability or postoperative outcome during EVLP. Additional studies are needed to further evaluate the use and clinical prognostic power of radiologic assessment with this promising score in the EVLP lung assessment.

P330 CAUSES FOR DISCARDING THE LIVING KIDNEY DONOR CANDIDATE: REVIEW OF THE LAST 20 YEARS AND 837 CANDIDATES

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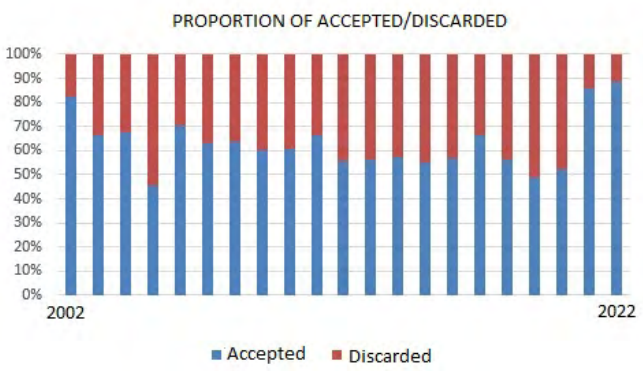
Background: Living donor kidney transplantation is the best therapeutic option for end stage chronic kidney disease. The assessment of the potential donor is exhaustive and a significant percentage of the initial studies will not progress to kidney donation. We aim to assess the characteristics of these donor candidates and the reasons for rejection of these kidney donors.
Methods: retrospective study and analysis of all patients evaluated for kidney donation at Fundació Puigvert during the last 20 years.
Results: a protocolized study for donation has been initiated in 837 candidates, 509 nephrectomies have been performed and 328 candidates have been rejected. The discard proportion has remained stable during these years (39.2% discards) (Table 1). The age of those dismissed is 54.7 ± 10.9 years, 37.2% are men. The age of potential donors, both accepted and discarded, has increased among years. In those discarded, the donor-recipient relationship is: spouse (36.5%) > siblings (30.7%) > parent-son/daughter (22.3%) > others (18.6%). The main reasons for dismissal are change of opinion of the donor (23%), kidney pathology of the donor such as lithiasis or renal mass (17%), medical pathology of the donor (12.7%), cadaver transplant (9%) and vascular complexity of the donor (9%). The complementary diagnostic test that determines the highest proportion of dismissals is abdominal computer tomography.
Conclusions: - The percentage of discarded donors remains stable among years, although their age of living donor candidate is ingreasing. - The percentage of discarded donors is not different based on age or gender or donor-recipient relationship. - The main reason for rejection is the donor's decision. The experience in the evaluation of these donors will possibly avoid unnecessary studies in this group.

Table 1:



P331 COMPARING PHYSICAL FUNCTION AMONG PATIENTS ON DIALYSIS, KIDNEY AND KIDNEY-PANCREAS TRANSPLANT RECIPIENTS USING PROMIS SCORES

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Background: Patients treated on dialysis have impaired physical function (PF) which is associated with poor outcomes. Kidney-pancreas (KP) and kidney transplant (KT) provide better outcomes; however, many transplant recipients have low PF. PF can be assessed using the Patient Reported Outcomes Measurement Information System (PROMIS) PF item bank, administered as either computer adaptive testing (CAT) or short form. Here we aim to assess PF among patients on dialysis, KP and KT recipients.
Methods: Secondary analysis of data from our research database, which include cross-sectional convenience sample of adult patients on dialysis, KT and KP recipients. Demographic data are self-reported, clinical data are from health records. Patients completed the PROMIS-29 profile domains, which include the PF domain. Higher PF scores correspond to better PF. Scores were compared using ANOVA and linear regression adjusted for age, sex, ethnicity, comorbidity and time since starting current treatment modality.
Results: Of 785 participants (285 dialysis, 93 KP and 407 KT), 472 (60%) were male, mean(SD) age was 55(16) years. Sex distribution was similar between treatment groups; patients on dialysis were significantly older than transplant recipients (mean[SD] age 64[14] vs 52[10] vs 51[16] years for dialysis vs KP vs KT, respectively; p<0.001). Females had lower mean(SD) PF scores 42(10) vs 44(11)(p=0.01). Age was negatively correlated with PF score (r=-0.39, p<0.001). Mean(SD) PF was significantly different in all 3 groups: 37(9) vs 44(8) vs 48(10) for dialysis vs KP vs KT, respectively; p<0.001. PF in both KP and KT remained significantly better after adjusting for potential confounders (coefficients [95% confidence interval] 4.9[2.6-7.2] and 8.0[6.4-9.6] for KP vs KT, respectively, p<0.001 for both). The difference between KP vs KT was also significant in the adjusted model.
Conclusions: These results suggest that both KP and KT recipients have better physical function compared to patients on dialysis, but all groups remain below the PF of the general population. Futures studies will need to assess if systematic physical rehabilitation improves PF in these patient populations.

P332 RISK MANAGEMENT AND SAFETY OF THE PEDIATRIC TRASPLANT PATIENT: THE ROLE OF THE NURSE IN THE PREPARATION OF THE CAREGIVER

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Background: Discharge represents a critical moment for the caregiver, characterized by two types of uncertainty: lack of preparation for future experiences and lack of adequate information (M. Boughton, 2009). The literature shows that from 40% to 80% of the medical information that a patient/caregiver receives, is immediately forgotten, and nearly half of the information retained is incorrect (Farris, 2015). If we are talking about foreign patients, discharge becomes an even more difficult moment, given the linguistic and cultural barrier.The aim of our study is to respond to the caregiver's need for information, especially for the management of home drug therapy, to reduce the related risks. The ultimate goal is to develop an audiovisual application that is always available, to clarify any parental doubts regarding the dilution, preparation and administration of therapy.
Methods: The project is designed for a patient of Kazakh origin undergoing liver transplantation, with an illiterate parent. After obtaining informed consent, videos were processed with the addition of audio files recorded by a Kazakh-speaking interpreter. At the time of administration of the various therapies, in addition to the classic sound alarm that attracted the attention of the parent, an illustrative video was available on the preparation of the drug and its administration. This work was then developed in 4 different languages to allow the training of as many caregivers as possible.
Results: All the parents obtained a good level of training after a total of 10 days (7 of practical/theoretical training and 3 of re-evaluation). Thanks to the teach-back method, all doubts were clarified along the way. Thanks to this new educational method, we obtained a reduction in the caregivers' uncertainty at discharge regarding the management of the therapy and an improvement in the well-being of the caregiver himself. All this translated into a reduction in calls to the transplant coordination to resolve doubts regarding the management of home therapy (the patients included in the project never contacted the coordination for this issue) and in a drastic reduction of errors regarding drug dosages.
Conclusions: According to the results obtained during the project period, the new method of communication and caregiver training used was found to be effective.

P334 DIALYSIS VINTAGE MATTERS: THE PROFOUND IMPACT OF DIALYSIS VINTAGE ON TRANSPLANT OUTCOMES

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Background: Optimized transplantation timing constitutes a complementary, still largely unexplored strategy to reduce the impact of donor shortages. While a (too) early transplantation introduces an aspect of (transient) futility; delayed transplantation, in particular dialysis vintage associates with compromised outcomes, and thus suboptimal use of the donor pool. A negative association between dialysis vintage and outcomes was first reported by Wolfe et al in 1999, this study is followed by a number of further publication confirming or denying an association between dialysis vintage and transplant outcomes. Unfortunately, interpretation of available data is interfered by aspects such as time-related changes in outcomes, absence of preemptive control groups, a focus on specific sub groups, and/or suboptimal case mixes.
Preemptive transplants are common practice in the context of living donor transplantations. Since outcomes for living donor transplantations are minimally interfered by donor and procedural factors, we reasoned that these transplantations provide the optimal opportunity to explore a possible impact of dialysis vintage on transplant outcomes. We here report a retrospective analysis of all primary living donor transplantations performed after 2000 in The Netherlands and the UK.
Results: A history of dialysis profoundly impacted transplant utility (i.e. transplant loss by any cause) with hazard ratios of 1.59 (Netherlands) and 1.51 (UK) (both p<.0001). The benefits of preemptive transplantations were granular, with both superior short- and long-term outcomes. For example, Dutch recipients with a dialysis vintage had a >5-fold higher 90-days mortality risk, and a respectively 1.67 and 1.54-fold higher risk for long-term graft loss or death. Data for Dutch recipients of a living donor graft cohort indicated a critical tipping point at approx. 6-months of dialysis. No tipping point was observed for procedures with deceased donor grafts, nor for UK recipients of a living or deceased donor graft.
Conclusions: Dialysis vintage has profound and persistent impacts on graft and recipient survival. No indications were found for an ingenuous dialysis interval for recipients of deceased donor grafts, however Dutch data implied a 6-months dialysis holiday for recipients of a living donor graft.

P335 TREATMENT OF COMPLEX UROLITHIASIS IN ORTHOTOPIC KIDNEY TRANSPLANT BY ENDOSCOPIC COMBINED INTRARRENAL SURGERY (ECIRS)

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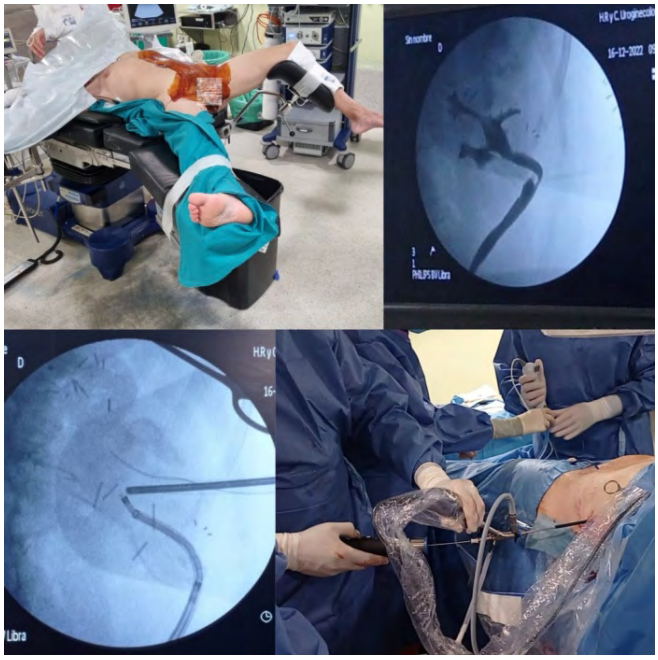
Background: Urolithiasis treatment has evolved greatly with technological advances in endoscopic material and miniaturization of percutaneous surgery instruments. However, there are still complex cases that can pose a challenge for the urologist, such as litiasis treatment in patients with an orthotopic kidney transplant or any type of urinary diversion.
Methods: We report a case of a 46 year-old male with a personal history of spina bifida and lumbosacral myelomeningocele. Tubeless cutaneous transureterostomy is performed for this reason at 6 months of age. Eventually, the patient develops chronic kidney disease secondary to chronic tubulointerstitial nephritis due to recurrent urolithiasis. Consequently, our patient received an orthotopic left kidney transplant in 2014. Pyeloureteral anastomosis to native uréter was performed. During follow-up the patient maintains a stable kidney function (baseline Creatinin 1.64 mg/dl) and in a control CT scan a staghorn litiasis is visualized, which occupies renal pelvis and superior calyx. Given the complexity of the case, endoscopic combined intrarrenal surgery isproposed (ECIRS). For that purpose, retrograde flexible ureteroscopy is performed, with partial laser fragmentation of the lithiasis. Mini percutaneous nephrolithotomy is added to complete stone fragmentation using ultrasonic and shockwave energy (ShockPulse-SE Lithotriptor®). At the end of the procedure, 18Fr nephrostomy tube and mono J catheter are placed.
Results: Immediate postoperative period went by with no incidents. Nephrostomy tuve was closed on the 3rd day after surgery (Creatinin 2.03 mg/dl), and 24h later it was removed. The patient was discharged on the 6th day after surgery. Mono J catheter is removed 16 days after surgery. At the present time, kidney function has returned to baseline values (Creatinin 1.76 mg/dl) and ultrasound scan was performed, without new litiasis or ureterhydronephrosis.
Conclusions: Endoscopic combined intrarrenal surgery is feasible, safe and useful for the treatment of complex urolithiasis. In particular cases such as orthotopic kidney transplant or cutaneous ureterostomy, surgical planning is crucial to succeed in litiasis treatment and minimize surgical risks.



P337 THE RISK FACTOR FOR DELAYED GRAFT FUNCTION IN THE DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: Delayed graft function (DGF) is a common and significant complication in deceased donor kidney transplantation (DDKT). DGF is characterized by a temporary or permanent loss of kidney function after transplantation, which is associated with increased morbidity and mortality for transplant patients. But the exact cause of DGF is not well understood. The aim of this study is to identify the risk factors associated with DGF after the DDKT.
Methods: Between June 2011 and December 2022, 88 patients underwent DDKT at department of surgery at Konyang university hospital, Daejeon, Korea. We compared two groups according to delayed graft: no delayed graft function group (n=75), delayed function group (n=13). The following characteristics were evaluated retrospectively through the medical records.
Results: The 5-year patient survival in the DGF group was 69.2% compared to 94.1% of the no DGF group (P <0.001). The 5-year graft survival were 76.9% and 97.1% in the DGF group and no DGF group (P = 0.005) retrospectively. The eGFR level by period of recipients was significantly more increased in no DGF group (1week: 61.4±25.5 ml/min vs. 22.0±12.2 ml/min, P<0.001, 12th months; 73.0±22.2 ml/min vs. 47.8±14.5 ml/min, P=0.001) but the eGFR level of recipients at 60th months was not significantly different in both groups (79.8±21.5 ml/min vs. 79.7±13.6 ml/min, P=0.989). Also, we found that significant independent risk factors associated with DGF after DDKT were extended criteria donor (OR = 6.002, 1.586-22.722 95%CI, P=0.008) and recipient BMI >25 kg/m2 (OR = 4.881, 1.249-19.074 95% CI, P=0.023) in multivariate analysis. During the follow periods, pneumonia increase in the DGF group (30.8% vs. 16.0%, P = 0.041) and AVN occurred 2 cases (15.4%) of DGF group (P = 0.020).
Conclusions: We should anticipate a high possibility of DGF after DDKT, when recipient's BMI is high or using the graft from extended criteria donor.

P339 ISCHEMIA-FREE KIDNEY TRANSPLANTATION: A PILOT STUDY

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Background: We previously performed the first case of ischemia-free kidney transplantation using normothermic machine perfusion in 2018. Here we report the first pilot study to compare the short-term outcome between ischemia-free kidney transplantation and the traditional kidney transplantation.
Methods: We have performed 9 cases of ischemia-free kidney transplantation since 2018. For each pair of donor kidneys, the right kidney was used in ischemia-free kidney transplantation by normothermic machine perfusion, the left kidney was used in traditional kidney transplantation by cold storage. The clinical data of donors and recipients were collected, and the recipients were followed up for at least 1 year. The incidences of delayed graft function (DGF), recovered time of DGF, acute rejection, bleeding, infection, the 1-month serum creatinine levels and the biomarkers of kidney injury after reperfusion of kidneys were compared between these two groups.
Results: 3 patients (33.3%) had DGF in ischemia-free group compared to 4 patients(44.4%) in traditional group(p=0.628). Recovered time of DGF was significantly shorter in ischemia-free group compared to traditional group (10.22±2.44 vs. 16.11±4.11 days, p=0.002). 1-month serum creatinine level was significantly lower in ischemia-free group(109.78±13.69 vs. 148.89±26.23, p=0.002). The serum levels of kidney injury biomarkers(KIM-1 and NGAL) after reperfusion were also significantly reduced in ischemia-free group(p<0.01). The incidences of acute rejection, bleeding and infection were similar between the two groups. There were no graft loss and patient death during the follow up period.
Conclusions: The ischemia-free kidney transplantation may reduce the recovered time of DGF, and improve short-term graft function compared to traditional kidney transplantation.

P340 HLA INCOMPATIBILITY AND PANEL REACTIVE ANTIBODIES PRIOR TO RENAL TRANSPLANTATION CAN ADVERSELY AFFECT RENAL FUNCTION OUTCOME AND IMMUNE PROFILE

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Background: The presence of Panel Reactive Antibodies (PRA) prior to renal transplantation (RT) and HLA incompatibility influence graft function and may cause immune profile alterations. The aim of this study was to estimate the effect of HLA class I and II incompatibility and the presence of PRA on lymphocyte changes and renal function outcome during the first year post-transplant.
Methods: One hundred six Renal Transplant Recipients (RTRs) were typed for HLA class I and II and assessed for PRA presence just before RT, subsequently followed for 12months. Lymphocytes, CD4, CD8, CD4+CD28null, CD8CD-28null, CD3-CD16+CD56+ (NK) and CD4+CD25+FoXP3+ (Tregs) were estimated with Flow cytometry on peripheral blood samples collected just before RT and at 3, 6, 12 months post transplantation (T0, T3, T6, T12, respectively).
Results: RTRs with at least 2/4 common HLA class II antigens (either DR or DQ), N=80/106 (75.4%), were younger at RT, 38.9±14 vs. 47.4±14yrs, p=0.04. At time point T12, they had increased lymphocytes 2200(1012) vs. 1600(563) p=0.001, CD4 897(697) vs. 595(465) p=0.008, CD8 cells 629(397) vs. 471(247) cells/μL, p=0.04, and Tregs 24(21) vs. 17(17), p=0.05. No difference was noticed regarding HLA class I incompatibility or other T cell subpopulations. RTRs with PRA(-), N=83/106 (78.3%), with no clinical differences compared to PRA(+) at time of RT, had increased lymphocytes 1700(1043) vs. 1200(800) p=0.006, CD4 788(615) vs. 507(242), p-0.002, and Tregs 27.6(31) vs. 21.3(9.9), p-0.05 at T6. Interactive effect of HLA class II and PRA with patients age was excluded by performing type III ANOVA. No difference on renal function based on eGFR was recorded during follow-up between patients groups, either based on HLA incompatibility, or presence of PRA, at any time point.
Conclusions: MHC class II incompatibility and presence of PRA seem to affect RTRs T cells subpopulations independently, at different time points, with no interaction with age. No influence was noticed to graft function during 12mo follow-up.

P341 EDTCO CONGRESS. ORGAN DONOR COORDINATORS' LEADERSHIP IN ORGAN DONATION AND TRANSPLANTATION PRACTICE AND POLICY

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Background: Increasing demand for transplantations has motivated many countries worldwide to move their organ donation policies towards opt-out consent systems. Organ donor coordinators' role involves a series of challenges related to leading practice and policy implementation within health institutions. Despite their paramount role, limited studies have explored how coordinators engage professionals and families towards a culture of donation in the Global South.
Methods: Constructivist grounded theory study. Six months of observations across two hospitals in Chile, documents (n=80), interviews (n=27), and focus groups (n=14) from 71 participants, including healthcare professionals (n=51) and families (n=20) were collected and analysed following Charmaz's constructivist grounded theory (Charmaz, 2014).
Results: Organ donor coordinators lead the organ donation process within health institutions using edgework emotion management strategies. Organ donation remains conflictive among professionals and families due to the sociological and philosophical implications of death and loss in this context. As a result, managing others' emotions might facilitate changing culture toward organ donation and end-of-life care, alluding to emotional commitment, engagement and a sense of purpose, balancing ethical values.
Conclusion: The essential role of coordinators leading organ donation practice and policy is not new. However, the findings provide evidence of how organ donation culture can be promoted and fostered within healthcare institutions in the Global South and worldwide. The study informs clinicians, educators, and policymakers and suggests strategies to support organ donation teams better, acknowledging cultural diversity.

P343 N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE LEVEL AS A PREDICTOR OF ADVERSE RENAL AND CARDIOVASCULAR OUTCOMES IN STABLE RENAL TRANSPLANT RECIPIENTS

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Background: Cardiovascular (CV) morbidity and mortality are highly prevalent in renal transplant recipients (RTRs). Assessments of CV status using N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentrations could help to identify patients at risk for death or CV events and as a predictor for deterioration of graft function. The aim of the study was to investigate the biomarker NT-proBNP for the prediction of adverse renal and cardiovascular outcomes in stable RTRs.
Methods: 305 stable RTRs with a median age of 53 years, (60.6% male) transplanted between 1994 and 2018, were enrolled in the study. At baseline, troponin, NT-proBNP, carotid-femoral pulse wave velocity (cfPWV) and pulse pressure (PP) were measured. NT-proBNP was measured during a routine baseline visit in stable RTR without cardiac symptoms and heart failure (HF) exacerbation. The median NT-proBNP concentration (292ng/l) was used as cut-off. Patients were divided into two groups (high (≥292ng/l) and low (<292ng/l) NT-pro BNP) and followed for 54 months. During this time CV events (stroke, myocardial infarction, peripheral artery thrombosis), death, graft loss and deterioration of renal graft function (increase creatinine ≥30% or proteinuria (urine protein creatinine ratio (UPCR) increase ≥500mg/g)) were monitored.
Results: At baseline, significant differences were observed between groups in terms of creatinine, eGFR, NT-pro BNP, UPCR, PP, and PWV. In the group with baseline NT-pro BNP ≥292ng/l, more patients had coronary artery disease/peripheral obliterans artery disease (CAD/POAD) and HF. Baseline NT-pro BNP correlated only weakly with age (R=0.41), cfPWV (R=0.31) and eGFR (R=-0.52). During follow-up, patients with high NT-proBNP experienced more frequently an increase creatinine ≥30% (28.7% vs 15.8%), doubling creatinine (11.1% vs 2.6%) and an increase of UPCR (22.2% vs 8.5%). Furthermore, high NT-proBNP at baseline was associated with graft loss (16.3% vs 0.6%), death (11.7% vs 0.6%) and CV events (7.2% vs 3.9%) during follow-up.
Conclusion: Age, arterial stiffness and eGFR only have a weak impact on NT-proBNP in stable RTR Higher NT-proBNP is associated with poor outcomes and might be useful not only for the identification of patients with high-risk CV events but also for the prediction of deterioration of allograft function.

P345 MINIMALLY INVASIVE INGUINAL APPROACH IN KIDNEY TRANSPLANT SURGERY BRINGS EXCELLENT OUTCOMES

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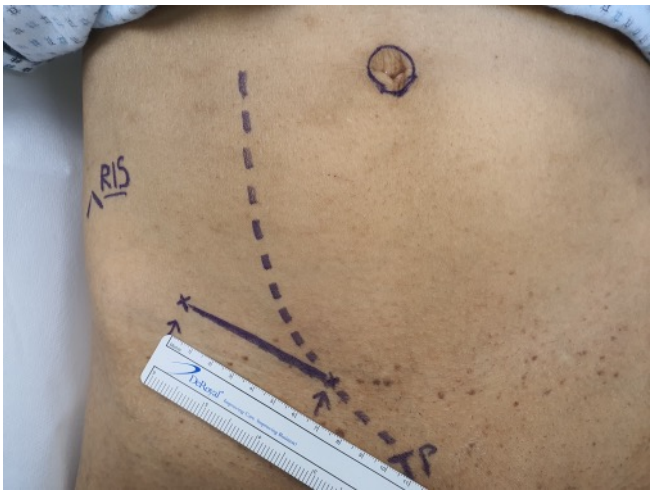
Background: Minimally invasive surgery (MIS) has been in use in Solid Organ Transplantation for the last three decades. However, in kidney transplantation, this approach is generally favoured for the donor surgery rather than for the recipient's. Our centre used a novel MIS approach, mini-inguinal access kidney transplant (MIAKT) technique that additionally spared vessels and nerves of the abdominal wall during transplantation in 50 kidney transplants.
Methods: Between November 2020 and May 2022, a consecutive series of 50 patients underwent MIAKT performed by a single senior surgeon. The surgical procedure (see figure) involves an incision of the cutaneous and subcutaneous layer, restricted to 6 to 8 cm, between the anterior superior iliac spine and the pubic tubercle. Instead the muscles receive an 8 cm J shape para-rectal dissection from the pubic tubercle. The dissection to create a retroperitoneal pouch is also minimal. The kidney that has been submitted to a meticulous back table preparation is then suspended ex-situ during the vascular anastomosis time, and can be concurrently cooled to reduce the warm ischaemia, whereas the Lich-Gregoir technique is used for the uretheral anastomosis
Results: The mean (+/- SD) age of the recipients was 52 +/- 6 years (range 21-71), the body mass index was 24 +/-0,2 (range 17-28), the procedural time was 136 +/- 18 minutes (range 98-170 minutes), anastomoses time of 40 +/-4 minutes (range, 24-43 minutes), skin incision (+/- SD) of 7,5 +/- 0,7 cm (range 6-8 cm). Despite one patient experiencing an occult ureteral dehiscence requiring surgical revision, no infection or hernia at incision site were observed. Furthermore, no vascular complications occurred during follow-up period of 9 months.
Conclusions: The mini-inguinal incision results in minor tissue trauma that does not add to possible delayed wound healing induced by peri and post-transplant immunosuppression protocols. Kidney transplant recipients deserve the best surgical approach to guarantee best outcomes not just in terms of graft function but also health-related quality of life.



P346 A NOVEL APPROACH USING BACTERIOPHAGE FOR MULTI-DRUG RESISTANT BURKHOLDERIA GLADIOLI IN A POST-LUNG TRANSPLANT PATIENT

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Background: We present a case of a 27-year-old immunosuppressed male colonised with multi drug resistant *Burkholderia Gladioli* with sternal osteomyelitis, infected superior vena cava thrombus and recurrent bacteraemia post bilateral sequential lung transplantation. Traditional antimicrobial therapy including regular surgical debridement over a year failed. Emergency compassionate access was sought for bacteriophage usage which successfully eradicated the organism.
Methods: This patient underwent bilateral sequential lung transplantation for cystic fibrosis in June 2017 and was known to be colonised by *Burkholderia Gladioli*. Subsequently he developed necrosis and osteomyelitis of the lower sternum, isolating *Burkholderia Gladioli* with limited antibiotic sensitivities. Despite extended admissions for intravenous (IV) antibiotics (meropenem/tigecycline/tobramycin), numerous surgical debridement with involvement of specialists from Plastics/Reconstructive surgery and use of extracorporeal photopheresis (as a pharmacological immunosuppression sparing agent) the patient continued to deteriorate with life-limiting infectious disease and prognosis was extremely poor. Emergency compassionate access was sought for use of bacteriophage in November 2018. After counselling, bacteriophage KS14 specific to the specific organism was given daily IV and topically with dressing changes.
Results: Following bacteriophage therapy, time spent in hospital greatly reduced (fig 1). By one month, patient was testing negative on sternal swabs. By six months all therapy was stopped, with no further organism growth. Lung function was 4.8L (111% predicted value), with preserved liver and renal function, and sternal wound fully healed (fig 2). Bacteriophage also significantly reduced resource burden. Antibiotics during September 2017 – November 2108 is estimated at £400,969; ward admissions estimated at £178,704 not accounting for surgical procedures, dressings, or imaging.
Conclusions: This highlights the potential use of bacteriophage therapy in multi-drug resistant organisms where conventional therapy has failed. The patient's trajectory reversed from life-limiting to being fully active, in employment and exercising regularly; as well demonstrating the cost-effective implications.

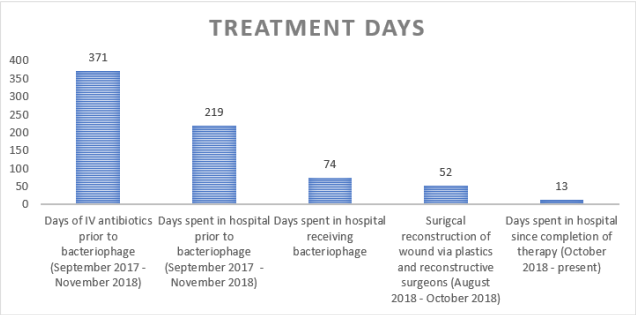

Fig 1: Days spent receiving IV antibiotic therapy and days spent in hospital prior to bacteriophage therapy September 2017 – November 2018, compared to days in hospital following successful bacteriophage treatment

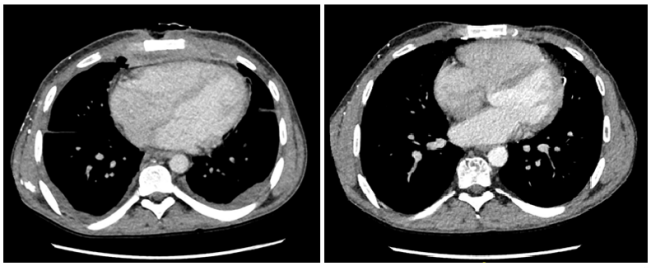

Fig 2: Cross sectional CT imaging chest. (L) revealing soft tissue thickening and retrosternal collection along the lower half of the body of the sternum despite 10 months treatment (August 2018). (R) revealing complete resolution of soft tissue thickening and retrosternal collection following bacteriophage therapy (August 2019).

P347 A FEASIBILITY STUDY EXPLORING THE IMPACT OF A LOW ADVANCED GLYCATION END-PRODUCT DIET ON SKIN AUTOFLUORESCENCE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Advanced glycation end-products (AGEs) are uremic toxins that result from hyperglycaemia and oxidative stress. AGEs are also formed in food, especially during cooking using dry-heat methods. AGE accumulation can be measured by skin autofluorescence (SAF) and increased SAF is a strong predictor of death and graft loss in kidney transplant recipients (KTR). The aim of this feasibility study was to investigate whether a low-AGE diet leads to a reduction in SAF levels in KTR.
Methods: Thirty-eight KTR were randomly allocated to a usual diet (control group, n=19) or a low-AGE diet (intervention group, n=19) and then followed-up for 6 months. The goal was to reduce dietary AGE intake to <8000 kilounits/day (kU/day). SAF was measured at baseline, 3 and 6 months. Rate of change in SAF (i.e., SAF trend) was calculated using the SLOPE function in Microsoft Excel. Dietary AGE intake, biochemistry and nutritional assessments were performed at baseline and 6 months.
Results: There were no significant differences between the intervention and control groups at baseline in SAF, dietary AGE intake, estimated glomerular filtration rate (eGFR), demographics, and clinical, biochemical and nutritional characteristics. Baseline SAF was negatively associated with eGFR (r= -0.387; p=0.02), energy intake (r= -0.464; p=0.003) and fat intake (r= -0.438; p=0.006). Seventeen participants in the control group and 13 participants in the intervention group completed 6 months of follow-up (Figure 1). Adherence to the low-AGE diet was moderate (69%). Dietary AGE intake decreased significantly in the intervention group but remained high in the control group. Body weight, energy, and fat intake decreased in the intervention group but there was no significant change in SAF (Table 1). The mean SAF trend observed was a decrease of 0.45±1.19 and 0.22±0.75 AU/year in the intervention and control groups, respectively (p=0.7 for comparison between groups).
Conclusions: In this feasibility study, we observed a high drop-out rate in the intervention group, which may explain our finding that reduction in dietary AGE intake did not seem to have any significant effect in decreasing SAF levels. This highlights the need for a larger trial to determine the effect of dietary AGE restriction on SAF levels in KTR.

P348 MANAGING THE DEFECT IN THE RIGHT RENAL VEIN IN DECEASED DONOR ORGAN PROCUREMENT: A SINGLE CENTRE EXPERIENCE

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Background: Vascular complications, including loss of the graft in renal transplantation are frequently due to surgical difficulties related to the venous area when procuring the right kidney. In addition, a shorter right renal vein (RRV) may be a contributory factor. An approach to avoid these complications is employing a surgical technique first used in our centre to compensate the possible procurement RRV injury and related loss of venous tissue.
Methods: Ten right kidneys macroscopically viable for the transplant bench, had an iatrogenic lesion of the renal and caval vein complex (RCVC) due to excessive transection of the inferior vena cava which resulted during liver procurement. RRV extension by transverse closure of the transected inferior vena cava would have involved important stenosis, with a high risk of venous thrombosis. Our novel surgical technique submitted all the kidneys to a Y-shape reconstruction to extend the vein without risk of stenosis when closing the transection margins of the cava with running sutures. Prophylactic anti-coagulation regimen, low molecular weight heparin 2000 s.c daily in the first week and subsequent oral relay with acetylsalicylic acid 100 mg daily was given, to minimise intimal inflammation and risk of thrombosis.
Results: No complications were observed including, bleeding; stenosis; thrombosis. Post-transplant serial ultrasounds, serum creatinine levels and eGFR confirmed optimal function in all grafts. Notably, in all patients, no vascular complications or delayed graft function occurred using this procedure.
Conclusions: Our technique compensates the loss of venous tissue related to the RCVC injury with no adverse vascular complications. This approach allows the recovery and transplantation of damaged right kidney that potentially could have been discarded. This novel technique, is another tool in the surgeon's armamentarium to ensure excellent graft and patient outcomes in kidney transplantation.

P349 EXTENDED RELESE TACROLIMUS IN SIMULTANEUS KIDNEY PANCREAS TRANSPLANTATION (SKPT). PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

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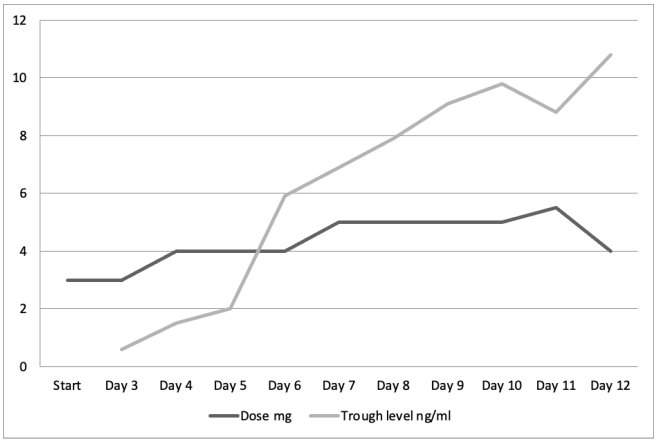
Background: Extended release tacrolimus (ER-T) is a novel formulation of drug using a MeltDose delivery technology that enables improved absorption of tacrolimus throughout the gastrointestinal tract and better bioavailability, leading to lower peak blood concentrations. ER-T is reported to have comparable efficacy and safety profiles to immediate release tacrolimus in kidney recipients and it allows more compliance to the young population.
Although ER-T is largely and safely used as immunosoppressive drug in kidney transplant recipients, few studies have been done on ER-T efficacy and safety in SKPT. Given that SKPT recipients are at risk of low early absorption of immunosuppressive drug because of surgery (intestinal anastomosis of pancreatic graft) and diabetic gastroparesis, we think that ER-T based immunosoppressive protocol could be more effettive in this group of patients.
Methods: We started to use ER-T in SKPT since January 2022 in patients with 0 panel reactive antibody (PRA). Our immunosuppressive protocol included basiliximab (20 mg in day 0 end 4), steroids, mycophenolic acid (720 mg bid from day 1) and ER-T starting on postoperative day 2 (median starting dose: 0.03 mg/Kg), aimed to reach trough level of 8-10 ng/ml.
Results: Five patients underwent SPKT (M/F: 3/2, median age 47 years) in 2022, median follow up was 6 months (range 3-11 months). All patients had uneventfully recovery with no surgical complication and neither rejection episodes. Graft function was excellent for both kidney and pancreas. Dosage in mg and trough level are summarized in tab.1. ER-T reached acceptable trough level at postoperative day 6 (median 6 ng/ml) , with low administration of drug (median dose was 4 mg qd).
Conclusions: Our preliminary study shows that ER-T associated to basiliximab, steroids and micophenolic acid can be safely used in SKPT. The low dose required to rapidly achieve trough level reflects the improved absorption provided by the MeltDose formulation even in SPKT patients.

Tab.1. Trend of ER-T dose (mg) and tacrolimus trough level (ng/ml) early post SKPT.



P350 EVALUATION OF DONOR'S QUALITY OF LIFE AFTER KIDNEY DONATION: SINGLE CENTER EXPERIENCE

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Background: Living kidney donation is considered a supreme act of altruism, especially because it has a favorable effect solely to the recipient. Therefore, it is essential to ensure kidney donors ideal pre- and post-operative conditions, as well as excellent long-term health and life quality. The purpose of our study was to evaluate the quality of life of kidney donors as well as to identify the association with potential influencing factors.
Methods: Over a pre-specified one-year time period (01/01/2022 to 31/12/2022), we recorded, in a cross-sectional study, information on demographic, laboratory and morbidity parameters in clinically stable kidney donors, attending the Outpatient Kidney Donor Clinic of our department. We also assessed the donors' quality of life through the questionnaire SF-36. The SF-36 questionnaire aims, through 36 questions, to study eight different health-related parameters,which are summarized in two general categories, that of physical (PCS) and mental health (MCS).
Results: The study population consisted of 199 stable kidney donors, who had donated at our center between 2000-2022. The majority (72%) were females, with mean age 62.8±10.3years and estimated glomerular filtration rate (eGFR) 60.6±14.1mL/min/1.73m^2.The total PCS and MCS score (52.5 & 52.73 respectively) was excellent and comparable to that of the general population (52.6 & 53.3 respectively). In addition, the analysis, performed 2.93±3.53 years after kidney donation, showed that men had significantly higher PCS and MCS scores (56.57 and 58.27 respectively) compared to women (55.03 and 53.3 respectively). Furthermore, younger age, both at the time of donation and evaluation, was correlated to a better quality of life on the physical scale (p=0.038 and p=0,07 respectively), whereas laparoscopic nephrectomy was strongly associated with increased mental health compared to open surgery (p<0.001). Last but not least, comorbidities, BMI, and donor-recipient relationship did not seem to affect donor's quality of life.
Conclusions: Overall, it seems that, postdonation, kidney donors have very good quality of life, which is mainly influenced by non-modifiable factors such as gender and age.

P351 HAEMODYNAMICS IN THE EXTERNAL ILIAC ARTERY: THE UTILITY OF CARDIOVASCULAR IMAGING FOR INVESTIGATING TRANSPLANT RENAL ARTERY STENOSIS

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Background: Magnetic resonance angiography (MRA) is a sensitive, non-invasive test for transplant renal artery stenosis (TRAS) but lacks specificity; up to 45% of TRAS cases identified by MRA have the diagnosis refuted at formal intra-arterial digital subtraction angiography. Using cardiovascular imaging (CVI) software, it is possible to assess haemodynamics in the external iliac artery (EIA) proximal (Point A) and distal (Point B) to the transplant artery anastomosis.
Methods: 787 MRAs were performed at our centre between January 2019 and February 2021. To date, 279 MRAs have been reviewed using CVI software. MRAs were excluded from the study if the software did not generate a typical arterial wave form (fig.1) or if the origin of the internal iliac artery was within the measurement points A and B on the external iliac artery. Accurate measurements were performed on 88 MRAs. 65 MRAs showed no evidence of TRAS and were analysed further. Paired sample t-tests were used to assess the relationship between measurements at point A and B.
Results: The maximum pressure gradient was greater at Point A than Point B (3.76 vs 3.25 mmHg, 95%CI -0.9 - -0.09, p=0.017). The mean pressure gradient was greater at Point A than point B (0.84 vs 0.64 mmHg, 95%CI -0.32 - -0.07, p=0.0027) (fig2). There was no difference in maximum velocity between Point A and Point B (45.94 vs 43.72 cm/s, 95%CI -15.37 – 10.94, p=0.74). Maximum flow was greater at Point B than Point A (8.70 vs 4.37 ml/s, 95%CI 2.75 - 5.92, p<0.0001).
Conclusions: This study demonstrates that, in recipients with no TRAS, there are statistically appreciable differences in haemodynamics at points proximal (A) and distal (B) to the transplant artery anastomosis on the external iliac. Determining why these differences exist, and normal parameters, may improve the specificity of MRA. Analysis of MRA-measured haemodynamics in a cohort of patients with IADSA-confirmed TRAS is underway.

Figure 1.

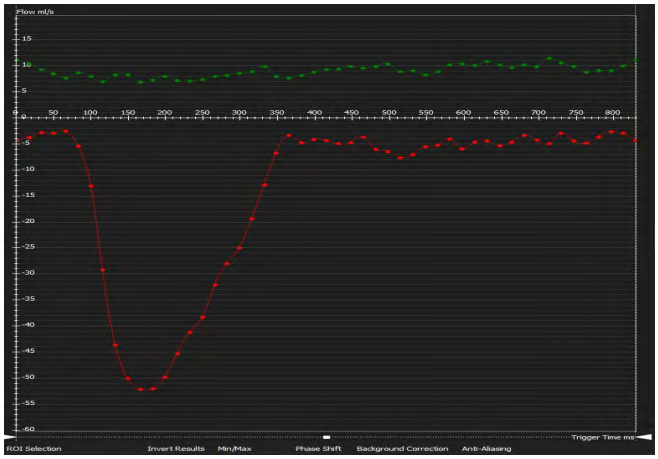
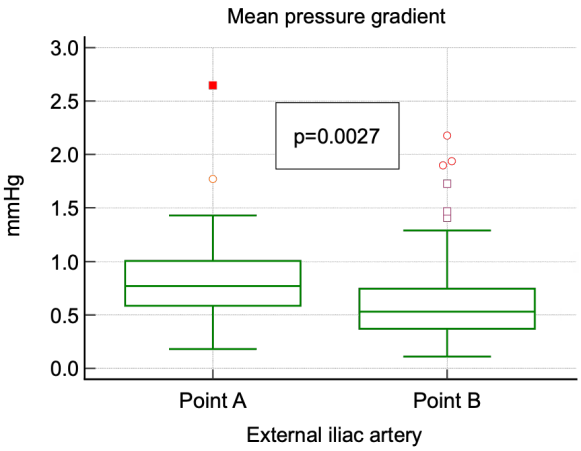


Figure 2.



P352 IMPACT OF PEG35-BASED SOLUTION ON STEATOTIC LIVER COLD PRESERVATION: INSIGHTS INTO MITOCHONDRIAL PROTECTION AND CELL SIGNALING

Arnau Panisello Rosello*[1;2], Raquel Gómez Bardallo[3], Njikem Asong Fontem[2], Teresa Carbonell Camós[3], Joan Rosello Catafau[1], René Adam[2]

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Background: The need for liver transplants has increased the use of steatotic livers, which are more susceptible to injury during preservation. PEG35 is a commonly used oncotic agent in organ preservation solutions, but its impact on liver preservation is not well understood.
Methods: To investigate this, the study aimed to evaluate the protective effects of three preservation solutions (UW, HTK, and IGL-2) on steatotic livers during hypothermic preservation. Male obese rats were used for liver preservation for 24 hours at 4°C using the solutions. IGL-2 was also compared to Belzer-MPS for hypothermic preservation with HOPE. A control group of SHAM livers was included for comparison.
Results: The results showed that after 24 hours of preservation at 4°C, ATP levels decreased significantly in the UW and HTK groups compared to the control and IGL-2 groups. The IGL-2 group had improved ATP levels and increased autophagic markers such as LC3B and beclin1. Cold preservation increased oxidative stress, measured by endoplasmic reticulum stress, lipid peroxidation, and protein oxidation, but the damage was reduced in the IGL-2 group. The IGL-2 solution, which contains higher amounts of GSH, showed significantly lower oxidative stress and better antioxidant activities compared to the other solutions. These benefits were confirmed when IGL-2 was used in HOPE with Belzer-MPS. The IGL-2 solution showed less presence of inflammasome mediators and improved energetic status, reducing oxidative stress and lipoperoxidation, and resulting in less inflammation. The data suggests that IGL-2 is a suitable solution for static and dynamic preservation techniques as a unique solution.
Conclusions: Steatotic livers are vulnerable to ischemia-reperfusion injury, and understanding the molecular mechanisms is important. Cold preservation of steatotic livers with the PEG35-based IGL-2 solution showed better results in reducing damage during static and dynamic preservation, but further research is needed.

P353 VAR-T CELLS: AN INNOVATIVE CELLULAR PLATFORM TO OPTIMIZE THE RESPONSE OF TRANSPLANTED PATIENTS ON THERAPEUTIC IMMUNOSUPPRESSION TO VACCINATION

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Background: Solid Organ transplantation is the best option for patients with vital organ failure. Because the donor is genetically distinct from the recipient, the latter need to receive immunosuppressive drugs that block T cell activation (calcineurin inhibitor, CNI) to prevent graft rejection. However, CNI that act regardless of T-cell receptor (TCR) specificity, also inhibit T cells involved in the response against pathogens and vaccines, making transplant patients extremely vulnerable to infectious complications, as illustrated during the recent SARS-CoV-2 pandemic. Elaborating on the recent success of Chimeric Antigen Receptor (CAR)-T cells, we propose an innovative approach named Vaccinal Antigen chimeric Receptor (VAR)-T cells aiming at optimizing the vaccinal responses of immunocompromised transplant recipients without increasing their risk of rejection.
Methods and Results: Lentivector have been designed to induce the expression on the surface of purified CD4+ T cells of a chimeric receptor made of the vaccinal antigen on the extracellular side and the signaling domains of CD3ε and CD28 in the intracellular side.In vitro experiments conducted with human and murine cells suggested that when contacting antigen specific B cells, VAR-T cells simultaneously deliver BCR dependent- and receive VAR dependent-signal 1 of activation. As a result, VAR-T cells upregulate the surface expression of costimulatory molecules, which represent the second mandatory signal triggering the differentiation of cognate B cells into Ab-producing plasma cells.In vivo experiments demonstrated that CD3εKO mice (devoid of T cells) transferred with OVA- or SARS-CoV-2 Spike-VAR-T cells efficiently generated detectable levels of, respectively anti-OVA or anti-Spike antibodies. Additional experiments are under way to specifically confer to VAR-T cells resistance to CNI.
Conclusions: VAR-T cells represent a promising innovative cellular platform to optimize the response of transplanted patients on therapeutic immunosuppression to vaccination.

P355 POST-TRANSPLANT THROMBOTIC MICROANGIOPATHY (PT-TMA) AFTER ABO-INCOMPATIBLE LIVING KIDNEY TRANSPLANTATION: TWO CASES WITH LOW ISOAGGLUTININ TITLES

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Background: PT-TMA is a rare condition but it was shown that ABO-incompatibility (ABOi) is a risk factor for de novo TMA after kidney transplantation (KTx).
Methods: We describe 2 cases of PT-TMA after ABOi living KTx.
Results: Case 1: a 49-years-old male, blood type A Rh+, with chronic kidney disease (CKD) secondary to a mesangial proliferative glomerulopathy without immunofluorescent study. The donor was a female, blood type B Rh+ and 7/8 HLA mismatches were present. Five days before KTx, IgM and IgG isoagglutinin were 1:4. He received a single dose of 375 mg/m2 of rituximab (RTX) and on day 0 isoagglutinins stayed ≤1:4, with normal blood count and lactate dehydrogenase (LDH). Induction was done with basiliximab, mycophenolate mofetil (MMF), tacrolimus (FK) and methylprednisolone (MP). On day 1, Hb was 7.4 g/dL, platelets 85 x 10^3/uL, LDH 313 U/L, FK levels 28,2 ng/mL. He suspended FK, but blood count and LDH get worse, with consumed haptoglobin, negative direct Coombs and schizocytes on blood smear. On day 4, he started plasma exchange (PE), goting a total of 4 PE sessions with increased in platelet count. Kidney biopsy showed intraluminal thrombi in two glomeruli and one arteriole. Eculizumab was started. On day 19, he had serum creatinine of 1.66 mg/dL, LDH 286 U/L, Hb 9.7 g/dL, platelets 127 x 10^3. Complement genetic study was negative and it was decided to continue eculizumab until 6 months. Case 2: a 57-years-old male, blood type B Rh+ with CKD secondary to atrophic left kidney. The donor was female, with blood type AB Rh+. They had 8/12 HLA mismatches. Isoagglutinin titers were 1:8 and he received a single dose of RTX. Induction was done with basiliximab, MMF, FK and MP. On day 1, Hb was 7.3 g/dL, platelets 64 x 10^3/uL, LDH 471 U/L, FK 5,5 ng/mL. He started PE (total of 7 sessions). Due to dysfunctions, we started eculizumab. After two doses, blood counts improved. His kidney graft biopsy was postponed due to thrombocytopenia. Isoagglutinin titers remained <1:2 since KTx day.
Conclusions: ABOi is a risk factor for PT-TMA. In both cases isoagglutinin titles were low and none received PE before KTx. Both received eculizumab with improved kidney function.

P356 PERFUSATE FROM NORMOTHERMIC MACHINE PERFUSED DISCARDED HUMAN DONOR KIDNEYS HAS AN ANTI-INFLAMMATORY EFFECT ON MONOCYTE-DERIVED DENDRITIC CELLS

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Background: Information about the immunological state of the kidney during machine perfusion is limited. We hypothesize that immunogenicity of the organ might be reflected by the release of damage associated molecular patterns (DAMPs) into the perfusate. Dendritic cells (DCs) are potent antigen presenting cells, and are able to sense DAMPs. We hypothesized that a DC model could be used to monitor the release of DAMPs by analysing the DC activation state.
Methods: Perfusate was obtained from the PROPER trial where discarded and transplanted human donor kidneys were perfused for 6h at 37°C. This study used perfusate from the discarded kidneys (n=15). Monocytes were isolated from buffy coats and differentiated into DCs. DCs were incubated for 24h with 4x diluted perfusate from 4 timepoints. DC supernatant was analysed by Luminex (27plex) and relevant cytokines were validated with ELISA. DCs were analysed with flow cytometry for expression of co-stimulatory markers. DCs were also cocultured with allogenic T cells.
Results: DCs showed a decrease of costimulatory marker CD86 when incubated with perfusate from 3 and 6h of normothermic machine perfusion (NMP) compared with the start of perfusion. Luminex analysis of DC supernatant showed increased levels of G-CSF, IL-8 and IL-10. However, IL-8 and G-CSF were released from the kidney and already increased in the perfusate. In contrast, IL-10 was specifically produced by DCs. DCs incubated with perfusate showed less T cell stimulatory capacity compared with non-exposed perfusion solution, as shown by reduced alloreactive CD4 and CD8 T cell proliferation and lower levels of IFN-y production. One perfusate sample induced a pro-inflammatory DC profile with high expression of CD80, CD83, CD86 and HLA-DR, along with high IL-6 levels. However, also in this case, the alloreactive T cell proliferation was still reduced.
Conclusions: The addition of perfusate obtained during prolonged NMP of discarded human donor kidneys to human monocyte-derived DCs leads to a more anti-inflammatory DC phenotype and function. The compound responsible for this anti-inflammatory profile appears strong enough to override a pro-inflammatory DC phenotype. Further studies should focus on identifying the compound(s) responsible for this anti-inflammatory DC profile.

P357 DESENSITIZATION WITH IMLIFIDASE IN CROSS-MATCH-POSITIVE, HIGHLY SENSITIZED KIDNEY TRANSPLANT RECIPIENTS: A SINGLE-CENTER EXPERIENCE

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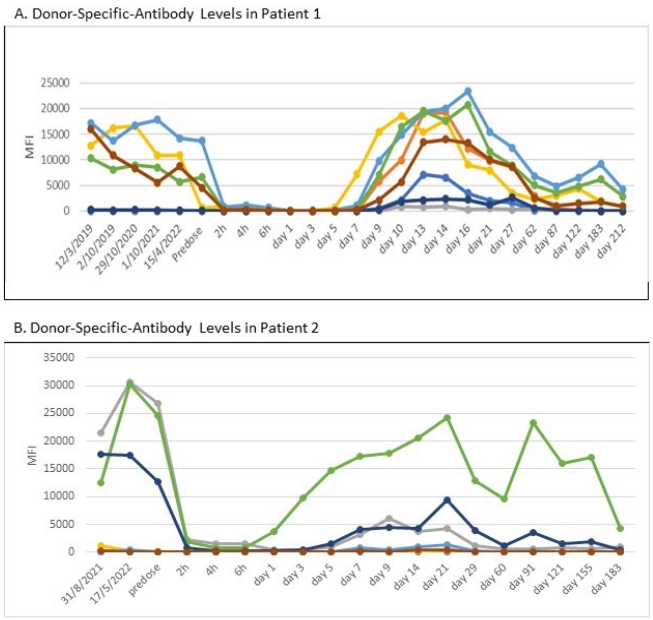
Background: HLA sensitization is a significant immunological barrier in kidney transplantation, resulting in prolonged waiting times and inferior patient survival. Imlifidase acts by eliminating all IgG subclasses, leading to a rapid conversion of a positive crossmatch (XM) to negative. Here, we report the first three cases treated with imlifidase in our centre.
Methods: Three highly sensitized patients (cPRA ≥ 97%) received priority for deceased donor kidney transplant after their HLA incompatible living donor donated a kidney to the national waiting list. Single antigen bead analysis, CDC and Flow XMs were performed pre- and post-imlifidase administration. Immunosuppression regimen included rabbit anti-thymocyte globulin, rituximab, and intravenous immunoglobulin (IVIG) in addition to mycophenolate mofetil, tacrolimus and methylprednisolone.
Results: The first patient was a 49-year-old male with preformed HLA class II donor specific antibodies (DSA) with a cumulative mean fluorescence intensity (cMFI) of 35858 and positive B-Flow XM. At 2 h post-imlifidase dose, the XM was negative. DSAs rebounded on day 9, whereas renal function continued to improve. No kidney biopsy was performed. On day 259, creatinine level was 0.93 mg/dl. The second patient was a 43-year-old female with preformed HLA class I & II DSA (cMFI: 64158) and positive CDC and T/B Flow XMs. Both XMs were negative at 2hours post-imlifidase. The patient developed antibody-mediated rejection on day 4, which was successfully treated with plasma exchange and IVIG. On day 185, creatinine level was 0.78 mg/dl. The third patient was a 24-year-old female with preformed HLA class I & II DSA (cMFI: 73377) and positive CDC and B-Flow XMs. At 2hours post-imlifidase, both XMs were negative. The patient developed hyperacute rejection and the graft was removed during surgery. Renal graft biopsy revealed intense IgM expression on glomerular and peritubular capillaries in the absence of IgG, findings suggestive of IgM-induced hyperacute rejection.
Conclusions: Imlifidase offers a rational therapeutic approach for kidney transplantation to highly sensitized patients. Besides IgG, other antibodies that are not routinely screened prior to transplantation, may have harmful effects on the renal graft.



P358 LUMINAL INTESTINAL PRESERVATION FOLLOWING BRAIN DEATH MAY REDUCE INNATE IMMUNE SYSTEM ACTIVATION

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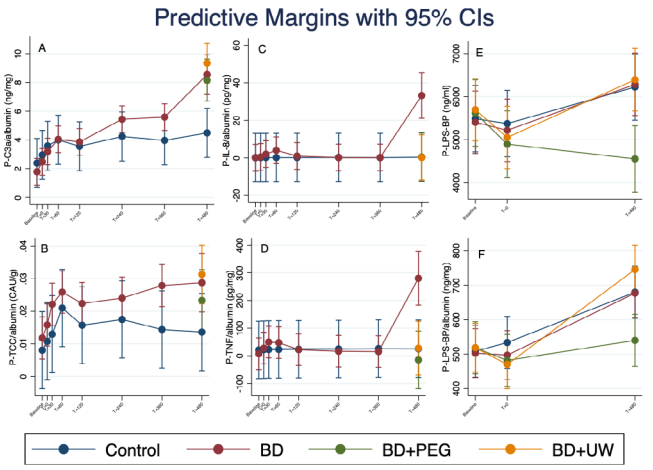
Background: Organs obtained from brain dead (BD) donors often have worse outcomes. Activation of the complement system and translocation of intestinal bacteria could be causative. We aimed to examine activation of the complement system following BD and evaluate the effect of adding luminal intestinal preservation to vascular preservation.
Methods: BD was induced in 30 pigs (four groups: control (n=7), BD alone (n=8), BD + luminal intestinal polyethylene glycol (PEG, n=7) and BD + luminal intestinal University of Wisconsin solution (UW, n=8) using a previously validated method. All animals were observed for 6 hours before organ retrieval. In the PEG and UW groups, 2000 ml of the selected solution was instilled into the duodenum during the organ procurement. Repeated measurements of C3a, Terminal Complement Complex (TCC), IL-8 and TNF were performed in plasma at baseline, BD, 30, 60, 120, 240 and 360 minutes after BD, and following the intestinal intervention (480). Plasma lipopolysaccharide binding protein (LPS-BP) was measured at baseline, BD, and 480 minutes after BD. All were normalised to albumin concentration.
Results: All animals were kept circulatory- and respiratory stable until organ procurement. At 480 minutes, C3a was significantly higher in BD, BD+PEG, and BD+UW groups compared to control group (all p<0.05) (fig. 1A). TCC was significantly higher in the combined BD group compared to control at 360 minutes, at 480 minutes, the BD and BD+UW groups. TCC was significantly higher compared to the control group (all p<0.05) (fig. 1B). IL-8 and TNF were significantly higher in the BD group compared to all other groups at 480 minutes (p=0.003 and p=0.001) (fig. 1C and D). LPS-BP increased following induction of BD in all groups except BD+PEG, which at 480 minutes were significantly lower (p=0.002) (fig. 1E and F) compared with all other groups.
Conclusions: The complement system is activated following BD independently of intestinal and luminal preservation and may lead to inflammation. Luminal intestinal preservation during organ procurement led to reduced cytokine and LPS-BP expression, which may be due to reduced bacterial translocation occurring during surgery independent of BD. Luminal PEG intervention may be combined with early innate immune system inhibition in BD donors to prevent systemic inflammation.



P359 ANASTOMOTIC BILIARY LEAKAGE AFTER HEPATICO-JEJUNOSTOMY IN PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION – INCIDENCE, MANAGEMENT AND OUTCOME

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Background: Introduction of living-donor liver transplantation (LDLT) have significantly reduced waiting list mortality. However, a higher morbidity is observed after LDLT, including an increased rate of anastomotic bile leaks (ABL). This study aimed to investigate the incidence, management and outcomes of ABL after hepaticojejunostomy creation in paediatric LDLT.
Methods: Retrospective cohort study of 331 children (<18 years of age) who underwent a primary LDLT between 2005 and 2020. Patients with duct-to-duct anastomosis were excluded from the analysis.
Results: The incidence of ABL in analysed group was 11,4% (n=33). In 3 patients additional leak on the cut surface was also recognized. All patients with ABL were treated surgically. In 28 cases existing hepaticojejunostomy was reinforced with additional sutures and in 5 cases complete reanastomosis was necessary due to major anastomotic leak. Primary surgical intervention was successful in 87,9% of patients (n=29). Remaining 4 patients required further surgical interventions with a good result. Five patients (15,1%) with ABL developed anastomotic biliary stricture afterward. Two patients with ABL required retransplantation and 1 patient died, but none of this events was related to ABL.
Conclusions: ABL is a common early complication after LDLT. Early surgical approach to ABL treatment is legitimate and effective. Such approach ensures good result with acceptable frequency of anastomotic biliary strictures.

P360 REDUCED CARDIOVASCULAR DISEASE ASSESSMENT FOR KIDNEY TRANSPLANT RECIPIENTS- A RETROSPECTIVE COHORT STUDY

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Background: Screening for asymptomatic cardiovascular (CV) disease in potential kidney transplant recipients (KTR) remains controversial. There is increasing evidence that cardiac screening prior to transplantation does not significantly improve patient outcomes. Since 2015 our centre has reduced CV screening for potential KTR, particularly removing the requirement for cardiac stress testing in asymptomatic patients. The aim was to assess the perioperative and one year post transplant CV event incidence in our KTR following this change of practice.
Methods: This was a single centre retrospective cohort study using a prospectively designed clinical database. The study included all KTR aged ≥ 18 years who had received a transplant between January 2015-December 2021. Key demographic details, perioperative/early (≤3-month post-transplantation) and one-year post-transplantation CV events were recorded. Logistic regression identified variables of statistical significance that predicted CV events.
Results: A total of 895 individuals received a kidney transplant between January 2015 and December 2021. 193 (22%) of the KTR had a diagnosis of diabetes prior to transplantation. 209 (23%) of KTR had a formal previous CV diagnosis. A total of 18 patients had a perioperative/early CV event representing 2.0% of the KTR. There was a 5.7% incidence of CV events in this cohort one year post transplantation. The results of the logistic regression analysis of multiple clinical variables exploring predictive variables and CV event one-year post-transplantation are shown in *Table 1*.
Conclusions: This study demonstrates comparable rates of CV events early and one-year post-transplantation to previous studies despite reduced cardiac screening in asymptomatic KTR. Our results add further evidence that the economic cost and delay to listing incurred by extensive cardiac screening prior to transplantation may not be offset by reduced rates of CV events.

Clinical Variable	Odds Ratio	95% CI	p value
Male Gender	0.03	-0.28-0.34	0.86
Deceased Donor Dialysis pre-transplant Diabetes Mellitus*	0.49 0.14 1.29	0.17 -0.81 -0.2-0.48 0.96-1.62	0.12 0.67 0.48
Cardiovascular Disease* Cerebrovascular Disease*	1.36 0.4	1.05-1.67 -0.15 -1.01	<0.01 0.46
Peripheral Vascular Disease*	1.51	0.96 -2.06	0.25

*Pre-transplantation diagnosis

P361 INCIDENCE OF ANTIBODIES AGAINST HUMAN NEUTROPHIL ANTIGENS-3A IN KIDNEY TRANSPLANT CANDIDATES

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Background: Human Neutrophil Antigens 3 (HNA-3a/3b) are expressed on neutrophils, lymphocytes, platelets and other tissues including kidney endothelium. Approximately 95% of Europeans are HNA-3a and 36% HNA-3b positive. Interestingly, ~5% are homozygous for HNA-3b and therefore at risk of developing HNA-3a antibodies (anti-HNA-3a). Anti-HNA-3a have been frequently associated with transfusion-related acute lung injury (TRALI) and immune neutropenias. Their role in kidney transplantation (KTx) is still not fully elucidated. In limited cases, is reported an association of anti-HNA-3a with unexplained positive T/B Flow crossmatches (T/B-FCM) in patients without HLA donor specific antibodies (HLA-DSA) as well as early rejection and poorer outcome post KTx. The aim of this study was to determine the incidence of anti-HNA-3a in patients who are waiting for KTx and to correlate them with the detection of Human Leucocyte Antigen (HLA) και Major-histocompatibility-complex (MHC) class I–related Chain–A antibodies (anti-MICA).
Methods: Anti-HNA were tested in 368 patients (107 females) registered in the kidney transplant waiting list using Luminex (Multi kit, One Lambda). We considered the normalized background values≥10 and Mean Fluorescence Intensity–MFI≥1000 as a positive result for anti-HNA-3a.
Results: Anti-HNA-3a were detected in 6 patients (5 females), 1.63% of the total cohort and 4.67% of the females, with mean MFI=7227 (1404-15420) and NBG=57,5 (13-105). Although all females had previous pregnancies, only one had anti-HLA. There was no correlation with anti-HLA or anti-MICA. Deceased donor kidneys were offered, so far, in only 2 out of 6 cases according to their ranking on the match list. In both 2 cases, although no HLA-DSA or autoantibodies were detected, the T/B-FCM were unexpectedly positive with 2 and 3 different donors respectively, resulting in graft refusal.
Conclusions: Monitoring of anti-HNA is important in order to identify patients with high risk to develop early rejection and graft loss although have no HLA-DSA, to evaluate unexplained positive T/B-FCM and to decide for patient selection for the virtual crossmatch program. The data are limited and further work is required to understand better the immunological risk associated with anti-HNA-3a and their clinical significance.

P362 THE IMPACT OF APPLYING UCSF CRITERIA TO PATIENTS UNDERWENT LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN A LOW VOLUME CENTER

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Background: There are many studies in patients with hepatocellular carcinoma applying the expanded Milan criteria. The University of California San Francisco (UCSF) criteria are considered as the most promising expansion rules so far. Based on UCSF criteria, we selected the patients underwent liver transplantation for hepatocellular carcinoma since 2008. Here we reported the long-term outcomes of patients underwent liver transplantation for hepatocellular carcinoma to assess the validity of the UCSF criteria instead of Milan in a single center.
Methods: Between 2008 and 2020, a total of 201 liver transplantation were performed, of which 39 were liver transplantation for hepatocellular carcinoma patients. Among them, living donor transplantations were 29 cases and deceased donor transplantations were 10 cases. Based on radiologic examination prior to operation, patients were prospectively categorized into 2 groups: within Milan (n = 32) and beyond Milan within UCSF (n = 7). Clinical outcomes were reviewed retrospectively.
Results: Mean age of patients was 51.2 years, and 28 patients were male. Mean MELD score was 11.2 ± 8.7. Mean follow-up period was 63.7 ± 54.6 months. The 5-year overall survival rates in 'within Milan' and 'within UCSF' groups were 84.4% and 74.7%, respectively ($p < 0.041$). The 5-year disease-free survival rates in 'within Milan' and 'within UCSF' groups were 94.7% and 76.0%, respectively ($p < 0.001$). Generally, 5-year disease-free survival rate in total patients was acceptable (n=39, 76.0%). However, 7 expanded patients from Milan were revealed very poor long term both 5-year overall survival rate and disease-free survival rate (n=7, 26.8%, 0%, respectively).
Conclusions: The Milan criteria are still optimal in seeking for long term good results in patients with hepatocellular carcinoma. When the UCSF criteria are applied to hepatocellular carcinoma patients, the overall long-term results are acceptable, however there is a higher risk of recurrence compared to the Milan criteria.

P363 A NOMOGRAM FOR PREDICTING MAJOR ADVERSE CARDIOVASCULAR EVENTS AFTER KIDNEY TRANSPLANTATION

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Background: N-terminal Pro-Brain Natriuretic Peptide (NT-proBNP) as a cardio-related biomarker indicated an increasingly valuable prognosis in renal transplant recipients (RTRs). This study aimed to develop and validate a nomogram based on preoperative data with NT-proBNP for predicting major adverse cardiovascular events (MACEs) in RTRs.
Methods: A retrospective study was conducted using data from 582 RTRs in The First Affiliated Hospital of Sun Yat-sen University from January 2015 to September 2020. The LASSO-Cox regression analyses were used to identify potential predictors. Then nomogram was developed and evaluated with respect to discrimination, calibration, and clinical usefulness and compared with previous predictive models. Finally, NT-proBNP was added to previous models for evaluation of model improvement.
Results: Overall, 58 (9.9%) patients developed MACEs during 2.8 (2.0 - 3.8) years of follow-up. Five variables including Log_2NT-proBNP (HR=1.43, 95%CI 1.25 to 1.64), Age (HR=1.05, 95%CI 1.03 to 1.08), BMI (HR=1.08, 95%CI 1.02-1.15), Diabetes (HR=3.00, 95%CI 1.67 to 5.39), Retransplant (HR=2.72, 95%CI 1.16 to 6.42) were incorporated in the nomogram. Area under the receiver operating characteristic curve was 0.864 at 6 months, 0.859 at 1 year, 0.838 at 3 years, with good consistency and clinical value showed by calibration curve and decision curve analysis respectively. The nomogram exhibited a higher predictive capacity than previous models in this cohort, and previous models were remarkably improved when adding NT-proBNP.
Conclusions: A nomogram including preoperative NT-proBNP may predict cardiovascular risks in renal transplant recipients more accurately than conventional models.

P364 THE OUTCOMES OF BK VIRUS INFECTION IN RENAL TRANSPLANT RECIPIENTS; SINGLE CENTRE EXPERIENCE

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Background: Polyomaviruses are small DNA viruses that can infect humans and animals like rabbits, rodents, and birds. In renal Tx recipients, BK virus can lead to tubulointerstitial nephritis, ureteral stenosis and hemorrhagic cystitis in bone marrow Tx. The current consensus on management of BKV viremia is to decrease immunosuppression and to regularly follow up BK viral polymerase chain reaction (PCR) along with renal functions to prevent allograft BKV nephropathy (BKVN) which increase the risk of graft failure. The challenging part in managing BKV infection is the balance between the fear of rejection, due to reduction of immunosuppression, and maintaining the same level of immunosuppression-causing more BKV viremia and consequently BKV nephropathy (BKVN. BKV is one of the most common infections in renal transplant patients. Our study aimed at evaluating the effect of BK virus reactivation poon both graft and patient survival in renal transplant recipients.
Methods: A single-center retrospective analysis of 492 patients who received their renal transplant between January 2010- October 2017.
Results: A total of 492 patients (337 males, 155 female) with a mean age of 54.1 ± 13.7. 73 years. About 14.8% of the patients had BK Viruria out of which 33 patients developed BK viremia. 10 patients were biopsy-proven BKVN and three of them had graft loss. The mean duration between transplantation and viruria was 8.92 ± 11.55 months, between viruria and viremia was 2.83 ± 3.16 months, and between viremia and development of BKVN was 3.29 ± 4.88 months. Finally, the duration between BKVN and development of graft failure as a result of BKVN was 14.49 ± 19.39 months. There was no statistically significant difference between the overall graft survival or patient survival for patients with positive BKV infection and that of negative BKV infection. No statistically significant difference in the incidence of acute rejection between both BKV infected group and the non- infected group.
Conclusions: Patients who developed BKV infection have a poorer graft function when compared to other renal transplant patients who did not. However, no significant statistical difference between both groups regarding both graft and patient survival.

Figure 1: Flowchart Description of the studied population from January 2010 to Oct 2017

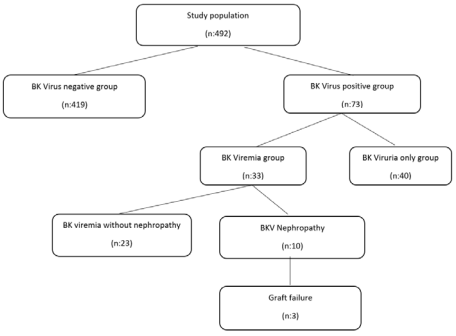

Table 1. Baseline characteristics of the renal transplant recipents

Variables	Total patients (n= 452)	BK negative (n= 419)	BK positive with viremia (n= 33)	p-value
Gender, n (%)				
Male	313 (69.2)	286 (68.3)	27 (81.8)	0.119 [a]
Female	139 (30.8)	133 (31.7)	6 (18.2)	
Age (year), mean ± SD	54.38 ± 13.74	53.91 ± 13.82	60.55 ± 11.15	**0.006** [b]
Race, n (%)				
White	407 (90)	337 (90)	30 (90.9)	0.751 [c]
Asian	8 (1.8)	8 (1.9)	0 (0)	
Pakistani	16 (3.5)	15 (3.6)	1 (3)	
Black	7 (1.5)	6 (1.4)	1 (3)	
Mixed	3 (0.7)	3 (0.7)	0 (0)	
Others*	11 (2.4)	10 (2.4)	1 (3)	
Diabetes Mellitus, n (%)	84 (18.6)	79 (18.9)	5 (15.2)	0.654 [a]
Malignancy, n (%)	30 (6.6)	22 (5.3)	8 (24.2)	**0.001** [c]
No. of renal transplantations, n (%)				
One time	384 (85)	355 (84.7)	29 (87.9)	0.831 [c]
two time	56 (12.4)	53 (12.6)	3 (9.1)	
Three times	12 (2.7)	11 (2.6)	1 (3)	
Type of Transplant, n (%)				
Deceased brain death	288 (50.4)	209 (49.9)	19 (57.6)	0.658 [a]
Deceased cardiac death	87 (19.2)	81 (19.3)	6 (18.2)	
Living Donor	137 (30.3)	129 (30.8)	8 (24.2)	
Induction Immunosuppressant, n (%)				
Basiliximab	386 (89.1)	357 (89.3)	29 (87.9)	0.543 [c]
Alemtuzumab	34 (7.9)	30 (7.5)	4 (12.1)	
Anti-thymocyte globulin (ATG)	10 (2.3)	10 (2.5)	0 (0)	
Rituximab	3 (0.7)	3 (0.8)	0 (0)	
Maintenance Immunosuppressant, n (%)				
TAC PRED MMF*	369 (81.8)	340 (81.3)	29 (87.9)	0.767 [c]
TAC PRED only	42 (9.3)	40 (9.6)	2 (6.1)	
TAC MMF only	21 (4.7)	20 (4.8)	1 (3)	
Sirolimus	7 (1.6)	6 (1.4)	1 (3)	
Azathioprine	12 (2.7)	12 (2.9)	0 (0)	
DR mismatch, n (%)	244 (54)	244 (53.5)	20 (60.6)	0.472 [a]
Acute rejection, n (%)	27 (6)	22 (5.3)	5 (15.2)	**0.038** [c]
Delay graft function, n (%)	161 (35.6)	149 (35.6)	12 (36.4)	1.000*
Graft failure, n (%)	41 (9.1)	39 (9.3)	2 (6.1)	0.756 [c]

*others: Afro Carribean, Somali and Mixed White and Asian, * TAC PRED MMF: tacrolimus, prednisolone mycophenolate mofetil based therapy.
[a] P values are based on Chi-Square test. Statistical significance at P < 0.05
[b] P values are based on Mann Whiney U test. Statistical significance at P < 0.05
[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Table 2. Comparison of eGFR at 1st, 3rd and 5th year follow up time post-transplantation between renal transplant recipients with/without BKV

Variables	Total patients (n= 452) mean ± SD	BK negative (n= 419)	BK positive with viremia (n= 33)	p-value
1-year GFR post transplantation	55.88 ± 24.61	57.12 ± 24.74	42.21 ± 18.48	**<0.001** [a]
3-year GFR post transplantation	53.20 ± 26.35	54.35 ± 26.39	39.33 ± 22.03	**0.008** [b]
5-year GFR post transplantation	50.99 ± 29.95	52.36 ± 29.74	29.64 ± 25.90	**0.014** [b]

[a] P values are based on Mann Whiney U test. Statistical significance at P < 0.05
[b] P values are based on Independent t test. Statistical significance at P < 0.05

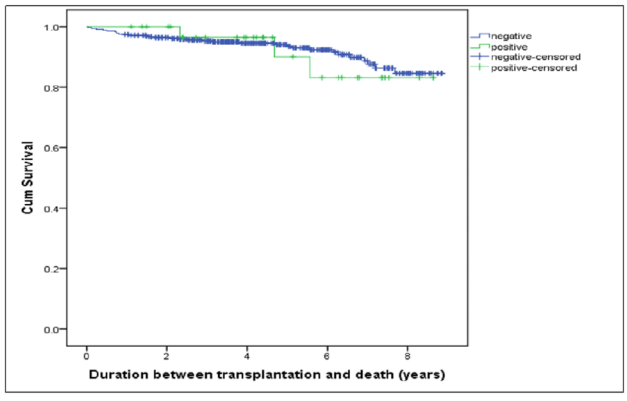

Figure 2. Kaplan Meier curve of renal transplant recipents survival according to BKV status

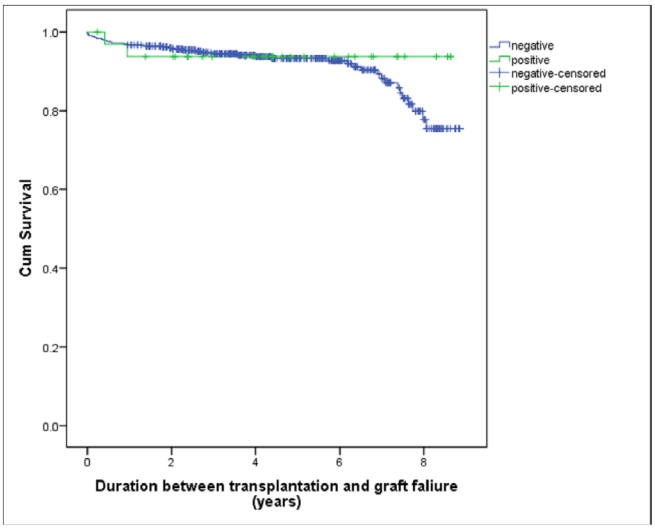

Figure 3. Kaplan Meier curve of graft survival after kidney transplantation according to BKV status

P367 COMPARISON IN ANALGESIC EFFICACY BETWEEN NEFOPAM AND ACETAMINOPHEN IN LIVING KIDNEY DONOR

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Background: Nefopam and acetaminophen are the most popular and commonly used postoperative pain relief drugs in multimodal analgesic regimen. There are different mechanisms of each drug's antinociceptive action, but no surgery-related studies are present to compare the pain relief efficacy between two drugs. Therefore, we investigated that administration of nefopam or acetaminophen, to postoperative healthy living kidney donors with parietal pain alleviated by rectus sheath block (RSB), limits the amount of subsequent opioid necessary to produce adequate analgesia.
Methods: A prospective randomized controlled trial with two parallel groups was performed from November 2021 to July 2022. A total of 72 living kidney donors undergoing laparoscopic nephrectomy were divided into two groups: the nefopam group (n = 36; 40mg IV nefopam) and the acetaminophen group (n = 36; 2g IV denogan). Ultrasound-guided RSB was performed preoperatively in all enrolled donors. The primary outcome of the study was total opioid consumption of IV-PCA during postoperative day (POD) 1. In addition, the numeric pain rating scales (NRS) of flank (visceral pain) and umbilicus (parietal pain) at rest and cough and quality of recovery-15 questionnaire (QoR15) were investigated on POD 1.
Results: There were comparable in demographic findings. Total opioid consumption of IV-PCA was higher in the acetaminophen group than in the nefopam group (70.2±29.0 mL vs. 44.5±19.3 mL; p<0.001). NRSs of flank and umbilicus at rest and cough were lower in the nefopam group than in the acetaminophen group in post-anesthesia care unit. Sub-division score related to severe pain was better in the nefopam group than in the acetaminophen group in QoR15.
Conclusions: Nefopam may provide better analgesic effect to reduce opioid requirement rather than acetaminophen in living kidney donors with pain relieved by RSB. Further randomized controlled studies are needed to determine an effective and safe dose in advanced multimodal analgesia for living donors.

P370 IMMUNOSUPRESSIVE TREATMENT AND CD4/CD8 T-CELL EXHAUSTION IMPACT SARS-COV-2-SPECIFIC ADAPTIVE RESPONSES AFTER VACCINATION IN SOLID ORGAN TRANSPLANT

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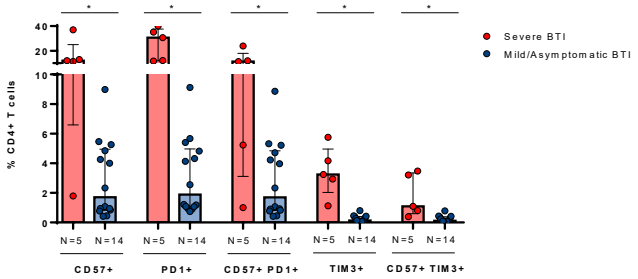
Background: Due to their immunocompromised status, lower immune responses to SARS-CoV-2 mRNA vaccination have been observed in solid organ transplant (SOT) recipients. However, scarce data is available regarding the impact of the different immunosuppressive treatments (IS). T-cell exhaustion abrogates effective proliferative and functional antigen specific immune responses. Therefore, characterizing different exhaustion T-cell phenotypes could identify patients more likely to respond to booster vaccination.
Methods: Within a large, prospective, multicentre study investigating serological and cellular memory immune responses specific to SARS-CoV-2 in 148 SOT undergoing three booster mRNA vaccination we assessed functional and phenotypic immune profiles related to distinct maintenance immunosuppressive therapies such as TAC/MMF, MMF-monotherapy, TAC monotherapy and TAC/mTORi. Antigen-specific neutralizing antibodies (NAb), memory B and Th1/Th2 cells, and exhaustion markers (PD-1, TIM3 and CD57) in CD4 and CD8 T-cells were assessed in 700 biological samples at 5 different time points.
Results: After three doses of SARS-CoV-2 mRNA vaccine, 32.3% of SOT did not achieve a successful neutralizing antibody response. 12.5% (2/16) TAC/mTORi patients did not achieve NAb versus 40% (24/78) and 50% (4/8) of patients in TAC/MMF and MMF (p=0.038 and p=0.023, respectively). Similarly, all functional T and B memory immune responses were significantly lower in patients on TAC/MMF than TAC/mTORi (p=0.015 for mBc; p=0.050 for IFN-γ T-cells). Notably, SOT patients not developing NAb after three booster vaccines exhibited a significantly more exhausted CD4+ T-cell phenotype prior to vaccination than those with NAb (p=0.001 PD1+/CD57+, p<0.001 CD57+, p=0.001 PD1+ and p=0.048 TIM3+/CD57+). Patients with an exhaustion phenotype were non-responders for T and B memory immune responses and were receiving TAC/MMF IS. Patients with severe breakthrough infection (BTI) exhibited a significantly more exhausted CD4 T-cell phenotype than those with mild/asymptomatic BTI (Figure).
Conclusions: T-cell exhaustion phenotypes seem to drive poor antiviral immune responses after SARS-Cov2 booster vaccination and favour severe BTI if infected, this feature being more likely observed among patients under TAC/MMF IS.



P371 A CASE OF ISOLATED KIDNEY TRANSPLANTATION IN A PATIENT WITH PRIMARY HYPEROXALURIA TYPE 1 RECEIVING LUMASIRAN THERAPY

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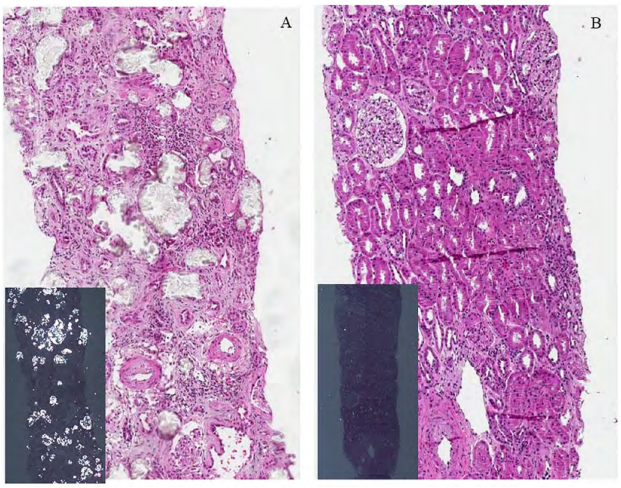
Background: Primary hyperoxaluria Type 1 (PH1) is an autosomal recessive inborn error of glyoxylate metabolism due to mutation of AGXT gene encoding for the hepatic enzyme AGT. The defect of AGT results in an excessive oxalate urinary excretion (uOx) that leads to chronic kidney disease up to ESKD. The suggested treatment of ESKD in PH1 is a combined liver-kidney transplantation. Nevertheless, an isolated kidney transplant (IKT) should be considered in PH1 due to AGXT mutation responsiveness to pyridoxine (VB6). Recently, lumasiran, an RNA-interference based-therapy, has been proven to be effective to reduce uOx and plasma oxalate (pOx) in PH1
Methods: We report the case of a 36-year-old male patient admitted in 2020 with ESKD due to oxalate crystal nephropathy, Fig. 1A. Genetic analysis showed a pathogenic variant in homozygosis c.33dupC of the AGTX gene. Four months after starting hemodialysis (HD) pOx was 190 µmol/L (n.v. 30-70 µmol/L). In March 2021 lumasiran was started and pOx dropped to 88 µmol/L with a plasma glycolate (pGly) of 367 µmol/L. Based on these positive effects of lumasiran: additional pOx reduction by half compared to pOx measured after HD and strongly elevated pGly, the patient was listed for IKT. On December 16, 2022 IKT was performed. pOx prior transplantation was 60 µmol/L. Although the immediate graft function, patient underwent daily HD until post-operative day (POD) 15 to remove the pOx rebound avoiding oxalate precipitation in the graft. pOx was 16 µmol/L when HD was stopped. Additional dose of lumasiran was administered on POD 5.
Results: At discharge sCr was 1.2 mg/dl. One month after transplantation sCr was 1.5 mg/dl. Thus, an allograft biopsy was performed. Histological analysis excluded rejection and showed negligible oxalate crystals.Fig. 1B.
Conclusions: Awaiting a long-term follow-up, our case suggest that isolated kidney transplantation may be considered in patients with ESKD due to PH1 treated with lumasiran.

Figure 1. (A) allograft kidney biopsy showed oxalate crystal nephropathy in hematoxylin-eosin stain (in inset birefringent calcium oxalated crystals under polarized light); (B) allograft kidney biopsy showed negligible oxalate crystals in hematoxylin –eosin stain (in inset the same field under polarized light).



P372 CIRCULATING IRISIN LEVELS IN KIDNEY TRANSPLANT PATIENTS

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Background: There is increasing evidence that skeletal muscle acts as a secretory organ. Irisin is a myokine, which promotes insulin sensitivity, body weight, and glucose tolerance in mice. There has been controversy regarding its role in glucose metabolism and development of diabetes in humans. Irisin serum concentrations were not previously analyzed in transplant patients and in post-transplant diabetes mellitus (PTDM).
Methods: We analysed irisin serum levels in 47 patients without diabetes (M28, F19, mean age 48.5 years) before and after kidney transplantation (KT) performed in our centre between 2020 and 2022. We present preliminary results. Blood samples were obtained before KT and at the following time points: 1, 2, 3, 4 and 5 weeks after KT. The serum was separated after centrifugation, mixed with aprotinin and stored at −80 °C pending analysis. Quantification of serum irisin was based on competitive enzyme immunoassay kits.
Results: We found an outstanding increase in ISL measured after KT reaching more than 1000 times in 44% of patients – (21/47). All measurements of irisin serum levels before KT levels were lower than 25ng/ml (median 8,4 ng/ml). The increase appeared at the first measurement (one week after KT) and remained stable for at least a month. Median values of all measurements after KT procedure in the group with increase in ISL was: 1220 ng/ml (min- max: 158-5884) and in the group without increase was: 6 ng/ml (min-max: 2-20). Factors connected to large growth were obesity, with BMI>30 (p=0,04), longer cold ischemia time (p=0,05), time spent on dialysis before KT (p=0,02) and subsequent KT - 2nd and 3rd (p=0,0006). In the group characterized by an irisin increase, glycemic disturbances requiring permanent insulin therapy occurred at a rate of 19% (4/21), while in the group without an irisin increase, 27% (7/26), difference not statistically significant. We did not find the influence of the type of calcineurin inhibitor and delayed graft function on the increase of the irisin level. The increased level of irisin was not connected to pre-transplant HbA1c, glucose, C-peptide, insulin, HOMA index and cholesterol.
Conclusions: Irisin serum levels are increased in some KT recipients. Whether the increase has an impact on reducing the risk of post-transplant diabetes requires further study.

P374 MACHINE-PERFUSION FOR LIVER TRANSPLANTATION IN HIGH VERSUS LOW/MID-VOLUME CENTRES: AN INTERNATIONAL SURVEY

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Background: Machine perfusion (MP) was developed to expand the available donor pool and improve liver transplantation (LT) outcomes. Despite optimal results in clinical trials, the real-life scenario of the MP benefit in LT center with low/mid-volume activity is still being determined.
Methods: An online 22-item survey on MP for LT outside clinical trials was distributed to worldwide LT centres representatives. Variables of interest included MP logistics, technicalities, and outcomes. Responding centres were grouped into high-volume centres (HVCs) (>55 LTs/year) and low/mid volume centres (LVCs) (≤55 LTs/year). Results from HVCs and LVCs were compared.
Results: Sixty-seven centres were included, 36 HCVs and 31 LCVs. Between HVCs and LCVs, significant differences were found regarding: I) the existence of an established MP program (80.6% vs. 41.9%;p=.02), II) the presence of a dedicated perfusionist (58.3% vs 22.6%;p=.006), III) the duration of MP (>4 hours: 47.2% vs. 16.1%;p=.01), IV) the routine MP use (20-40% vs. 5-20%;p=.002), V) the graft utilization (>50%: 75% vs. 51.6%;p=.009), VI) the 90-day patient survival rates (90-100% vs. 50-90%;p=.001) and VII) the subjectively perceived benefit of MP (always vs. only in selected ECD;p=.009). Concordance was found for indications of MP use, type of MP technology, viability tests, graft salvage rate, 90-day graft loss and major complications.
Conclusions: This study captured a picture of the real MP use in LT practice. Significant disparities have surfaced between LVCs and HVCs regarding the logistics, utilization and results of MP, including patient survival. Further studies are required to define the future role of MP worldwide.

P377 DISPARITIES IN ORGAN DONATION RATES INSIDE THE EUROPEAN REGION

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Background: World Health Organization (WHO) is advocating for the development of self-sufficiency in donation and transplantation (D&T) worldwide. European countries represent 8 from the 10 worldwide countries with highest organ donation rates. Nevertheless, many countries in the region still present low rates with great opportunities for improvement. The International Registry for Organ Donation and Transplantation (IRODAT registry) is the oldest worldwide registry for organ donation and transplantation activity, reporting information since 1996 from 106 different countries.
Methods: A retrospective analysis of the organ donation activity from the information reported from European countries between 2019 to 2022 in the IRODAT registry has been conducted. European countries have been selected according to the World Health Organization's classification. Data from the actual deceased organ donors per million population (PMP) rate, living organ donors PMP rate and actual donors after circulatory death PMP rate has been analyzed.
Results: From the 53 countries in the European region, 43 have submitted data to our registry. COVID pandemic showed a big impact in the programs' activity, with 30 countries having a decrease in their deceased donation rates during 2019 and persist until 2021. In the analysis of total deceased donation activity, 3 countries (7%) did not report deceased donation in the period studied, and only 23 countries (52%) reported more than 15 donors PMP in at least 1 of the 3-year period studied, with 20 of them maintaining this level during 2021. 34% (15) countries reported having an active Donation after Circulatory Death (DCD) program and 27% (12) of the countries reported having more living than deceased donation activity.
Conclusions: To achieve self-sufficiency in organ transplantation in the European region, more efforts should be allocated to develop efficient deceased donation programs. Despite the WHO's third guiding principle which mentions that donation from deceased persons should be developed to its maximum therapeutic potential, many European countries have living donation programs with poor or no deceased donation activity at all.

P378 MANAGEMENT OF INCISIONAL HERNIA FOLLOWING ABDOMINAL ORGAN TRANSPLANTATION

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Background: Incisional hernia (IH) remains one of the most common complications following abdominal organ transplantation with no consensus on the optimal management. This study is a narrative review on the incidence, risk factors, diagnosis, and management of IH post-transplantation.
Methods: A literature search using the EMBASE and MEDLINE from 1.1.2016 to 15.8.2002 was conducted. Included studies reported on IH after open abdominal organ transplantation. The outcomes included in our analysis were the incidence of IH, significant patient risk factors, the diagnostic approach used to detect IH, and proposed strategies for the management of IH. 33 publications that involved 9336 transplant patients who developed IH were included.
Results: The incidence of IH ranged from 1.7% to 43% in liver transplant patients and was reduced following kidney transplantation (1.1%-7.0%). Patient risk factors predisposing to IH were body mass index>30, age (>50), smoking history, previous open abdominal surgery, open surgical repair, a Mercedes or inverse T incision and surgical site infections. The most common diagnostic approach for IH is clinical examination, followed by US or CT imaging in cases of complex IH. Following IH repair, recurrence rates ranged from 0-76.9%, and complication rates from 12% - 52.9%, the most common of which were surgical site occurrences (16.0 - 79.2%) including infection (0 - 65.4%) and seroma formation (0-8%). Management of IH should include preoperative optimisation of patients through weight reduction, smoking cessation and adjustment of immunosuppression using a multidisciplinary (MDT) approach. Mesh repair, either open or laparoscopic, is the gold standard for the treatment of IH, resulting in a significantly lower recurrence rate than primary closure. There is no consensus on the type and positioning of mesh, and very limited studies have reported on other perioperative factors such as wound closure.
Conclusions: Prehabilitation and MDT approach are important in ensuring good outcomes following IH repair. Further prospective studies and the establishment of a relevant registry are required to propose a consensus pathway for IH repair in the transplanted population.

P379 TRANSPLANTATION OF UNCONTROLLED DCD KIDNEYS AFTER RECONDITIONING BY A NOVEL EX-VIVO PERFUSION METHOD - REVIVEME TRIAL

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Background: Transplantation of kidneys from patients dying from uncontrolled circulatory arrest outside hospital (uDCD) has been published from several large populations. Overall, 2087 patients show a 65,1%-76,0% frequency of DGF and a 6,8%-12,3% frequency of PNF. The high frequency of DGF, in combination with the labour-intensive and expensive methods for utilizing these donors, is the main reason why uDCD kidneys are rare among all DCD kidney transplantations in Europe. Based on animal data in pigs, we have strong reason to believe that a novel developed method significantly can reduce the frequency of delayed graft function (DGF), increase the quality of renal grafts, and increase the donor pool for successful kidney transplantation. The present study protocol describes a first-in-human trial, in which uDCD kidneys are reconditioned and preserved using this new perfusion method and then transplanted to patients on the waiting list for diseased donors.
Methods: This is a first-in-human phase 1-2a safety study in eight patients, using only one kidney from each uDCD donor in four patients, followed by both kidneys from two uDCD donors in four more patients. Patient safety data, including patient death, PNF, and any effect of drug toxicity from the drugs in the device solutions, will be studied. Kidneys from the uDCD donor will be retrieved up to 4 hours after death, followed by ex-vivo perfusion, using lys-plasminogen and tPA to remove/prevent clot formation and allow oxygenation of the kidneys.
Results: We have extensive preclinical data published in Transplantation and will use the protocol in humans. The primary objective is to perform a safety study with minimal risk for patients. Preclinical data from pigs suggests a low risk of complications. A limited number of patients will be used. Proof of Concept (PoC) will be declared if 50% or fewer patients (≤4 of 8 Pts) experience DG, and less than 13% will have primary non function (PNF) i.e., substantially lower frequency than published data, The protocol will be presented. Inclusion of patients is estimated to start August 15th 2023.
Conclusions: Kidneys from *extended* uDCD donors, allowing warm ischemia times of > 4 hours, will be transplanted to patients. The novel method has the potential to change organ allocation and abolish organ shortage, globally.

P380 PRO-INFLAMMATORY PROFILE OF ADIPOKINES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Adipokines, such as leptin and adiponectin, are adipocyte-specific secretory cytokines. They play an important role in the metabolic regulation of body weight. Alterations in leptin and adiponectin concentrations are associated with CKD-related cardiovascular problems. Data on the association between inflammatory processes and leptin and adiponectin in people after kidney transplantation are unclear. The aim of this study was to investigate the levels of adipokines and assess its relation to nutritional and inflammatory parameters in overweight/obese and normal weight kidney transplant recipients (KTRs).
Methods: The 66 KTRs in stable clinical condition were enrolled in the study (mean time after Tx was 137 ± 83 months). Assessment of nutritional status was determined by the level of s- albumin, body mass index (BMI), percentage of body fat (%F), lean body mass (LBM), Fat Tissue Index (FTI) and lean Tissue Index (LTI). Analysis of body composition was performed using the BCM (Fresenius SA). The routine laboratory parameters (creatinine, urea, potassium, lipidogram, albumin, blood whole morphology) were measured in serum. Leptin, adiponectin and hsCRP levels were measured by ELISA methods. eGFR was calculated by CKD-EPI formula. The statistical analysis was done used Statistica 13.0.
Results: Overweight and obesity were found in 65% and decreased LTI in 84 % KTRs.The most high leptin level and increased ratio leptin to adiponectin was observed in obese KTRs. Leptin positively correlated with BMI ($R= 0.9$; $p<0.05$), body fat ($R=0.8$; $p<0.05$) and with hsCRP level ($R= 0.61$; $p<0.05$). The association between graft function (eGFR CKD EPI) and leptin was observed ($R=-0.3$; $p<0.05$).
Conclusions: Obesity and its association with high level of leptin, decreased adiponectin and biochemical signs of inflammation may increase cardiovascular risk in KTRs. Results suggests need nutritional education that could prevent the consequences of adipose tissue accumulation in KTRs.

Table. Selected results (* normal vs overweight/obese KTRs p<0.05).

	Leptin ng/ml	Adiponectin pg/ml	Leptin/ Adiponectin ratio	hsCRP mg/dl
Normal weight KTRs	4.5 ± 5.9*	2.4 ± 2.2	1.8*	2.9 ± 2.9
Overweight/ Obese KTRs	17.8 ± 14.8	3.8 ± 3.3	4.6	4.9 ± 2.7

P381 PROTOCOL BIOPSY IN LIVING KIDNEY DONOR TRANSPLANTATION

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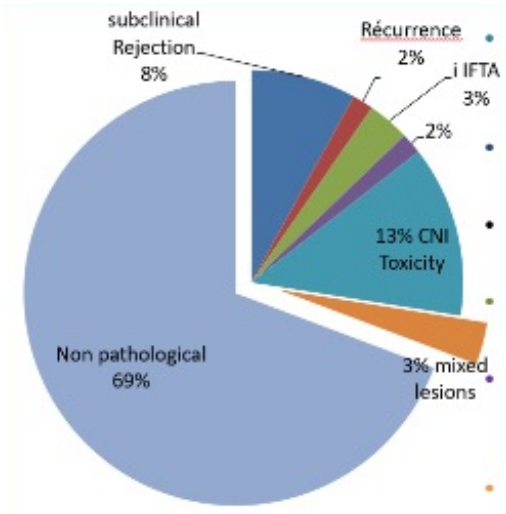
Background: The benefit of protocol biopsies is supported by the fact that histological lesions precede biological disturbances; We were the first center in our country that established protocol biopsies at 3 and 12 months. The aim of our study was to demonstrate the utility of the screening at 3 months by reporting a significant rate of pathological findings.
Methods: We conducted a descriptive, prospective study,which included patients transplanted with ABO compatible living donors who have stable creatinine and no significant proteinuria. Out of a total of 67 patients, we retained 62 pts who benefited at M3 from routine testing for DSA, graft ultrasound Doppler and biopsy, biopsies were analysed twice,locally and a second time in France or Belgium in a reference center.The Mean of serum tacrolimus during the 3M was calculated for each patient and correlated to the histological lesions. At M12 a 2nd screening was performed to evaluate the evolution of patients.
Results: The mean age was 34yo, sex ratio:1,69,The causal nephropathy was underterminated for about ¾ of patients,85% of pts had no DSA even if 54% experienced sensitizing events. ATG was used in 76 % of cases, a minimisation strategy of CNI was adopted. elementary lesions were classified according to Banff 2017, we found 13% of CNI toxicity, 8% subclinical rejection, 2 hyper metaboliser patients had mixed lesions(toxicity and rejection),1 patient recurrence of IGAN,1patient an acute pyelonephritis.We found a significant correlation between Tubular vacuolisation and higher means of tacrolimus during the 3 months, but no correlation was found between the presence of CV, Ah1, Medial Vacuolisation, IFTA and higher means of serum tacrolimus.Patients with Ah1 at M3 had a better creatinine at M12 but it wasn't statuesquely significant.At M12, we found a slight increase in inflammatory lesions, and most patients that have a slight tubular atrophy.
Conclusion: Protocol biopsy is a safe and useful procedure,perfectly stable patients can present a pathological biopsy, even if the elementary lesions are moderate and at early stages. subclinical rejection was found in our study in 8% of a moderate immunological risk population mainly treated with ATG and Tacrolimus.These results encourage us to continue our strategy.



P382 SHOULD INFECTION IN DECEASED ORGAN DONORS INHIBIT THE DECISION FOR KIDNEY TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE

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Background: THe decision to accept a deceased organ donor with infection can be a subject of controversy among physicians due to the possibility of transmitting the disease to the recipient. Here, we report the impact of the infections of deceased donors to 87 recipients in our centre.
Methods: We retrospectively collected data from 68 deceased donors who donated their kidneys to 87 recipients in our centre from 1/1/2016 until 1/9/2022. The donors had been diagnosed with microbemia, urinary tract infection or both diseases. The minimum follow-up of recipients was 3 months.
Results: The median age of donors was 65.5(51.7-79.3) years and the median age of recipients was 52(41-63) years. Fifty-eight (66.6%) patients received a kidney from a donor diagnosed with microbemia, 13(14.9%) patients were transplanted by a donor diagnosed with UTI, while the donors of 16 (18.3%) recipients suffered from both microbemia and UTI. The median stay of donors in the ICU was 10 days. Infection by the same pathogen developed in none of the recipients. No serious adverse effects of the antibiotic regimen on recipients were reported. The one-year survival rate of renal recipients was 98.8%, while the one-year survival rate of renal grafts was 95.4%.
Conclusions: Although the harmful effects of donor-derived infections on renal recipients have been described, the careful acceptance of some infected donors could be a safe and reasonable way to expand the donor pool in countries with long waiting lists for kidney transplantation.

P385 COMPARISON OF PROGNOSIS AND RISK FACTORS OF GRAFT FAILURE BETWEEN PEDIATRIC AND ADULT RECIPIENTS WHO RECEIVED PEDIATRIC DONOR KIDNEY TRANSPLANTATION

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Background: The number of patients receiving pediatric donor kidney has been increasing in recent years in China. However, it is unknown whether the long-term prognosis and risk factors of graft failure in pediatric recipients (age <18 years) differ from those in adult recipients (age ≥18 years).
Methods: We retrospectively analyzed clinical data of kidney transplant patients who received pediatric deceased-donor kidneys in our hospital from August 2011 to July 2018. The long-term outcomes of grafts, in addition to risk factors of graft failure were compared between the pediatric recipients and adult recipients.
Results: We enrolled 33 pediatric recipients and 114 adult recipients who received pediatric donor kidneys. The 1-,3-,5-year graft survival rates in the pediatric group were 90.6%, 81.3%, and 81.3% versus 96.5%, 94.6%, and 93.0% in the adult group, and Kaplan–Meier curves showed that the survival rate of the graft in the adult group was higher than in the pediatric group(P=0.014). The main cause of graft failure in the pediatric recipients was renal vascular thrombosis (57.1%). Multivariate Cox regression analysis suggested that the independent risk factors for graft failure were renal vascular thrombosis and acute rejection in the pediatric recipients, compared to chronic rejection and urinary tract stenosis in the adult recipients. The rates of vascular thrombosis and acute rejection were much higher in pediatric group compared to adult group.
Conclusions: The graft survival rates of pediatric recipients were worse than adult recipients who received pediatric donor kidneys, mainly due to renal vascular thrombosis and acute rejection.

P386 DEVELOPMENT OF RENAL ALLOGRAFT LYMPHANGIECTASIA AFTER 14 YEARS FROM KIDNEY TRANSPLANTATION

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Background: Renal lymphangiectasia is known to be a very rare disease, and in particular, it is confirmed that very few cases occur in the setting of transplant kidney. Here, we report a rare case of renal lymphangiectasia after kidney transplantation
Methods: A 43-year-old man received living donor kidney transplantation due to IgA nephropathy, treated with two episode of acute and chronic antibody-mediated rejection, on post-transplant 1 year and 7 year respectively.
Results: On post-transplant 14th year, he presented with abdominal distension, and dyspnea gradually progressing for 2 months. Serum creatinine level was elevated to 1.6mg/dL from baseline 1.1mg/dL. Computed tomography (CT) and Magnetic resonance imaging (MRI) showed multi-septated cystic lesions around the graft kidney with a large amount of ascites. Ascites profile showed transudative, non-chylous, suggesting lymphatic fluid. (Protein 289.3mg/dL, Serum ascites albumin gradient(SAAG) 3.1g/dL, Triglyceride 3mg/dL). There was no evidence for infectious or malignant disease. At first, tacrolimus was switched to sirolimus, which has an anti-lymphangiogenic effect, consequently the amount of ascites was significantly reduced and abdominal distension improved, and the patient was eventually discharged from the hospital on the 5th day after changing the medication. However, 3 weeks after discharge, he returned to the hospital with abdominal distension, and again a large amount of ascites was confirmed. In this time, surgical approach with explore laparotomy and argon coagulation and helixor injection through Hemo-vac drain inducing adhesion were done. Also, lymphatics embolization was performed using lipiodol. Afterwards, the abdominal distension and ascites resolved. However, massive ascites recurred just after 1 week from procedures, therefore, allograft nephrectomy was inevitable.
Conclusions: Post-transplant renal lymphangiectasia is a rare but critical complication of allografts, still poorly understood. However, massive ascites due to lymphangiectasia could result serious situation, so efforts to active treatment is required.

Fig 1. Abominal computed Tomography

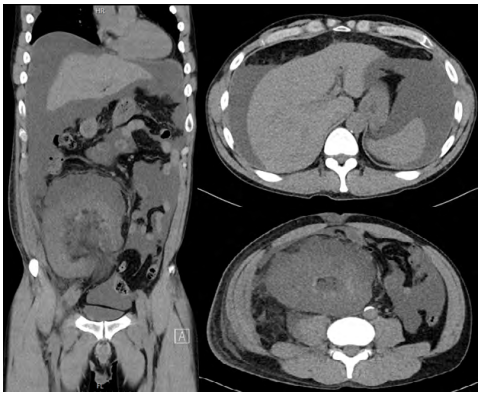


Fig 2. Kidney magnetic resonance imaging

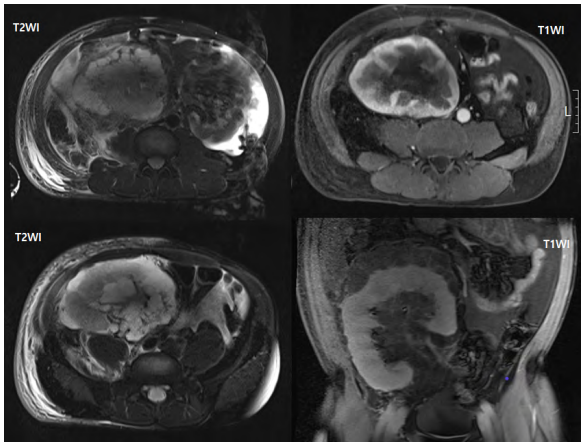
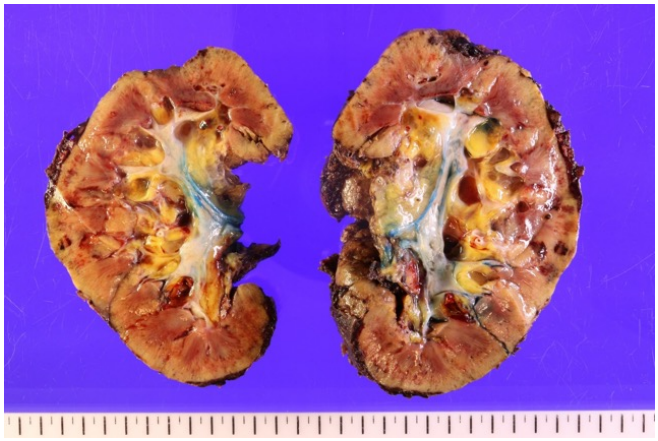


Fig 3. Gross pathology of transplant nephrectomy



P387 LONG-TERM OUTCOME OF PEDIATRIC LIVER TRANSPLANTS: THE IMMUNOSUPPRESION AND PSYCHO-SOCIAL DEVELOPMENT

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Background: To review the long-term outcome of pediatric liver transplantation at NTUH, with attention to immunosuppresion regimen and psycho-social development.
Methods: 174 liver transplants were performed at age <18 y/o. All patients were followed till December 2021 or death. Their medical records were reviewed for biologic outcome and immunosuppresion regimen. Psycho-social developments were studied for 51 patients with final age ≥15 y/o by questionnaire.
Results: Of the 174 patients, 10 were excluded due to death within 6 months. The 5 and 10 year patient survival are 85% and 75%. Most of the transplants were performed between 0.5 to 2 y/o. 19 patients are on CsA-based therapy and the other 145 patients are under TAC-based immunosuppresion. Most of them are with two combined immunosuppressants. There is no significant change of TAC dose along with age, and then the standardized TAC daily dose decreased along with time. At age of 15 (n=49), the average TAC level was 2.82 ng/ml, and 1/5 of cases with level below the detectable limit. This level is far lower than that in adult liver transplant patients. For patients with age ≥15 years, 87% of them are with compatible academic degree in their learning process. 20% patients need special education program in their junior-high or high school stage. 23% patients had one to two years delay in their education process. Around 17 % of patients had the feeling to be discriminated by their peer group.
Conclusions: The long-term survival of pediatric liver transplantation is good. The age standardized TAC dose decreased with age, but there is no parallel decrease of TAC concentration. The long-term TAC level is very low. Though they survived with normal liver function and body built, but significant percentage of patients have obstacle/delay in their learning process, and they have the feeling of being discriminated psychologically.

P390 PREVALENCE OF EARLY ACHIEVEMENT OF THERAPEUTIC LEVEL OF MYCOPHENOLATE AFTER A LOADING PROTOCOL AMONG THAI KIDNEY TRANSPLANT RECIPIENTS

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Background: Loading protocol with daily mycophenolate mofetil (MMF) dosage of 3 gram for 5 days resulted in superior accomplishment of target MPA level and reduction of acute rejection. However, with lower MMF dosage usage in Asian population, data regarding MPA-AUC in early phase after KT is lacking.
Methods: We performed a prospective cohort study in patients who underwent KT at Siriraj Hospital between July 2019 and March 2020. All enrolled patients received MMF loading protocol of 2 gram daily for 7 days after KT then adjusted to 1 – 1.5 gram per day. Full MPA-AUC was measured at 3rd and 5th day after KT. MPA-AUC was also measured at 1 month after transplantation by mean of abbreviated AUC model. The CMV, BK infection and rejection were monitored for 2 years after KT.
Results: We enrolled 37 patients with mean age of 38.9 ± 11.8 years. Most (75.7%) received deceased donor KT. At 1-month post KT, 82.4% patients received daily MMF dosage of 1.5 gram. Achievement of therapeutic MPA-AUC (≥ 30 mg.hr/L) at 3rd, 5th and 30th day after KT were revealed in 82.9%, 80% and 85.3% of patients, respectively. However, high MPA-AUC (≥ 60 mg.hr/L) at 3rd and 5th day was observed in 37% and 51.4% patients, respectively. Most of patients whose BW < 65 kg (96%), but 50% of patients with higher BW had MPA-AUC ≥ 30 mg.hr/L at 3rd day. Early acute rejection was found in 2 patients. Both patients had MPA-AUC at 3rd day < 40 mg.hr/L (15.4%). CMV and BK viremia was found in 40.5% and 16.2% of patients, respectively. Patients who had CMV viremia tended to have higher MPA-AUC at 3rd day after KT (62.2 ± 34.4 vs 47.1 ± 22.7 mg.hr/L; p = 0.13).
Conclusions: A MMF loading protocol of daily 2 gram in Thai KT patients resulted in early therapeutic MPA-AUC achievement, especially in patients with BW < 65 kg. Monitoring MPA exposure at day 3 after KT is advantageous for prevention of transplant complication.

P391 PREGNANCY AFTER LUNG TRANSPLANTATION IN THE NETHERLANDS

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[1]University Medical Center Groningen , Department of nephrology, Groningen, Netherlands, [2]University Medical Center Utrecht, Department of pulmonology, Utrecht, Netherlands, [3]University Medical Center Utrecht, Department of Gynecology and Obstetrics, Utrecht, Netherlands, [4]University Medical Center Groningen, Department of pulmonology, Groningen, Netherlands, [5]University Medical Center Groningen , Department of Nephrology, Groningen, Netherlands

Background: Data on pregnancy after lung transplantation (LTx) is scarce. Most data on pregnancy after solid organ transplantation comes from pregnancies after kidney or liver transplantation. Data from the American National Transplant Pregnancy Registry (NTPR) shows that these pregnancies (n=46) are associated with a high risk of complications such as (pre)eclampsia, graft rejection, kidney function decline, preterm birth and maternal mortality. The primary aim of this study was to examine neonatal and maternal outcomes of pregnancy after LTx in the Netherlands.
Methods: In this retrospective multicenter cohort study all patients with a pregnancy after LTx in the Netherlands were eligible. Data on demographics, pregnancy complications, kidney function (slope) and lung function, was collected from medical files. Due to small sample size mainly descriptive statistics were used.
Results: We included 11 pregnancies of 8 women. For 7/8 women cystic fibrosis (CF) led to LTx and 1/8 pulmonary hypertension. Hypertension during pregnancy occurred in 3/11 pregnancies and preeclampia in 2/11. One patient with pre-existent CF-related diabetes had progressive renal insufficiency during pregnancy. In one patient post-transplant lymphoproliferative disorder (PTLD) was diagnosed in the second trimester. Lung function remained >80% of FEV1 % of baseline at last follow-up in all patients. One woman died 3.5 years after her first pregnancy and 2 years after her second due to PTLD (distinct from the former PTLD patient). All children were born alive, 10/11 were born preterm and their median gestational age was 35 weeks (range 27-38). All children had a birth weight <3500 grams with a median weight of 2340 grams (range 1020-3300). Median follow-up after pregnancy was 5 years (range 2 months-7 years). All children were reported as healthy on last follow-up. However, no specific tests were performed.
Conclusions: This cohort study in the Netherlands found that pregnancy after LTx led to an increased risk for pregnancy complications for both mother and child. This is in line with existing research. In the longer term results show no deterioration of lung function after pregnancy and healthy children. However, 13% of the mothers died, which is in line with the survival of women with a pregnancy after liver of kidney transplantation

Table 1. Characteristics of pregnancies after lung transplantation in the Netherlands

Case	Age	Diagnosis	Time tx-conception (years)	Gestational age (weeks)	Birth weight (grams)	Neonatal outcome	Maternal outcome	Lung function last before 1st conception (%FEV1 of baseline)	Lung function at last follow-up (%FEV1 of baseline)
1a	37	PAH	5	36	2340	alive	death (PTLD) 3.5 years after birth		99%
1b	38		6	36	2750	alive	death (PTLD) 2 years after birth		99%
2	28	CF	4	34	2295	alive	alive (3 yr FU)	95%	98%
3	28	CF	5	35	2420	alive	alive (7 yr FU)	94%	82%
4a	28	CF	4	38	3300	alive	alive (7 yr FU)	92%	92%
4b	31		7	37	3300	alive	alive (4 yr FU)		92%
5a	33	CF	5	33	2140	alive	alive (6 yr FU)	94%	88%
5b	35		7	31	1700	alive	alive (5 yr FU)		88%
6	32	CF	8	36	2420	alive	alive (4 yr FU)	95%	94%
7	37	CF	5	29	1317	alive	alive (0.5 yr FU)	96%	95%
8	33	CF	12	27	1020	alive	alive (2 mo FU, PTLD diagnosis second trimester)	99%	96%

Abbreviations: FU: follow-up, mo: months, PAH: pulmonary hypertension, PTLD: post-transplant lymphoproliferative disorder, tx: transplantation, yr: years

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P393 EARLY COMPLICATIONS AFTER DESENSITIZED LIVING DONOR KIDNEY TRANSPLANTATION: ANALYSIS OF KOREAN ORGAN TRANSPLANTATION REGISTRY (KOTRY) DATA

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Background: Transplantation of kidneys to highly sensitized patients has become a common practice in recent years. Desensitization is commonly used in sensitized recipients, but its relation to non-infectious complications is unclear. The aim of the study was to evaluate the effect of desensitization on early complications in kidney transplantation.
Methods: Based on the Korean Organ Transplant Registry (KOTRY) data, a retrospective analysis was conducted of 5038 living donor kidney transplants (LDKTs) between 2014 and 2021.A comparison was made between the outcomes of 1819 desensitized patients and those of other recipients. The incidences of early complications such as delayed graft function (DGF), urinary leak, hemorrhage, thrombosis and embolism at graft vessels, wound infection, and vascular stenosis and their associated risk factors were analysed.
Results: The desensitized group had a higher rate of hemorrhage (2.1% vs. 0.8%, P < 0.001) and DGF (1.2% vs. 0.6%, P = 0.03). Desensitization did not appear to be responsible for any other complications. Except for desensitization, other demographic data and baseline factors were not associated with hemorrhage. Univariate and multivariate analysis revealed that diabetic (OR 2.0, P = 0.028) and/or desensitized (OR 2.0, P = 0.03) recipients had higher DGF. DGF eventually resulted in graft failure (GF) for 12 of the 40 patients. In desensitized recipients, GF was more likely to occur, and the period between transplantation and GF was shorter. A higher rate of early acute rejection was observed in patients who underwent desensitization (OR 1.4, P < 0.001).
Conclusions: More frequent postoperative bleeding and DGF were observed in desensitized kidney transplant recipients. The only risk factor for bleeding was desensitization. In regards to DGF, DM was also considered a risk factor. DGF and GF may be associated with the increased incidence of early acute rejection in desensitized recipients.

P394 KOMPARTE. REGISTERING MORE AND BETTER THE DONATION PROCESS

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Background: The development of a digital platform for the registration and exploitation of data that facilitates inter-professional transmission of information in real time during the donation process may improve the communication errors that jeopardize the safety these procedures. We present an analysis of the 2022 deceased organ donation activity of a third level University Hospital (HUVH) registered in this digital platform named "Komparte".
Methods: In 2021, the first operative version of "Komparte" was launched for clinical use at HUVH. This is a multi-professional, multi-device, secure, reliable, and exploitable digital database that links with hospital and regional registries, allowing the introduction and consultation of patient and process data generated during the organ and tissue donation in real time by all professionals involved in the procedure . It is composed of 4,500 variables arranged in different tabs that reproduce the clinical sequence of the donation process according to the definitions of the Critical Pathway (1) in an easy and intuitive way thanks to the use of Lean® visual management techniques. Fig1a
Results: A total of 277 possible donors (PD) were notified and followed until death of discharge during 2022, of which 126 became potential-PT (45.5%), 72 eligible (57.1%) and 50 actual-AD (69.4%) donors, the majority of which (98%) were utilized. Two hundred and one PD did not progress to PT due to favorable outcome (35.7%) and medical contraindication (36.8%). Lack of consent (21%) or logistical problems (4.3%) where the main modifiable causes that precluded the progression to AD of the remaining PT. Fig1b.
Conclusions: "Komparte" is a useful tool that facilitates the organization and transmission of interprofessional information, teamwork and optimization of time and resources ensuring the safety of both the patient and the professional.
(1) Dominguez-Gil B, et al. Transpl Int 2011; 24 (4): 373-8)

Figure 1a. Scheme of "Komparte" variables included

Figure 1.b. HUVH 2022 Donation activity.

P395 ROBOT ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY

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[1]İstanbul Florence Nightingale Hospital, Kidney Transplantatiom, Istanbul, Turkey, [2]Demiroğlu Science University, Faculty of Medicine, Istanbul, Turkey, [3]Demiroğlu Science University, Faculty of Medicine, İstanbul, Turkey

Background: After initial experience with robot assisted laparoscopic donor nephrectomy (12 cases), we adopted Robot Assisted Retroperitoneoscopic Donor Nephrectomy (RARDN) as an alternative to hand assisted retroperitoneoscopic surgical technique in our center.
Methods: We performed 34 RARDN with Da Vinci robotic system in between March 2018 and November 2022. The mean age was 53 (9 females). The median BMI was 26.8 kg/m2 (SD± 4.78). 7 cases had right nephrectomy (due to double left renal artery (n=1), millimetric stones (n=2) and simple cysts (n=4) at right kidney). 7 cases had 2 renal arteries and 2 cases had 2 renal veins. We performed hybrid surgery with hand and robotic assistance for ease and safety. Initially, a Pfannensteil incision was performed for creation of retroperitoneal space and introduction of 3 robotic trocars with hand assistance. Permanent hook cautery, fenestrated bipolar forceps and grasper were robotic instruments used in surgery. Ligasure and vascular stapler were introduced from the Alexis port.
Results: The robotic dissection time was 115 min for the initial half and 100 min for the second half of the series. Also, preparation time to surgery decreased (34 min for the initial half vs 27 min for the later series). The time for staplering and removing the kidney was less than 4 min in all cases. 2 cases had major peritoneal opening. 1 case had 70 cc of bleeding. None of the cases had subcapsular hematoma or vascular sacrifice of accessory renal arteries. One recipient died after 2 months with functional graft because of pneumatosis intestinalis. Other had lost kidney secondary to rejection 1 week after transplantation. The rest had uncomplicated course with a mean creatinine of 1.28 mg/dl. Questionnaire showed all cases had cessation of pain less than 1 week except 2 cases (4 weaks). 1 case had superficial wound infection requiring antibiotic treatment. All donors had good memory and recommend robotic surgery.
Conclusions: RARDN enabled uncomplicated nephrectomy with good donor satisfaction. The improved ability to operate in tight spaces with robotic assistance allowed us to adopt retroperitoneoscopic access and enabled comfortable dissection at the retroperitoneal space with no intraabdominal complications. It can be a good alternative to hand assistance especially in low BMI living donors.

P396 ENHANCED RECOVERY AFTER SURGERY IN LIVER TRANSPLANTATION. A NATIONAL SURVEY ON CURRENT PRACTICES AND TRENDS IN THE UNITED KINGDOM

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Background: Enhanced Recovery after Surgery (ERAS) is well established in many specialties but has yet to be widely adopted in liver transplantation. The aim of this survey was to understand current national practices and sentiment towards ERAS in liver transplantation.
Methods: A web-based survey was designed and sent to consultant surgeons, anaesthetists, hepatologists and transplant coordinators at all UK adult liver transplant centres between February and April 2022. Respondents were requested to answer the survey in the context of uncomplicated liver transplant. Data was analysed according to individual responses and where appropriate, grouped according to transplant centres.
Results: All disciplines, at all seven centres were represented in the responses. No units had a formal ERAS pathway for all recipients. Of the 116 eligible respondents, over half (54%) were considering implementing ERAS within 18 months. Perceived barriers to implementation included the complexity of post-operative management and the complex nature of liver transplant surgery (51%, 47% respectively); lack of a standardised protocol (49%) and embedded unit culture (48%). The majority of respondents (93%) regularly inserted NG drainage tubes whereas fine bore tubes were rarely or selectively inserted by most (76%). Only 12% of respondents routinely used portocaval shunts or portosystemic bypass. The commonest time to extubation was 2-6hr (44%). Opiate based PCA was most commonly used (79%), with routine discontinuation of PCA between 48-72hr for 55% of respondents. Routine discontinuation of prophylactic antibiotics within 24hr was most common (46%). Over half of respondents start oral or enteric diet within 24hr and 44% remove NG tubes within 24hr. 32% of respondents report central lines remaining beyond 48hr. 32% reported urinary catheter removal within 48hr, although 13% reported keeping them beyond 72hr. Average length of stay was reported to be between 7 and 15 days (90% respondents).
Conclusion: Despite slow uptake of ERAS in liver transplantation, appetite is increasing. The captured national practices and opinions of transplant specialists are now being used to help with standardisation of a local ERAS protocol for liver transplant recipients.

P397 EPIDEMIOLOGY OF CANCER AFTER SOLID ORGAN TRANSPLANTATION (EPCOT): AN ENGLISH POPULATION-COHORT PROJECT OF LINKED NATIONAL DATASETS

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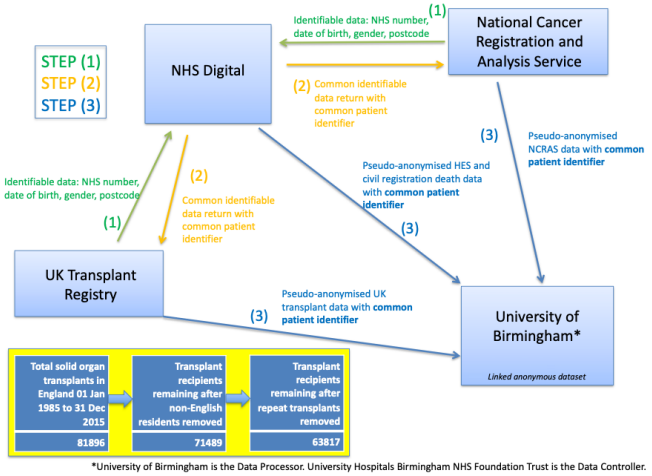
Background: Post-transplantation cancer is common, associated with increased healthcare costs and a leading cause of post-transplant mortality but remains poorly understood. Limitations include translation of data from different countries (e.g., United States), lack of contemporary population cohorts and epidemiological data being siloed across different registries and/or data warehouses. Epidemiology of Cancer after solid Organ Transplantation (EpCOT) overcomes these limitations by creating a comprehensive record-linked national dataset of solid organ transplant recipients.
Methods: EpCOT has gained approval for record linkage between the UK Transplant Registry (held by NHS Blood and Transplant) and Hospital Episode Statistics secondary care episodes/national cancer registry/civil registration deaths (held by NHS England). Deterministic record linkage, conducted by NHS England, has created an anonymised linked dataset available for analysis by the research team combining all individual datasets. The project obtained institutional support, ethical approval, and Section 251 legal approval back in 2014 but has taken 9 years to reach fruition.
Results: The EpCOT study cohort consists of 63,817 solid organ transplant recipients who received their first solid organ transplant in England between January 1st 1985 and December 31st 2015. Up-to-date clinical outcome data to 2022 is available, allowing the research team to study our pre-specified research questions which include: 1) compare observed and expected risks of specific causes of deaths between transplant and general population cohorts, 2) investigate survival and causes of death after cancer in post-transplant patients versus the general population, 3) compare observed and expected risks of specific cancer types post-transplantation versus the general population, and 4) estimate risk of morbidity requiring hospitalization for transplant recipients.
Conclusions: The EpCOT dataset is the largest record linked resource available to study post-transplantation cancer at a comprehensive national level. It is designed to help address some of the unmet need to further our understanding of the morbidity and mortality associated with post-transplantation cancer and will be ready for analysis from August 2023.



P398 REDUCED MONOSEGMENT LIVING DONOR LIVER TRANSPLANT IN A 4,5-KILOGRAM CHILD: A FIRST IN AFRICA

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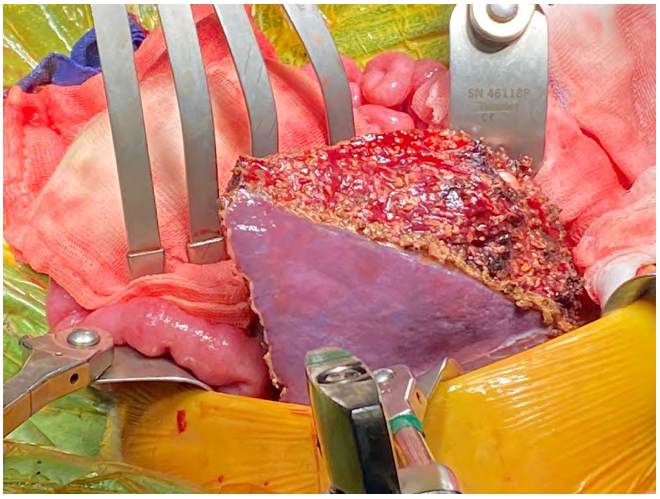
Background: Supply-demand mismatch of appropriately sized liver grafts for transplantation is particularly pronounced in small children. Advanced surgical techniques in reducing cadaveric and living donor liver grafts allow for access to life-saving transplantation. Living donor left lateral segment liver grafts have been successfully transplanted into small children in South Africa since 2013, however, this type of partial graft remains too large for children below 6 kilogram (kg) in body weight and requires reduction. We report the first case in Africa of a reduced monosegment, blood group incompatible, living donor liver transplant in a 4,5 kg child with fulminant liver failure.
Methods: An ex-prem male twin, at a corrected age of 3 weeks and a weight of 4,5 kg was referred to our unit in fulminant liver failure. Despite listing as a Status 1A recipient, no cadaveric donors became available. Both parents were found to be unsuitable for living donation. An altruistic donor consented to urgent donation and was found to be suitable. Computerized tomography (CT) volumetry calculated a 289 g left lateral segment graft which amounted to a graft to recipient weight ratio (GRWR) of 6.4%. The donor surgery involved the procurement of a standard left lateral segment graft, followed by an in-situ reduction of segment III parenchyma without dissecting around the segment III vascular pedicle. Further reduction of the graft on the lateral aspect of segment II followed to achieve a GRWR of 3.5%. The recipient transplant involved the standard implantation technique used for a left lateral segment graft. Cold and warm ischemic times amounted to 50 min and 20 min respectively. Primary abdominal closure was achieved. Doppler studies revealed excellent graft vascular inflow and outflow. Total operative time was 5 hours 30 min.
Results: The donor was discharged after 6 days without complications. The recipient suffered no technical surgical complications except for an infected cut-surface biloma and biliary anastomotic stricture and remains well and alive 10 months post-transplantation.
Conclusions: This case report describes the first hyper-reduced monosegment liver transplant performed in Africa This development is a critical landmark in ensuring access to liver transplantation for small infants on the continent.



P399 BLUE KIDNEY, A CHALLENGING CASE FOR LIVING DONOR KIDNEY TRANSPLANTATION

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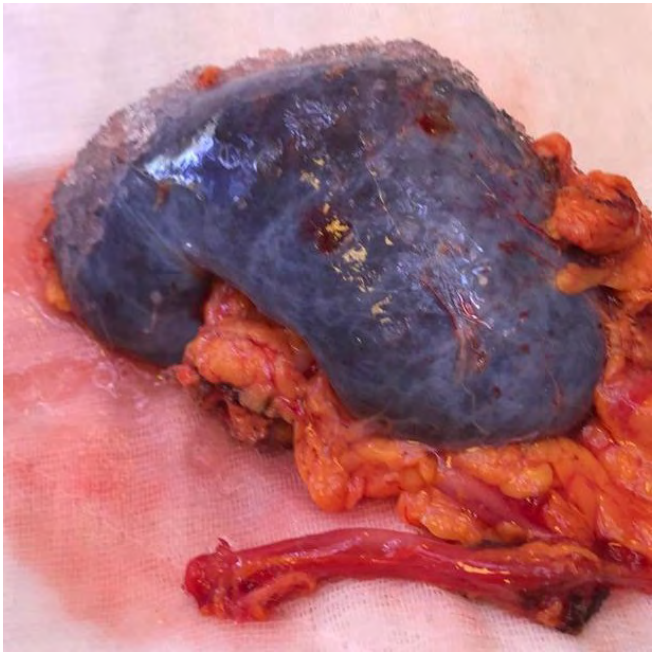
Background: Even though it is extremely uncommon, it is possible for a live kidney donor to have a blue kidney. In the body of published research, hemosiderin deposits, lipofuscin pigment, and melanosis have all been suggested as potential causes.
Methods: We present a case of 55 years old female donor. All preoperative lab and imaging tests showed normal renal function. During Hand Assisted Retroperitonoscopic Nephrectomy, the left kidney was noted to be blue in color which required a differential diagnosis for ischemia, subcapsular hematoma covering all kidney, vascular compromise of aorta and renal vessels. The donor was hemodynamically stable. The kidney was mobilized a.s.a.p, and hand assistance enabled to feel the arterial pulsation of aorta and the tonus of the kidney. Ureter and renal vessels were sealed and kidney was removed. Kidney perfusion was normal, and the blue coloration did not change at the back table. After transplantation to recipient, the perioperative doppler USG was performed. A wedge biopsy was carried out.
Results: Doppler USG showed no signs of ischemia or pathological findings. Kidney dimensions was 10x8x6 cm. Histopathological and immunohistochemical examinations showed deposition of reddish-brownish pigment (myoglobulin) in the tubules, and there was no evidence of glomerular, interstitial, or vascular pathology. Post-operative day 1 creatinine dropped from 13.7mg/dl to 13.4 mg/dl. Patient had 3 postoperative hemodialysis sessions. Discharge creatinine was 3.3mg/dl.
Conclusions: Facing with a dark colored kidney is a challenging situation during living donor nephrectomy. The immediate elimination of hemodynamic instability of the donor, renal artery perfusion defects and extensive subcapsular hematoma is mandatory. Hand assistance is useful to eliminate these complications and quick mobilization and removal of kidney. It should be kept in mind that there can be dark coloration of kidney without any complications in some rare instances.



P400 TISSUE DONATION ACTIVITY OF A THIRD LEVEL HOSPITAL ACCORDING TO THE NEW DEFINITIONS ESTABLISHED BY THE CRITICAL PATHWAY

Alberto Sandiumenge*[1], Jose Alejandro Marin Figuera[1], Zulaikha Zia[1], Anna Sole Fores[1], Carlos Marín Pérez[1], Gloria Arriscado Martin[1], Christopher Mazo[1], Aroa Gomez Brey[1], Teresa Pont[1]

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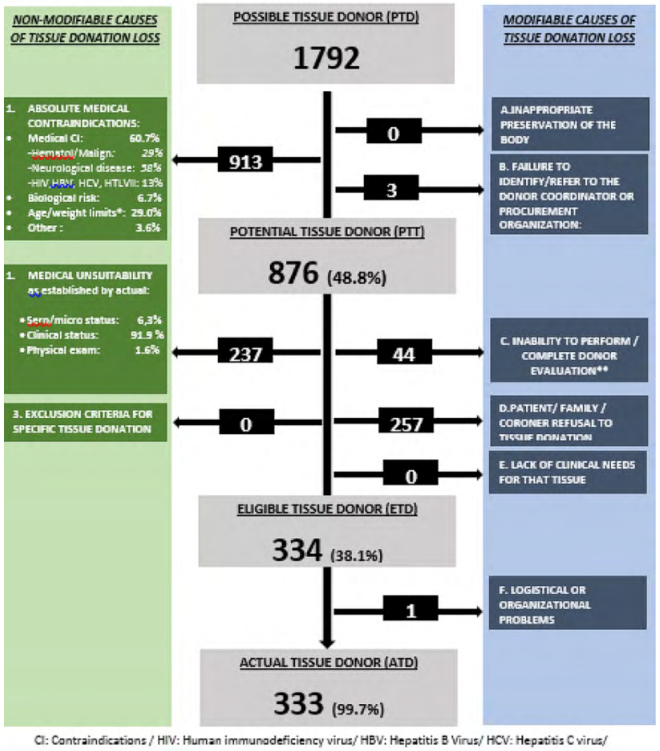
Background: The European Committee for Organ Transplantation of the Council of Europe (CD-P-TO) proposed a "Critical Pathway" with the aim to develop a common systematic approach and lay the foundations to standardize data used to measure efficiency and effectiveness of deceased tissue donation (1). We present the 2022 deceased tissue donation activity of a third level university Hospital (VHUH) on of the largest tissue procurement centers of Spain classified according to the new pathway.
Methods: The "Critical Pathway" defines thel steps of tissue deceased donation process following the definition similar to organ donors (2): Possible tissue donor-PTD- (person who has died or in a situation of imminent death); Potential tissue donor-PTT- (Dead PTD with no apparent absolute contraindication whose body has been preserved according to requirements for tissue procurement); Eligible tissue donor-ETD- (PTT consented donor medically suitable and meets specific criteria for the donation for at least one type of tissue) and Actual tissue donor (ATD) (ETD from whom at least one tissue was recovered with the intention of clinical application)
Results: A total of 1792 PTD were identified (male 58.8%, median age 76 (min 0- max 103) years old, 876 of whom (48.8%) became PTT. Three-hundred and thirty four (38.1 %) PTT became ETD, 99.7% of whom progress to ATD (18.5% of all PTD) generating a total of 330 corneal, 47 musculoskeletal, 39 skin, 14 blood vessel and 28 heart valve tissue grafts. Figure 1.
Conclusions: Despite an optimized donation process (few modifiable causes of loss), VHUH tissue donation potentiality is hampered by the profile of the possible donor (aged and high percentage of medical contraindications). Training in family approach could be implemented as a measure to increase efficiency.
(1) Sandiumenge A, et al. Transpl Int 2021; 34(5):865-871.
(2): Dominguez-Gil B, et al. Transpl Int 2011; 24 (4): 373-8)

FIGURE 1. CRITICAL PATHWAY FOR DECEASED TISSUE DONATION HUVH 2022



CI: Contraindications / HIV: Human immunodeficiency virus/ HBV: Hepatitis B Virus/ HCV: Hepatitis C virus/ HTLV: Human T-lymphotropic virus * Age and weigh limit: corneas 2 and 89 years old. Min weight: 2,5 kg **

P401 ORGAN DONATION AFTER CIRCULATORY DEATH – SHALL WE? PERCEPTIONS AND CHALLENGES OF GREEK NURSING PROFESSIONALS - A FOCUS GROUP STUDY

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Background: There has been growing interest in donation after circulatory death (DCD) in recent years with DCD accounting for about 20% of all deceased donations worldwide. In a European survey, 18 countries reported running DCD programs and 17 countries declared no DCD activity, due to a variety of reasons from legislative to organizational obstacles, yet with half of them interested in developing DCD. Greece appeared reluctant towards DCD. The current study aims to identify and understand the attitudes of Greek nursing professionals as key stakeholders in transplantation towards DCD in order to inform future policy.
Methods: We conducted a focus group study with nursing professionals of all levels and from institutions spread across the country regarding their attitudes towards organ donation, brain death vs circulatory death, decision-making, current donation practices and the nursing professionals' role. Data were analysed using qualitative research methods.
Results: The majority of participants showed a positive attitude towards organ donation in general as an act that attaches meaning to death and helps families process loss. Despite their positive attitude, they raised numerous conditions not favouring donation like organizational and medical-technical difficulties, lack of knowledge about donation, but also moral conflicts regarding the withdrawal of life support, violation of the donor body, and depriving donor families of a false sense of hope, which turns them subjectively into accomplices. All participants would welcome DCD, but expressed concerns regarding the definition of circulatory death, the ethicality of it, (time) management issues, conflicting roles of the staff and donor-family management issues. Interestingly, participants differentiated between personal and professional attitudes towards donation, which partially explains the conflicting areas. All expressed need for education, targeted training, clear role definitions and discussion in order to fulfil their potential role.
Conclusions: Nursing professionals seem open towards DCD despite the ethical and practical concerns. For a possible successful implementation of DCD in Greece, their views and dilemmas need to be acknowledged and treated through training, active involvement and reflection opportunities.

P402 CC GENOTYPE OF GNAS C.393C>T (RS7121) POLYMORPHISM HAS A PROTECTIVE EFFECT AGAINST DEVELOPMENT OF BK VIREMIA AND BKV-ASSOCIATED NEPHROPATHY

Tobias Peitz[1], Birte Möhlendick[2], Ute Eisenberger[1], Winfried Siffert[2], Falko Markus Heinemann[3], Andreas Kribben[1], Justa Friebus-Kardash*[1]

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Background: The GNAS gene encodes the alpha-subunit of the stimulatory G-protein (Gαs), the single-nucleotide polymorphism of GNAS, c.393C>T, is associated with elevated production of Gαs and increased formation of cyclic adenosine monophosphate (cAMP). In the present study, we analyzed the effect of this GNAS polymorphism on renal allograft outcome.
Methods: We screened a cohort of 436 renal allograft recipients who were retrospectively followed up for up to 5 years after transplant. GNAS genotypes were determined with polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) assays.
Results: The 393T allele was detected in 319 (73%) recipients and the CC genotype in 117 (27%). The CC genotype was associated with a significantly lower frequency of BK viremia (CC, 17 recipients [15%]; T, 84 [26%]); p=0.01) and BKV-associated nephropathy (CC, 3 recipients [3%]; T, 27 [8%]; p=0.03) after transplant. BKV-associated nephropathy-free survival was significantly better among CC-genotype carriers than among T allele carriers (p=0.043). Multivariate analysis indicated an independent protective effect of the CC genotype against the development of both BK viremia (relative risk. 0.54; p=0.04) and BKV-associated nephropathy after renal transplant (relative risk. 0.27; p=0.036).
Conclusions: The GNAS 393 CC genotype seems to protect renal allograft recipients against the development of BK viremia and BKV-associated nephropathy.

P403 GNB3 C.825C>T (RS5443) POLYMORPHISM AND RISK OF ACUTE CARDIOVASCULAR EVENTS AFTER RENAL ALLOGRAFT TRANSPLANT

Tobias Peitz[1], Birte Möhlendick[2], Winfried Siffert[2], Falko Markus Heinemann[3], Andreas Kribben[1], Ute Eisenberger[2], Justa Friebus-Kardash*[1]

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Background: The c.825C>T single-nucleotide polymorphism (rs5443) of the guanine nucleotide-binding protein subunit β3 (*GNB3*) results in increased intracellular signal transduction via G-proteins. The present study investigated the effect of the *GNB3* c.825C>T polymorphism on cardiovascular events among renal allograft recipients posttransplant.
Methods: Our retrospective study involved 436 renal allograft recipients who were followed up for up to 8 years after transplant. The *GNB3* c.825C>T polymorphism was detected with restriction fragment length polymorphism (RFLP) polymerase chain reaction (PCR).
Results: The *GNB3* TT genotype was detected in 43 (10%) of 436 recipients. Death due to acute cardiovascular event occurred more frequently among recipients with the TT genotype (4 [9%]) than among those with the CC/CT genotypes (7 [2%]; p=0.003). Rates of myocardial infarction–free survival (p=0.003) and acute PAOD–free survival (p=0.004) were significantly lower among T-homozygous patients. A multivariate analysis showed that homozygous *GNB3* c.825C>T polymorphism exerted only a mild effect for the occurrence of myocardial infarction (relative risk, 2.2; p=0.065) or acute PAOD (relative risk, 2.4; p=0.05) after renal transplant.
Conclusions: Our results suggest that the homozygous *GNB3* T allele exerts noticeable effects on the risk of MI and acute PAOD only in the presence of additional nonheritable risk factors.

P404 KIDNEY TRANSPLANT RECIPIENTS IN WHOM CONCENTRATION-CONTROLLED DOSE ADJUSTMENT OF MMF WAS PERFORMED HAD HIGHER REJECTION-FREE SURVIVAL AT THREE YEARS

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Background: We conducted a multicenter exposed vs. non-exposed study nested in a prospective cohort of about 900 unselected adult kidney transplant recipients (KTRs) to evaluate the effects of model-informed mycophenolate mofetil (MMF) individual dosing over the first three years post-transplantation.
Methods: Patients had up to 8 study visits over the first three years post-transplant. Independent from the cohort protocol, they benefited or not from MMF precision dosing to reach MPA AUC = 45 mg.h/L, and these two groups were compared for rejection-free survival and cumulative incidence of graft rejection episodes, before and after stratification on a propensity score for rejection.
Results: The exposed group included 377 and the control group 524 KTRs. At 3 years, the cumulative incidence of rejection was 2.5% vs. 5.8% per patient X year (HR=0.38 [0.24, 0.61], p<0.001) and rejection-free survival was 91.5% and 84.0% (p<0.001), respectively. These differences were confirmed in patients at high or low risk of rejection (p=0.011 and 0.015), and whether on tacrolimus or cyclosporine (p=0.00022 and 0.034). The group with MMF precision dosing also had slightly but significantly higher cumulative incidences of various adverse effects, but most of these AEs occurred before any dose adjustment.
Conclusions: In summary, model-informed precision dosing in routine is associated with a better MMF benefit-risk balance in KTRs over 3 years post-transplant, whatever their immunological risk and associated CNI.

P405 THE SF12 IS SHORTER AND AS EFFICIENT AS SF36 TO EVALUATE HEATH QUALITY OF LIFE IN KIDNEY TRANSPLANT PATIENTS

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Background: Evaluating Heath quality of life (HQOL) in kidney transplant recipients (KTRs) is a way to detect patient physical symptoms or distress, potentially associated with non-adhesion and poor outcomes. The 36-Item Short Form Health Survey (SF36) is the questionnaire most frequently used to evaluate HQOL, but it is hardly applicable in routine. The aim of this study was to validate a shorter health status instrument, the short form SF12, in KTRs.
Methods: Five hundred and fifty-five patients were invited to complete PROMs forms, including SF36 at 1, 3, 6, 9, 12, 18, 24, 30 and up to 36 months post-transplantation. The following psychometric properties of the SF12 were assessed: reliability (intra-observer reproducibility (ICC) and Cronbach's alpha) and validity ("construct validity" evaluated by exploratory factorial analysis and "criterion validity"). Correlation coefficients were calculated between SF-12 and SF-36 results regarding the MCS and PCS dimensions independently. To evaluate the "responsiveness to change", longitudinal clusters were set up using KML.
Results: We collected >2000 PROMs forms. Mean age was 53.4 years (SD = 13.3) and 65.0% of respondents were male. SF12 displayed characteristics comparable to SF36, with good accuracy, precision and reliability: for SF12 MCS and PCS scores, ICC (M12-M18) were 0.74 and 0.84 respectively, Cronbach's alpha = 0.890±0.005 and 0.850±0.004, respectively. Factorial analysis confirmed the bidimensionality of the questionnaire (KMO =0.87 and Barlett test<0.001). The MCS and PCS scores of SF12 and SF36 were well correlated (r=0.98 and 0.92 respectively, p<0.005). The same clusters of HQOL profile over time were found in 92.5% and 90.4% of the patients for MCS and PCS, respectively.
Conclusions: We showed that SF-12 has similar psychometric qualities to SF36 in KTRs. SF-12 is valid and reliable, and can be an efficient alternative for assessment of HQOL of KTRs in routine practice.

P406 VIRAL INFECTION CYTOMEGALOVIRUS AND POLYOMA BK VIRUS, IMMUNIZATION AND LONG-TERM RENAL GRAFT SURVIVAL

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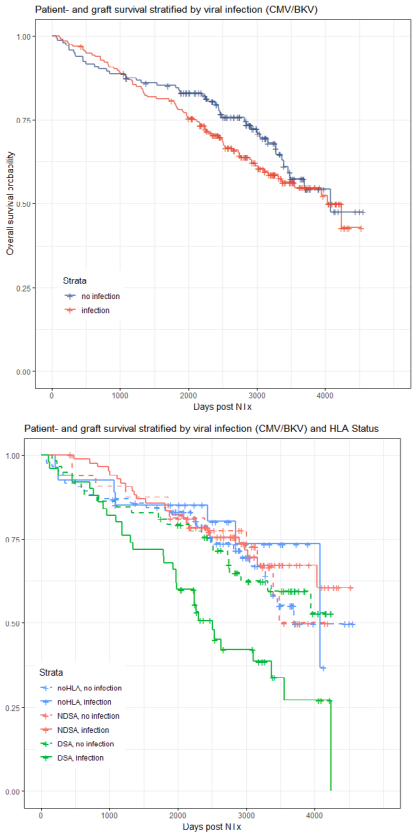
Background: Posttransplant kidney survival depends on several risk factors: Viral infections (cytomegaly (CMV) and polyoma BK (BKV)), or the development of HLA antibodies (ab) may hurt the graft. Vice versa, the absence of HLA donor specific antibodies (DSA) seems to determine the graft´s longevity.
Methods: Patient and graft survival (recorded by Kaplan Meier curves and logrank testing) was determined within an observational, single centre study including patients transplanted from 2010 to 2016 with a follow up until 2022. All patients presented in the outpatient-clinics with a standardized posttransplant work-up including (1) viral screening (BKV, CMV), and (2) screening the HLA antibody-status (no-HLA-ab, non-specific HLA-ab (NDSA) and donorspecific HLA-ab (DSA)) every 6 months in case of DSA free patients, and every 3 months in case of DSA + patients (for 2 years, and on the long-term every year per indication). CMV prophylaxis was administered according to the CMV risk status
Results: A full dataset was obtained from 336 patients. Viral infection with CMV or BKV (in terms of positive PCR, first event of CMV or BKV counted) had no impact on the overall patient and graft survival (Chisq= 1.3, p = 0.254). The patient and graft survival differed between the three groups no-HLA, NDSA, DSA (Chisq= 9.8, p=0.007), with a worse outcome for DSA+ patients. The cohort was further stratified for infection in addition to the DSA status (Figure 1). Log rank testing revealed a worse survival for DSA+ patients with viral infections (Chisq =20.3, p=0.001)
Conclusions: Applying standardized viral screenings and CMV prophylaxis after transplantation, CMV and BK viral infections didn´t harm patient and graft survival in our cohort, whereas the presence of DSA reduced survival. Further stratification showed, that the coincidence of DSA and viral infection significantly reduced patient and graft survival. This finding might impact the allocation process: Risks for viral infections- such as high-risk CMV-serostatus, should be minimized in patients with a high immunological risk.

Figure 1



P407 EVALUATION OF THE BENEFIT OF PHARMACEUTICAL INTERVIEWS (PI) FOR DE NOVO KIDNEY TRANSPLANT PATIENTS AT 6 MONTHS

Malissa Boucida*[1], Marguerite Vaillant[1], Marie Antignac[1], Benoit Barrou[1], Nadia Arzouk[1], Helga Junot[1]

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Background: As part of the department's therapeutic education program (TEP), the pharmacy set up a PI for de novo kidney transplant patients, at discharge (M0), to help them manage their immunosuppressive therapy (IT). Patients are recalled at 6 months (M6) to assess their knowledge at a distance from their transplant.
Methods: The PI takes place after the session with the TEP nurses and is designed to verify that the knowledge of IT treatments is acquired. To do this, the pharmacists fill out a questionnaire during this PI.
Six months later, during a telephone call back by the pharmacy, a new questionnaire is proposed to review knowledge and discuss tolerance and daily management. The benefit of PI is evaluated by comparing the results of the two questionnaires.
Results: All patients (N=23) seen since April 2022 were recontacted at M6. Of these, only 13 patients responded. Overall, the PI gained 1 point on the total response score (7.2/10 at M0 versus 8.1/10 at M6). Concerning knowledge about IT and other treatments related to the transplant, 100% of patients mastered all the notions at M6 (against 69% at M0). For the behaviour to adopt in sensitive situations, it was necessary to re-examine some notions, even at M6: in case of forgetfulness or vomiting (N=6 at M0 against N=3 at M6); self-medication (N=5 against N=3); recognition of the signs of an infection (N=4 against N=10). For the hygienic-dietary rules: 2 patients did not know how to adapt their diet at M6; 3 did not know how to identify foods to be avoided at either M0 or M6 (grapefruit, St. John's wort, pomegranate); 10 declared that they practiced a daily physical activity at M6. Among the new concepts at M6: 9 patients had set up a method to avoid forgetting their treatment (alarm, pillbox). 6 patients declared a problem of compliance: 3 sometimes, 3 more than twice a month. For tolerance: 3 patients had adverse effects related to ITs, mostly tingling. All knew how to warn the medical team and none of them interrupted their treatment.
Conclusions: The results show the benefit of PIs in providing essential assistance to patients in managing their IS treatment as well as in adherence to treatment. However, some notions need to be revisited at M6, suggesting that regular PIs should be organized throughout the patient journey. A link with pharmacists should therefore be developed in this context.

P408 LEUKOPENIA AFTER KIDNEY TRANSPLANTATION: SWITCH FROM MYCOPHENOLATE TO MTOR-I IS SUPERIOR TO REDUCE ALLOSENSITIZATION AND ACHIEVE CMV SEROCONVERSION

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Background: Mycophenolic acid (MPA) is a standard component of maintenance immunosuppression after kidney transplantation. MPA, however, increases the risk of leukopenia. In the past, mTOR inhibitors (mTOR-I), combined with calcineurin inhibitors (CNI), were considered immunologically safe but showed higher mortality in the long term.
Methods: We conducted a single-center observational cohort study analyzing 98 kidney transplant recipients (KTRs) under standard triple maintenance immunosuppression between 2020 and 2022 who developed leukopenia. We compared patient and kidney allograft outcomes between 31 KTRs who were temporarily switched from MPA to mTOR-I and 67 KTRs who underwent a reduction of MPA dose.
Results: A switch to mTOR-I was performed more often among CMV high-risk KTRs (50% vs. 21%, p=0.009), CMV primary infection (68.2% vs. 22%, p<0.001), and more severe leukopenia (median nadir of neutropenia: 0.52 G/L vs. 0.86 G/L, p=0.023). The median duration of leukopenia was comparable between the two groups (69 vs. 80 days). 9 of 67 KTRs (13%) developed de novo donor-specific antibodies (dnDSA) under reduced MPA compared to 1 of 31 KTRs (3%) under mTOR-I only (p=0.17). Biopsy-proven rejections were comparable between the two groups (1 in each). There was a slight but insignificant improvement of eGFR under mTOR-I compared to MPA (ΔeGFR +17 vs. +7 ml/min/1.73m2, p=0.13) and no difference in proteinuria. CMV seroconversion occurred more frequently (0.015) among CMV high-risk KTRs under mTOR-I (14/16 KTRs (88%) vs. 7/15 KTRs (47%) under reduced MPA) CMV high-risk KTRs (46.7%) under reduced MPA) and earlier (190 vs. 265 days, p=0.185).
Conclusions: A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leukopenia, especially in CMV high-risk KTRs. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy could reduce the risk of allosensitization. Under mTOR-I CMV high-risk KTRs achieved seroconversion earlier and more frequent.

P409 GLOBAL BURDEN OF IMMUNOSUPPRESSION AND ITS ASSOCIATION WITH BKV MORBIDITY IN ABOI VS. PRE-TRANSPLANT DSA-POSITIVE KIDNEY TRANSPLANT RECIPIENTS

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Background: ABO blood group-incompatible kidney transplantation (ABOi) may be associated with increased BK virus (BKV) replication. The reasons for this remain unclear, but might be attributable to more intense immunosuppression and/or use of rituximab. Global burden of immunosuppression can be estimated via quantification of Torque-Teno-Virus (TTV) in recipient blood and offer insight into this ABOi-specific phenomenon.
Methods: Longitudinal TTV-PCR was assessed in 38 ABOi and 143 pre-transplant DSA+ patients (Tx 2007-2018). TTV load was determined at baseline and at months 3, 6, 12 and 18. BKPyV-DNAemia was defined as at least two consecutive positive BKV-DNA detections in blood. Additionally, we recorded frequencies of presumptive (>10.000c/mL, without biopsy) or definite BKPyVAN (biopsy-confirmed).
Results: CD20 antibody rituximab was used in 63% of ABOi patients and ATG plus semi-selective immunoadsorption in 89% of DSA+ patients. TTV loads in ABOi patients were 7.6x10^4 at baseline and 1.5x10^9, 4.0x10^9, 5.3x10^6, and 9.1x10^5 at M3, M6, M12 and M18. In DSA+ patients, baseline TTV load was 5.3x10^3 and 1.1x10^8, 6.9x10^6, 9.7x10^5 and 9.8x10^4 at M3, M6, M12 and M18, respectively. Comparing ABOi with DSA+ we found higher TTV levels in ABOi at baseline (p=0.04), with significant differences at M6 (p=0.018) but not at M12 (p=0.64) or M18 (p=0.31). Incidences of any BKPyVDNAemia did not differ between groups (ABOi 23.7% vs. 30.8% in DSA+; p=0.53). The same was true for presumptive BKPyVAN (ABOi 15.8% vs. 11.9%, p=0.6), but definite BKPyVAN were observed more frequently in ABOi patients (13.2% vs. 3.4%, p=0.03). Interestingly 17.4% of presumptive BKPyVANs occurred 18 months or later after transplantation.
Conclusions: The overall higher TTV load in ABOi recipients may reflect the use of rituximab before transplantation. As suggested by the literature BKPyVAN rates were higher in ABOi patients, although BKPyVDNAemia did not differ between groups. Prolonged BKPyVDNAemia screening may be considered in these specific patient groups.

P411 PROTEINURIA AND TYPE OF ALLOGRAFT INJURY IDENTIFY KIDNEY TRANSPLANT RECIPIENTS BENEFITING MOST FROM BELATACEPT CONVERSION

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Background: Conversion to belatacept is associated with an improvement in kidney allograft function. Yet, not all kidney transplant recipients (KTRs) seem to benefit equally from this change in maintenance immunosuppression. Both type (alloimmune vs. non-alloimmune) and severity (assessed by proteinuria) of kidney allograft injury may impact the functional response.
Methods: We studied 37 KTRs from belatacept conversion to 1-year post-conversion. KTRs were categorized based on pre-conversion proteinuria: 21 KTRs with low (<500mg/day), 12 with moderate (500-1000mg/day), and 4 with high proteinuria (>1000mg/day). KTRs were analyzed concerning change of kidney allograft function, change of proteinuria, and type of allograft injury.
Results: 17 of 21 KTRs (81%) showed low proteinuria pre- and post-conversion, and 5 of 16 KTRs (31%) with moderate/ high proteinuria pre-conversion showed low proteinuria post-conversion (group 1, n=22). 8 of 12 KTRs (67%) showed moderate proteinuria pre- and post-conversion, and 1 of 21 KTRs (5%) with low proteinuria pre-conversion developed moderate proteinuria post-conversion (group 2, n=9). 3 of 4 KTRs (75%) showed high proteinuria pre- and post-conversion, and 3 of 21 KTRs (14%) with low proteinuria pre-conversion developed high proteinuria post-conversion (group 3, n=6). 16 of 22 KTRs with low proteinuria post-conversion (73%; group 1) showed an increase in eGFR at 1-year post-conversion (≥10% from pre-conversion baseline eGFR) compared to 6 of 9 KTRs (66%, group 2) with moderate proteinuria post-conversion, and 1 of 6 KTRs (17%, group 3) with high proteinuria post-conversion (p=0.008). Alloimmune injury was assumed in 5 of 22 KTRs (23%, group 1), 3 of 9 KTRs (33%, group 2), and 4 of 6 KTRs (75%, group 3), respectively.
Conclusions: KTRs with low proteinuria and non-alloimmune injury benefit most from belatacept conversion concerning improvement of kidney allograft function. While aggravation of proteinuria post-conversion is rare, some KTRs may show improvement post-conversion. If belatacept conversion is still beneficial compared to CNI-based immunosuppression among KTRs with high proteinuria and alloimmune injury needs to be studied.

P412 VITALISE-PILOT, A FEASIBILITY PROJECT: EX VIVO OPTIMISATION OF DONOR LUNGS WITH INHALED SEVOFLURANE DURING NORMOTHERMIC EX VIVO LUNG PERFUSION

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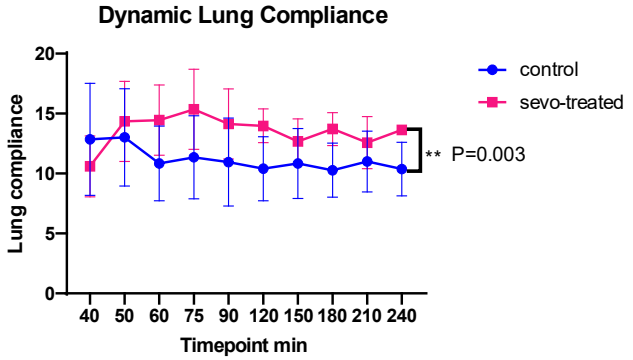
Background: Volatile anaesthetics have shown to reduce pulmonary ischemia reperfusion injury (IRI) in various animal models and humans and are associated with reduced levels of oxidative stress and inflammation, reduced pulmonary oedema and improved oxygenation. Ex vivo lung perfusion (EVLP) facilitates evaluation of potential grafts and enables extension of preservation time. In addition, EVLP could serve as therapeutic platform to improve quality of donor lungs. We hypothesize that ventilating lungs with sevoflurane during EVLP is feasible and improves lung quality.
Methods: We performed a pilot study to test the feasibility of ventilating lungs with sevoflurane during EVLP in a slaughterhouse sheep model, comparable with the clinical setting of a deceased circulatory dead donor. Lungs were harvested, flushed, and preserved cold storage for 3h, after which EVLP (4 hours) was initiated. When a temperature of 32°C was reached ventilation was started. The lungs were ventilated with a mixture of air and oxygen (EVLP, n 5) and in the intervention group sevoflurane 2% end tidal concentration (Cet) was added (S-EVLP, n 5). Perfusate and tissue samples were collected and functional measurements, including perfusate gas, were recorded and analysed. Compliance data were recorded every 30 minutes. Normally distributed, repeated measurements were analysed with a two-way ANOVA and a Mann Whitney test was used for not-normally distributed data.
Results: After approximately ten minutes a steady state of the target Cet sevoflurane was reached. Sevoflurane was measurable in the perfusate. Samples that have been taken right after the deoxygenation period showed decreased sevoflurane levels in the perfusate compared with samples taken during normal perfusion settings. The S-EVLP group showed markedly better dynamic lung compliance over time than the EVLP group (p = 0.003). Oxygenation capacity was non-significantly superior in treated lungs, indicated by a better delta pO_2 (+3,8 vs. -11,7 kPa, p = 0,151) and a higher P/F ratio (437 vs. 347 mmHg, p = 0,054). Perfusate AST levels in the S-EVLP group were significantly reduced compared to the EVLP group (198.1±93.66 vs 223.9±105.7 U/L, p=0.02).
Conclusions: Ventilating lungs with sevoflurane during EVLP is feasible and showed potential to improve lung quality.



P413 SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION AND ITS EFFECT ON BONE

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Background: Simultaneous pancreas and kidney transplantation (SPKT) is the treatment of choice for subjects with type 1 diabetes in advanced stages of diabetic nephropathy. Bone impairment in SPKT candidates is of combined etiology (diabetic osteopathy and renal bone disease) and the bone loss might be further accelerated in the early post-transplant period mainly due to the administration of high doses of corticosteroids.
Methods: The aim of our study was to compare retrospectively the development of bone mineral density (BMD) evaluated by dual energy absorptiometry (DXA) before SPKT and after the successful procedure in the same subjects. We analyzed 52 subjects (39 men, 13 women, mean age 41.9 ± 10.0 years) who entered the waiting list for their first SPKT in years 2011-16, waited more than 12 months for the surgery, were not on any antiresorbtive treatment and DXA was available from their pre-transplant examination, within ± 28 days from the date of the transplantation and 2 years after SPKT.
Results: Lumbar spine (LS) BMD was stable during the pre-transplant interval but increased significantly after SPTK (1.091 ± 0.133 vs 1.170 ± 0.125 g/cm2, $p < 0.001$). Femoral neck (FN) BMD decreased significantly during the waiting period (0.887 ± 0.136 vs. 0.864 ± 0.122 g/cm2, $p < 0.05$) with insignificant post-transplant increase. Trabecular bone score (TBS) declined during the pre-transplant interval (1.288 ± 0.118 vs 1.225 ± 0.113, $p < 0.001$) but significant increase after SPKT was registered (1.225 ± 0.113 vs 1.260 ± 0.123, $p < 0.05$). The difference in BMD development between the pre-transplant and post-transplant period was significant for all sites: LS ($p < 0.001$), FN ($p < 0.05$) and TBS ($p < 0.01$)
Conclusions: Despite intensive corticosteroid treatment in early post-transplant period successful simultaneous pancreas and kidney transplantation has a positive impact on bone metabolism probably due to the restoration of kidney function, normoglycaemia and increased mobility of patients.

P415 NON-HLA ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS WITH INDICATION AND FOLLOW-UP GRAFT BIOPSIES AT ONE AND THREE YEARS

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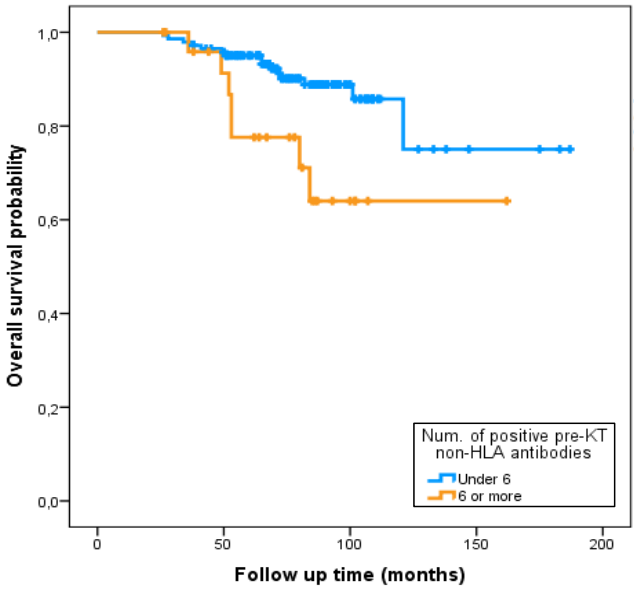
Background: Donor-specific HLA antibodies (HLA-DSA) contribute to antibody-mediated rejection (ABMR) after kidney transplantation (KT) and worse graft-survival. The role of non-HLA antibodies in the development of ABMR or microvascular inflammation (MVI) without HLA-DSA is less clear.
Methods: We evaluated 169 KT recipients (2006-2019) in our center with available serum samples preKT and at the time of biopsy. Patients had either one or two graft indication or protocol biopsies after KT with available serum samples. Biopsies corresponded to one (n=158) or three (n=146) years after KT. We analyzed the presence of 60 non-HLA antibodies in sera with a multiplex Single Non-HLA Beads kit (LIFECODES®) on a Luminex® platform. Then, we assessed the association of non-HLA antibodies at different time points with graft-survival and with ABMR/MVI at one and three years (n= 44 and 41 respectively).
Results: Altogether, non-HLA Abs were present in 84.6% before KT and 84,8 and 82,9% at one- and three-years' post-KT. We found that 15.4% patients with 6 or more non-HLA-Abs pre-KT had worse graft-survival (89.5 vs. 73.1%, p=0.012, Figure 1), being antibodies anti-thyroglobulin and PRKCZ the most frequent ones. Regarding the 60 distinct non-HLA antibodies, pre-KT and first year antibodies against GSTT1 associated with ABMR/MVI at one- and three-year biopsies (p=0.038 and 0.048, and p=0.027 and 0.004 respectively). Anti-P2RY11 and anti-IL2 antibodies at one year serum associated with ABMR/MVI at 3 years biopsies (p=0.017 and 0.016).
Conclusions: We detected non-HLA-Abs in around 80-85% patients before and after KT with a non-HLA Single Ab test. We found an association between the presence of 6 or more non-HLA-Abs pre-KT and graft-survival, and between anti-GSTT1 pre-KT and one year post-KT with ABMR/MVI at one and three year biopsies. Anti- P2RY11 and anti-IL2 antibodies at one year also associated with ABMR at 3 years.



P416 RESTING LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION CAUSING CRITICAL ILLNESS, TO TRANSPLANT OR NOT TO TRANSPLANT?

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Background: Left ventricular outflow tract obstruction (LVOTO) is well described in the literature among cirrhotic patients, and is found on preoperative testing with Dobutamine stress echocardiogram (DSE) or seen intraoperative post reperfusion. LVOTO often leads to significant intraoperative hypotension but has not been shown to affect overall mortality. Orthotopic liver transplantation (OLT) is curative. We present a case of resting LVOTO causing critical illness in the pre-, peri-, and post-operative setting found on preoperative transthoracic echocardiogram (TTE) which was not DES testing induced. As far as we know, this is the first case report of resting LVOTO prior to transplant.
Methods: This case report presents a 61 year old male patient with NASH cirrhosis and a MELD of 29 who was critically ill with significant resting LVOTO in the pre-operative setting. TTE measurements taken pre transplant in the ICU revealed resting LVOT gradients in excess of 140 mmHg with a mean above 50 mmHg. His cardiac dysfunction had become so profound that he was not expected to survive without OLT. The transplant team was presented with an ethical dilemma: a successful OLT would cure the patient of LVOTO but the chances of success were not clear given the severity of the patient's illness. Electing to attempt OLT without guarantee of success had to be weighed against the alternative of forgoing OLT and allowing the allograft to be allocated to another patient.
Results: The team elected to perform OLT. Anesthesia was able to successfully manage intraoperative hypotension with alpha agonists, vasopressin, volume resuscitation, and TEE monitoring. LVOT gradients ranged from 37 to 84 mmHg. However, he was transferred to the ICU post-op on two vasopressors with worsening LVOTO and a post-op peak gradient of 220. His condition did ultimately improve. He was weaned from pressors within 48 hours. He was discharged on post-op day 6 and continues to do well at three months.
Conclusions: We share our experience in order to help better elucidate the nuanced presentation of this well-known pathophysiology and we call for more case reports so that we may begin to develop a trend from which more informed management decisions can be made in the future for resting LVOTO.

P417 FACTORS ASSOCIATED WITH PREMATURE LOSS OF KIDNEY GRAFTS FROM DONORS > 70 YEARS

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Background: Kidney transplantation (KT) outcomes with kidneys from older donors are worse than with optimal donors. However, in some cases, the loss of grafts occurs prematurely with respect to their potential, the factors involved being unknown. Our objective was to determine the factors associated with premature loss of kidney grafts from older donors.
Methods: We analyzed 252 KT recipients from donors >70 years old (2011-2021). Previous KT (n=24) and early losses (<3 months, n=35) were excluded. The median survival of the graft (return to dialysis or eGFR<15ml/min) was determined, considering "premature loss" that survival of the graft <40 months.
Results: 193 recipients analyzed were 71±6 years old and the donors 77±4 years old. 47% suffered premature loss, especially due to death (61.5%). We observed no differences in donor/recipient age, donor type or cold ischemic time between groups. *Before KT*, donor creatinine was better in longer-lasting grafts, and recipients had less cardiovascular disease and more residual diuresis. *After KT*, recipients with premature loss presented more DGF, cardiovascular events and worse renal function the first year after KT (table). In the multivariate analysis, hemodialysis [HR 4.2, CI 1.0-19.4 p=0.041], DGF (HR 1.5, CI 0.9 -2.6), admissions for infections (HR 2.0 CI 1.0 – 3.8), and increased proteinuria at 6 months (P/C >1gr/gr) (HR 3.2 CI1.7-5.9) were associated with graft loss.
Conclusions: Donor and recipient factors influence the success of KT from older donors. The main cause of graft loss is premature death of the recipient. The early identification of KTs that will have a shortened survival is essential for the correct allocation and management of the transplant and the recipient.

P418 FACTORS ASSOCIATED WITH HEALTH RELATED QUALITY OF LIFE IN A GREEK COHORT OF KIDNEY TRANSPLANT RECIPIENTS: A PROSPECTIVE STUDY

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Background: : Improvement in short term patient and graft survival of kidney transplant recipients (KTRs) has shifted interest to the long term outcomes and Health Related Quality of Life (HRQoL) estimation is closely related. The aim of this prospective study was to assess possible changes in HRQoL during follow up and to identify factors that might affect these changes.
Methods: The Greek version of the Kidney Transplant Questionnaire 25 (KTQ-25) and the Greek SF-36 were administered twice in a cohort of KTRs, at study entry and after one year. Sociodemographic, clinical-lab data were collected at both time points. Inclusion criteria were, age≥18years old, time since transplant≥1 year, functioning graft.
Results: 74 out of 84 KTRs initially included (3 died, 4 denied reassessment, 4 changed center), completed the study. Patients mean age was 53.5 years (59 males), mean e-GFR 47.7±15ml/min/1.73m^2 and average time since transplant 56±48 months. The majority of KTRs was married (73.8%), non-smokers (81.6%), retired (60.7%), received hemodialysis before transplantation (62%) and had a deceased graft (59.52%). KTRs were receiving steroids in 84.3%, Tacrolimus 54.2%, Cyclosporine 40.9% and MMF 91.8%. The observed KTQ-25 and SF-36 scores in all dimensions both time-points were similar without significant changes. A multivariate regression analysis for the 5 KTQ-25 dimensions at the end of the study showed that variables significantly associated with Physical Symptoms dimension was age (p=0.02) directly and osteoporosis (p=0.02) inversely. Significant variables for Fatigue dimension remained, female sex (p=0.04) and higher serum cholesterol (p=0.01). Uncertainty/Fear dimension was significantly worse in KTRs with cardiovascular disease (CVD) (p=0.03). Appearance dimension was positively correlated with female sex and negatively with age and CVD (p=0.02, p=0.04 and p=0.04, respectively). Total KTQ-25 score was significantly correlated with female sex (p=0.02), while history of CVD had a negative impact on the score (p=0.01).
Conclusions: In this prospective study of HRQoL in a Greek cohort of stable KTRs, no significant changes were found in the scores of KTQ-25 and SF-36 instruments. Age, sex, osteoporosis, serum cholesterols' levels and history of CVD are some of the factors that might affect HRQoL of KTRs.

P420 FROM PALLIATION TO FULL-TIME OCCUPATION: CYSTIC FIBROSIS PATIENT WITH BURKHOLDERIA CEPACIA COMPLEX ON ECMO SURVIVES LUNG TRANSPLANT AND MENINGITIS

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Background: We report the evolution of a 18-year-old cystic fibrosis patient (compound heterozygote for F508/CFTRdele2.3), BMI 15.1 kg/m^2 on triple CFTR-modulator therapy without adequate response with subsequent pulmonary deterioration of end-stage lung disease leading to intubation, prolonged ECMO support and for whom lung transplant (LT) as therapeutic option was always considered to be non-viable due to the long-standing active infection with Burkholderia cenocepacia (BCC). Before activating a palliative therapy after 2 weeks on ECMO without signs of recovery, the treatment team decided to perform a LT despite the dismal prognosis based on the expected complicated course of BCC infection.
Methods: The bilateral lung transplantation was performed after 14 days on ECMO and ongoing antibiotic treatment with ceftazidime/avibactam and temocilline. Intraoperatively taurolidin rinses of the thoracic cavity were performed.
Results: The initial postoperative course was uneventful with continued combination antibiotic treatment (cefiderocol and meropenem) which were continued after discharge on day 55 for a total duration of one year (!) as outpatient and subsequently deescalated to one drug treatment and then stopped. After rehab she continued her vocational training as office clerk and finished her training 1 year later. She subsequently received a full-time employment in the company where she trained and has survived so far 2 years and 4 months to date. One major complication occurred 6 months postoperatively when despite ongoing dual antibiotic treatment, a basal meningitis occurred due to the local progression of the BCC infection with osseus defect leading to a communication between the left ear and the brain cavity. Surgical revision was imminent and besides debridement of the infectious cavity antibiotic beads were locally introduced to achieve better local control of the infectious focus (Dalbert et al., doi:10.1002/ccr3.5516) After extended duration of intravenous antibiotics we reintroduced triple CFTR modulator therapy to aid with better drainage of sections in the ear nose and throat region. The subsequent course has been uneventful so far.
Conclusions: Although formally listed as a contraindication, LT in highly selected BCC positive patients could be considered. Unusual case evolution.

P421 MATERNAL LIVING DONOR LIVER TRANSPLANTATION OFFERS NO PROTECTION AGAINST GRAFT REJECTION AND GRAFT LOSS

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Background: The effect of gender on graft prognosis is a recognized entity in adult liver transplantation with male recipients of female grafts exhibiting the lowest graft and patient survival. The effect on gender mismatch in pediatrics is less well defined. Related living donation adds the dimension of maternal antigen exposure prior to liver transplantation. The presence of non-inherited maternal antigens (NIMA) potentially induce a degree of tolerance to future maternal grafts in the child which bear the antigens shared by microchimeric cells. This study sought to determine the effect of receiving a maternal liver graft on graft rejection and survival rates relative to a non-maternal graft.
Methods: A retrospective cohort study was performed on all children below 18 years of age who underwent living donor liver transplantation at our institution from 2012 to 2020. Rates of graft loss and biopsy proven rejection were compared between patients who had received a maternal graft to those who did not. Recipient, donor and transplant characteristics were recorded as well as rates of biliary and vascular complications.
Results: A total of 87 children underwent related living donor liver transplantation. Donors were 60% maternal, 21% paternal and 19% non-parental. Median recipient age was 19 months (IQR 13 to 37 months) with equal gender distribution. Predominant indication for liver transplantation was chronic cholestatic liver failure, with 15% of the cohort presenting in acute liver failure. Mean PELD scores at transplantation were 16.2. The majority of recipients received standard immunosuppression of steroid and calcineurin-inhibitor. Between the two groups, rates of graft loss (18%), first episode biopsy-proven rejection (31%), biliary complications (38%) and vascular complications (12%) did not differ.
Conclusions: Maternal living donor liver transplantation offered no protection against graft loss, rejection, biliary or vascular complications compared to other related living donors in this cohort of patients. Current evidence to support preferentially selecting maternal donors for liver transplantation in the paediatric population is scanty. Further studies on the effects of current immunosuppression regimes on the immunotolerant arm of the immune system is warranted.

P422 REMARKABLE MORTALITY BEFORE LIVER TRANSPLANT IN BILIARY ATRESIA; PRELIMINARY OUTCOMES FROM A 14-YEAR COHORT STUDY

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Background: Biliary atresia (BA) is a leading etiology for liver transplantation (LT) in pediatric settings. Considering the surgical and anesthetic obstacles for LT at very young ages, Kasai portoenterostomy (KPE) performs to save naïve organs till when the patient can undergo LT. In this study, we have retrospectively surveyed the long-term outcomes of BA after KPE.
Methods: 196 confirmed cases of BA who underwent KPE between 2007 and 2021 included in the study. The patients' baseline demographic, clinical, paraclinical characteristics, as well as operation information and follow-ups were collected from medical records and telephone interview.
Results: Clinical and paraclinical characteristics are demonstrated in Table 1. We could not determine the end-point outcomes of 49 (25%) cases. From the rest, 22 cases underwent LT, of which 13 were alive, and 9 died. Furthermore, 56 cases survived without undergoing LT, and 69 died before LT. Higher level of pre-KPE AST, and total bilirubin, longer hospital stays and further hospital admissions were significantly associated with poor outcomes (death or LT).
Conclusions: Many lives are being lost after KPE on the LT waitlist due to inability to undergoing LT, limited organ pool, and mismatched parental donors. Considering prognostic determinants along with PELD for organ allocation and establishing newer techniques of LT in this age group may improve the outcomes significantly.

KPE age, day		71.47 ± 24.87	Hospital stay (day)	16.07 ± 8.40
Male gender		90 (45.9)	Post KPE jaundice	58 (29.6)
Jaundice age (week) (%)	1	128 (65.3)	Post-KPE Cholangitis	40 (20.4)
	>=2	40 (20.4)	Post KPE Hospital admissions	89 (45.4)
Dark urine		35 (17.9)	Liver transplant	22 (11.22)
Pale stool		78 (39.8)		
Hepatomegaly		81 (41.3)	Alive without liver transplant	56 (38.09)
Splenomegaly		25 (12.8)	Alive with liver transplant	13 (8.84)
Gall bladder	Absent	82 (55.4)	Dead without liver transplant	69 (46.93)
	Others	66 (44.6)	Dead with liver transplant	9 (6.12)
		Pre- KPE	Post-KPE	
BUN		7.65 ± 2.80	8.51 ± 3.95	
Cratinine		0.18 ± 0.14	0.18 ± 0.18	
AST		252.51 ± 130.70	207.13 ± 139.17	
ALT		148.27 ± 90.72	206.98 ± 129.17	
Alkaline phosphatase		1700.89 ± 690.96	747.82 ± 331.89	
Total bilirubin		10.28 ± 3.15	8.39 ± 2.66	
Direct bilirubin		5.54 ± 2.04	4.49 ± 1.85	
Albumin		4.06 ± 0.48	3.17 ± 0.56	
Platelet		442.93 ± 173.35	385.46 ± 195.51	

P423 THE INFLUENCE OF ANTIBODIES AGAINST MICA ON THE OUTCOME OF KIDNEY TRANSPLANTATION: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Major histocompatibility complex class I chain-related proteins A (MICA) are polymorphic antigens that induce considerable alloimmune response. The impact of anti-MICA antibodies (anti-MICA), alone or in association with HLA donor specific antibodies (HLA-DSAs), on the outcome of kidney transplantation (KTx) is investigated.
Methods: Anti-MICA and HLA-DSAs were retrospectively detected in 142 KTx recipients, 71 with biopsy proven acute or chronic active rejection (rejection group, RG) and 71 with comparable characteristics without rejection (control group, CG). Among 71 patients of the RG, 51 were diagnosed with T-cell mediated rejection (TCMR) and 20 with antibody mediated rejection (ABMR). Median follow- up was 3.7 (2.9-5.2) years. Anti-MICA were determined pre- and post-KTx by Luminex method.
Results: Before KTx, 4 (5.6%) patients in the RG, all with TCMR, were found anti-MICA positive vs. 2 (2.8%) patients in the CG (p=0.681). Preformed HLA-DSA were found in 19 (26.7%) patients in RG vs. 6 (8.4%) in CG (p=0.008). Simultaneous detection of preformed anti-MICA and HLA-DSAs was found in 2 patients of the RG, all with TCMR, vs. 0 of the CG (p=0.497). At transplant biopsy, positive anti-MICA were identified in 3 patients with TCMR, preformed in all cases. In 2 TCMR cases anti-MICA and HLA-DSAs were detected simultaneously at biopsy. During follow-up, 13 (18.3%) patients in RG, 8 with ABMR and 5 with TCMR, lost their graft vs. 1 patient (1.4%) in CG (p=0.001). One (1.4%) RG patient, with TCMR, who lost the graft, was found positive for anti-MICA pretransplant. Patient survival with functioning graft did not differ between anti-MICA positive and negative KTx recipients (log-rank p=0.300). Simultaneous detection of anti-MICA and HLA-DSAs did not have significant influence on patient survival with functioning graft (log-rank p=0.071). Graft function at the end of follow-up was better, but not significantly, in anti-MICA negative patients vs. anti-MICA positive ones.
Conclusions: Anti-MICA detection pretransplant is not associated with an increased risk of rejection in our cohort. Their absence appears to be associated, although not significantly, with better renal function without affecting long-term graft survival. Their role in kidney transplantation requires further investigation.

P425 INFECTION, VACCINATION OR BOTH? THE SARS-COV-2 IMMUNE FOLLOW-UP OF KIDNEY AND LIVER TRANSPLANT RECIPIENTS

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Background: The use of vaccination against severe acute respiratory syndrome coronavirus (SARS-CoV-2) significantly limited the spread of the coronavirus disease 2019 (COVID-19) pandemic around the world. However, it is known that over time from the vaccination, an immune response decreases in general population. The reports for immunocompromised individuals as solid-organ transplant (SOT) recipients or chronic kidney disease (CKD) patients appeared similar. Therefore, in order to prolong immunity, it was proposed to use an immune booster with the next, third or fourth vaccination dose. Knowing the importance of protection against COVID-19 for immunocompromised patients, we checked the role of SARS-CoV2 infection history during the vaccination schedules in kidney or liver transplant recipients (KTRs, LTRs) and CKD patients.
Methods: We retrospectively analyzed the data of randomly selected 78 SOT recipients (37 KTRs and 41 LTRs) and 40 patients with IgA nephropathy (IgAN) as representatives of the CKD group. They received two or three 30 µg doses of BNT162b2 vaccine. The follow up was prosecuted in five time points (TP1-5). We assessed the anti-SARS-CoV-2 spike protein IgG antibody (anti-S1 Ab) titer as well as graft function, COVID-19 history and patients' clinical condition.
Results: Ab titer in SOT patients was lower than in IgAN group (p = 0.05). KTRs achieved lower values than LTRs. The protective level after the 3rd dose of vaccination was not observed only in 8.4% at TP4 and 5% at TP5. We demonstrated the advantage in Ab levels of a 2 doses vaccination scheme with COVID-19 history over a 3 doses in a group of patients with no COVID-19 history in TP 1-4 (p= <0,001 - 0,005, respectively). Subjects in 2 doses schedule had a longer median time to infection from the last dose compared to the 3 doses schedule (31.5-39 vs. 9 weeks).
Conclusions: Our results showed that approach to the vaccination schedule should be individualized and should take into consideration vaccine response rate and medical history including COVID-19 history. So-called the hybrid immunization appears to be the most effective strategy to protect immunocompromised patients from SARS-CoV-2 infection.

P426 TRANSCRIPTIONAL PROFILES IN BLOOD AND URINE FROM KIDNEY TRANSPLANT PATIENTS WITH REJECTION AND GRAFT ACCEPTANCE

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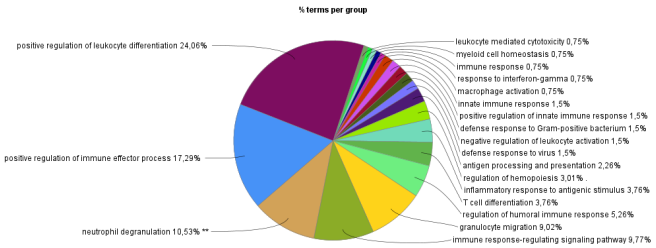
Background: Although the importance of defining the causality of the different transplant outcomes has been identified, to date, little is known about gene expression and the intracellular interaction networks that take place in each outcome. Several studies have proposed differentially expressed genes (DEGs) and microRNAs either as outcome biomarkers or outcome regulators. However, an expression profile that allows differentiating with greater sensitivity and specificity between groups of patients is unknown. We aim to identify DEGs between blood and urine samples from kidney transplant patients with rejection and acceptance processes.
Methods: Blood and urine were collected from patients with acute (AcutePre), chronic rejection (Chronic), long term allograft survival (LTS), and acute rejection after anti-rejection treatment (AcutePost). Blood was collected from dialysis patients (HD) and non-transplanted healthy individuals (HC). RNA was isolated from all samples using Tri Reagent. A minimum of 1 µg of RNA was purified and used for generating cDNA libraries using SureSelect XT RNA Direct Human. Libraries were sequenced using Illumina Novaseq 6000 system. DEGs were those with a Log2FC smaller or greater than -2 or 2, and a FDR smaller or equal to 0,05. For functional Analysis, GO categories were obtained using ClueGO in Cytoscape.
Results: DEGs (Table 1) were used for functional analysis. Because of the amount of data, we chose only functional categories observed in urine mainly because this sample is a striking alternative for the diagnosis and following of rejection and to identify molecules associated with each outcome. Immune system enriched categories associated to up regulated genes in urine of AcutePre (Figure 1A), Chronic (Figure 1B), and AcutePost (Figure 3) are depicted.
Conclusions: According the number of regulated genes in each sample, urine seems to be more transcriptional active when compared with blood. We suggest that urine might reflect the immune response associated to the allograft outcome, and that this sample might be suitable for the identification of transcripts associated with either acute or chronic rejection.

Table 1. Number of DEGs in each comparison described.

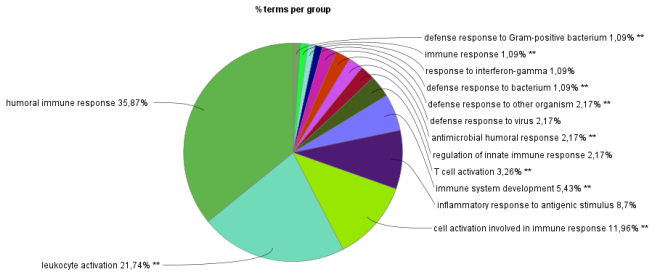
Urine				
Reference group	vs	AcutePre	AcutePost	Chronic
LTS	Up-regulated genes	1058	921	1264
	Down-regulated genes	5729	4658	7059
Peripheral Blood				
Reference group	vs	AcutePre	AcutePost	Chronic
LTS	Up-regulated genes	373	232	133
	Down-regulated genes	147	182	85
HD	Up-regulated genes	304	219	128
	Down-regulated genes	195	215	166
HC	Up-regulated genes	562	378	229
	Down-regulated genes	386	380	184

Figure 1. Immune enriched categories associated to upregulated genes in urine

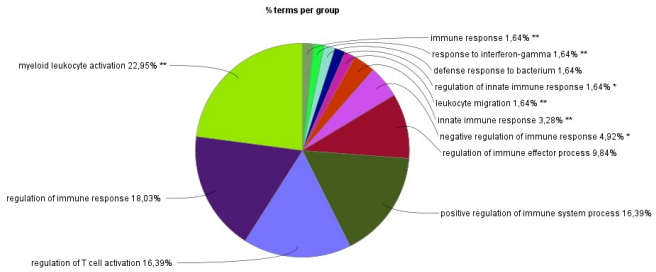
A. AcutePre



B. Chronic



C. AcutePost



P427 THE INFLUENCE OF ANTIBODIES AGAINST ANGIOTENSIN II TYPE-1 RECEPTOR ON THE OUTCOME OF KIDNEY TRANSPLANTATION: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Allo- and autoimmune mechanisms are involved in kidney allograft rejection and loss. The impact of anti-angiotensin II type-1 receptor antibodies (anti-AT1RAbs), alone or in association with HLA donor specific antibodies (HLA-DSAs) on outcome of kidney transplantation (KTx) is investigated.
Methods: Anti-AT1RAbs and HLA-DSAs were retrospectively detected in 142 KTx recipients, 71 with biopsy proven rejection (rejection group, RG); 51 T-cell mediated (TCMR) and 20 antibody mediated rejection (ABMR), and 71 with comparable characteristics without rejection (control group, CG). Median follow-up was 3.7 (2.9-5.2) years. Antibodies were determined by Luminex method for HLA-DSA (positive MFI>1000) and enzyme-linked immunosorbent assay for anti-AT1RAbs (positive ≥10 U/mL).
Results: Before KTx, 23 (32.4%) patients in RG, 16 TCMR and 7 ABMR, were found anti-AT1RAbs positive vs. 11 (15.5%) in CG (p=0.031). Preformed HLA-DSAs were found in 19 (26.7%) patients in RG vs. 6 (8.4%) in CG (p=0.010). Preformed anti-AT1RAbs and HLA-DSAs was found simultaneously in 5 patients of RG, 1 ABMR and 4 TCMR, vs. 2 of CG (p=0.355). At transplant biopsy, positive anti-AT1RAbs were identified in 4 patients with ABMR and 11 with TCMR, preformed (n=12) or de novo (n=3). In 3/4 ABMR and 4/11 TCMR cases anti-AT1RAbs and HLA-DSAs were detected simultaneously. During follow-up, 13 (18.3%) patients in RG, 8 ABMR and 5 TCMR, lost their graft vs. 1 patient (1.4%) in CG (p=0.001). Six out of 13 (46,2%) RG patients, 3 TCMR and 3 ABMR, who lost the graft, were found anti-AT1RAbs positive. Survival with functioning graft did not differ between anti-AT1RAbs positive and negative recipients (log-rank p=0.88) and was not significantly influenced by simultaneous detection of anti-ATR1Abs and HLA-DSAs (log-rank p=0.96). Graft function at the end of follow-up was better, but not significantly, in anti-AT1RAbs negative patients.
Conclusions: Anti-AT1RAbs detection characterizes KTx recipients at increased risk of rejection. Furthermore, anti-AT1RAbs pretransplant, either alone or in association with HLA-DSAs, appear to be associated with impaired graft function. The strong presence of alloimmune mechanisms may obscure our results. However, screening for anti-AT1RAbs may help identify KTx recipients at high immunological risk.

P429 HEART-FAILURE RECOVERY AFTER LUMASIRAN AND ISOLATED KIDNEY TRANSPLANTATION IN PRIMARY HYPEROXALURIA TYPE 1

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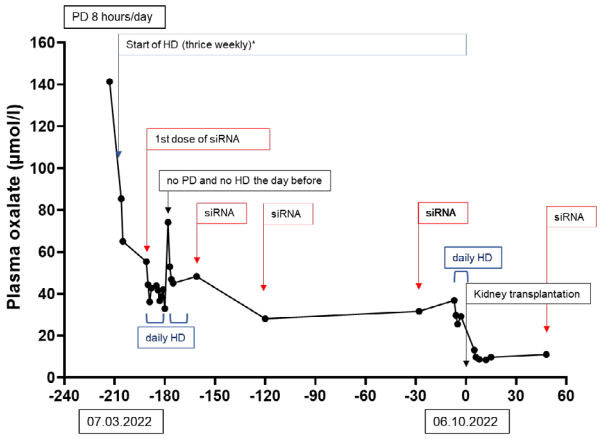
Background: Primary hyperoxaluria type 1 (PH1) is characterized by oxalate stones leading to kidney failure. In advanced stages of disease, systemic oxalate deposition may lead to heart failure. The small interfering RNA (siRNA), lumasiran, reduces the oxalate load and may improve organ impairment in systemic oxalosis.
Methods: We report a 29-year old male patient with PH1, who was referred to our center in March 2022 for evaluation for combined heart-liver-kidney-transplantation.
Results: Kidney failure was diagnosed in August 2021, a kidney biopsy revealed diffuse interstitial nephritis with massive oxalate depositions. Genetic testing confirmed two compound heterozygous Alanine-Glyoxylate Aminotransferase (AGXT) gene mutations. He was on peritoneal dialysis (PD) for 6 months. In addition, he suffered from severe heart failure (NYHA III) with a left ventricular ejection fraction (LV-EF) of 25%, marked left ventricular hypertrophy (septum of 14 mm) and NTproBNP >50,000 pg/mL. A biopsy revealed severe cardiac oxalate deposition. Hemodialysis (HD) therapy was commenced to optimize volume overload and to lower plasma oxalate (Pox) levels. The initial POx level was 141.3 µmol/L and decreased to less than half after combined PD and intensified HD (Fig.). After the start of treatment with lumasiran s.c. and high dose pyridoxine, POx levels further decreased to 29.2 µmol/L. Subsequently, cardiac output improved with an LV-EF of 35-40%. He received a living kidney donation from his father in October 2022 using standard immunosuppression and intensive hydration post KT. Daily pyridoxine p.o. and lumasiran s.c. every 3 months was continued. Kidney function stabilized with a creatinine of 2.0 mg/dL at 3 months follow up. An allograft biopsy one month after KT showed no oxalate deposition. His cardiac function improved further (NYHA I, LV-EF of 55%, NTproBNP level of 449 pg/mL) and his recent POx level was 11 µmol/L.
Conclusions: To our knowledge, this is the first case demonstrating complete remission of heart failure in a patient with PH1 following lumasiran therapy and isolated KT. Our experience underscores the utility of lumasiran and the conclusion, that the cardiac dysfunction related to PH1 is potentially reversible.

Figure



* 3x 4.5 hours/week, unless otherwise stated, PD= peritoneal dialysis, HD= hemodialysis,

P430 THE MINIMIZATION OF IMMUNOSUPPRESSION IN LIVER TRANSPLANT RECIPIENTS: A 3-YEAR PATIENT FOLLOW UP

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Background: The introduction of potent immunosuppression (IS) such as calcineurin inhibitors (CNIs) has increased the one-year survival rates post liver transplantation (LTx) to over 90%. However, due to the deleterious side effects associated with IS such as malignancies, cardiovascular disease, recurrent infections, and chronic kidney disease, no substantial progress had been made in prolonging their long-term survival. Thus, minimization is an approach where IS is decreased to levels that do not cause clinically significant side effects, yet at the same time prevent rejection. Due to the liver's unique ability to modulate its immunological response, it is feasible to introduce IS minimization protocols in liver transplant recipients (LTRs). In our study, IS minimization protocols were introduced to LTRs based on clinical and laboratory characteristics with the aim to establish predictive factors of successful IS minimization.
Methods: In this prospective observational study, adult LTRs were screened for eligibility and 97 LTRs were recruited after obtaining informed consent. Patients were deemed eligible if the primary cause of LTx was a non-autoimmune liver disease, they had a stable graft function for >3 years and no evidence of chronic rejection in histology was recorded. The dose of IS was minimized in 3-month intervals with laboratory tests performed at 2, 4 and 8 weeks after each dose reduction to evaluate liver function. Additional testing was performed to assess graft stability and evaluate IS related comorbidities.
Results: IS minimization was achievable in 87.6% of LTRs. After 36 months, 76 LTRs were on monotherapy with 47 of them being on subtherapeutic doses of CNIs and 2 were on spacing protocols with tacrolimus (table 1). In only 12/97 LTRs (12.4%), an episode of acute graft failure was recorded, which resolved in ALL cases when the dose of IS was returned to the previous amount. An average those, who successfully underwent minimization were of male gender (51.7% vs 40%), younger (54.5 years of age vs 60.1 years of age) and had a lower BMI (25.56kg/m^2 with 31% being overweight or obese vs 26.57 kg/m^2 with 70% being overweight or obese)
Conclusions: Minimization of IS seems to be safe for precisely characterized LTRs and should be implemented in eligible patients to reduce IS-related comorbidities.

Table 1 Immunosuppression therapy at baseline and at 36 months

	AT BASELINE (N=97)	AT 36 MONTHS (N=97)
COMPLETE WITHDRAWAL	1 (1.03%)	1 (1.03%)
SPACING*	0	2 (2.06%)
SUBTHERAPUTICAL# MONOTHERAPY	24 (24.7%)	47 (48.5%)
TAC	24 (24.7%)	45 (46.4%)
CsA	0	2 (2.06%)
MONOTHERAPY	55 (56.7%)	76 (78.4%)
TAC	43 (44.3%)	58 (58.8%)
CsA	5 (5.15%)	9 (9.28%)
MMF	6 (6.19%)	9 (9.28%)
EVE	1 (1.03%)	0§
DUAL THERAPY	39 (40.2%)	18 (18.6%)*
TAC + GCS	17 (17.5%)	6 (6.19%)
TAC + MMF	13 (13.4%)	9 (9.27%)
TAC + EVE	2 (2.16%)	1 (1.03%)
CsA + GCS	2 (2.06%)	0++
CsA + MMF	4 (4.12%)	2 (2.06%)
MMF + GCS	1 (1.03%)	0+++
TRIPLE THERAPY	2 (2.06%)	2 (2.06%)
TAC + GCS + MMF	1 (1.03%)	0++++
CsA + GCS + MMF	1 (1.03%)	1 (1.03%)
TAC + GCS + EVE	0	1 (1.03%)+++++

* TAC 0.5mg taken 5 times a week
\# trough serum concentration of TAC <5ng/ml or CsA <50ng/ml
§ patient switched to monotherapy with TAC
* decrease in number due to the patients being converted to monotherapy
++ patients converted to monotherapy with cyclosporine A
+++ patient converted to monotherapy with MMF
++++ patient converted to dual therapy with tacrolimus and MMF
+++++ addition of everolimus with the intent of withdrawing tacrolimus after consultation with oncological team
Abbreviations used: CsA cyclosporine A, EVE everolimus, GCS glucocorticosteroids, MMF mycophenolate mofetil, TAC tacrolimus

P431 CROSS-PLATFORM VALIDATION OF MOLECULAR MARKERS FOR REJECTION PHENOTYPES AFTER KIDNEY TRANSPLANTATION

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Background: Molecular analysis of allograft tissue is a promising tool to refine the diagnosis of kidney transplant rejection, which has led to the development of several independent diagnostic platforms. The ideal molecular classifier should be translatable from one platform to another to improve its accessibility and application in transplant clinics. Herein, we derived molecular markers for antibody-mediated rejection (ABMR) and T-cell mediated rejection (TCMR) using microarray analysis and evaluated their diagnostic value on the Nanostring nCounter platform.
Methods: In a discovery cohort of 224 kidney transplant biopsies, lasso regression was applied on microarray gene expression data to derive sparse molecular classifiers for ABMR and TCMR using genes from the B-HOT panel. The expression of these classifier genes was then examined by Nanostring nCounter analysis in two independent biopsy cohorts (n= 66 and n= 80, respectively).
Results: In the discovery cohort, a two-gene classifier was identified for ABMR, consisting of PLA1A and GNLY, and a two-gene classifier was identified for TCMR, consisting of IL12RB1 and CD1D. The expression of ABMR and TCMR genes correlated with the extent of microvascular inflammation (spearman correlation coefficient r= 0.66) and tubulointerstitial inflammation (r= 0.39), respectively. In the two Nanostring cohorts, ABMR genes obtained good diagnostic accuracy (AUC 0.82, 95% CI 0.71-0.93 and AUC 0.81, 95% 0.70-0.91, respectively) and TCMR genes obtained fair to good diagnostic accuracy (AUC 0.88, 95% CI 0.79-0.97 and AUC 0.71, 95% CI 0.59-0.83, respectively).
Conclusions: The diagnostic value of sparse molecular markers for ABMR and TCMR can be translated across platforms. However, platform-specific calibration remains necessary to obtain the best model for each molecular assay.

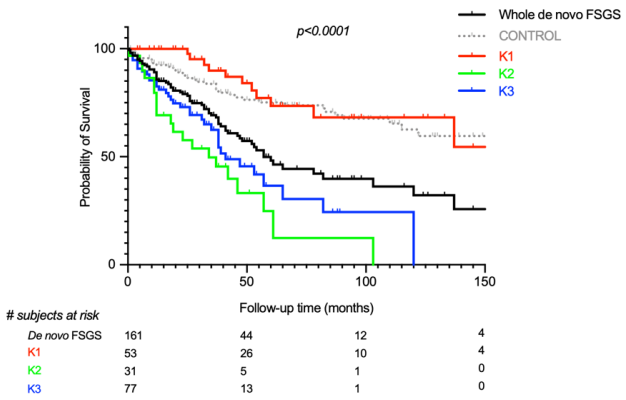
P432 DE NOVO FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN THE KIDNEY ALLOGRAFT: ONE LESION, DIFFERENT OUTCOMES

Juliette Leon[1], Dany Anglicheau[1], Julien Zuber[1], Adel Abderrahmane[1], Jean-Paul Duong van Huyen[1], Christophe Legendre[1], Marion Rabant*[1]

[1]Necker Hospital, Paris, France

Background: Focal Segmental Glomerulosclerosis (FSGS) can be found *de novo (Dn)* or as a recurrence in kidney allograft. While FSGS recurrence has been extensively described as a devastating cause of graft loss, the natural history and the prognosis of *Dn*FSGS remain unknown.
Methods: Using a monocentric prospective database, we analyzed a cohort of *Dn*FSGS in kidney transplant recipients (KTR). Pre- and post-transplant characteristics were recorded as well as graft outcomes. Propensity score matching was used to compare outcomes in the presence or absence of *Dn*FSGS.
Results: From 2001 to 2019, 171 KTRs had a diagnosis of *Dn*FSGS, half of them being at high immunological risk at transplantation. The diagnosis was made at a median time of 4.2 years post-transplant, with a proteinuria of 1.6 ± 1.6 g/g. Based on histological characteristics, a hierarchical clustering divided the cohort into 3 clusters (K1 to K3). K1 (n=58, 34%) was diagnosed earlier post-transplant, half within the first year, and was associated with chronic vascular lesions and ischemic glomeruli. K2 (n=32, 19%) was strongly associated with a concomitant ABMR, mainly chronic active, whereas K3 (n=81, 47%) was diagnosed later (9.3 ± 6.4 years) in the context of IF/TA and chronic vascular lesions. Sixty-seven KTRs (39%) lost their graft over a follow-up of 3.3 years. Overall, the presence of *Dn*FSGS was associated with poor outcomes in comparison to a control cohort of KTRs without FSGS (median graft survival of 57 vs 260 months, p<0.001). Among the clusters, K2 and K3 were significantly associated with an increased risk of graft failure (K2 = HR 7.1 [3.2-15.6], K3 = HR 4.8 [2.2-10.4]), whereas K1 had similar outcomes to the control, even after adjusting to the diagnostic time post-transplant
Conclusions: The occurrence of *Dn*FSGS lesions in KTRs can be seen in different settings. When associated with ABMR or diagnosed on a late biopsy, it is associated with a poor graft survival.

Figure : Kaplan Meier survival curve of time to graft dysfunction in de novo FSGS and matched control cohort.

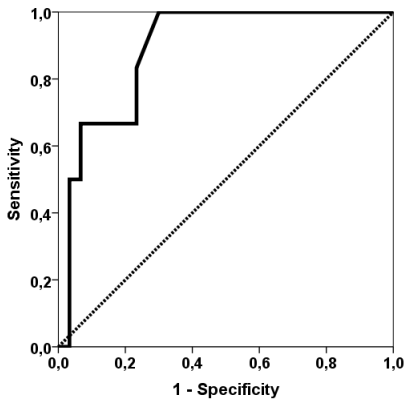


P433 DONOR-DERIVED CELL-FREE DNA IDENTIFIES "TROUBLED" KIDNEY ALLOGRAFTS

Elena González-López[1], Lucía Cañamero[2], J. Gonzalo Ocejo[1], Lara Belmar[2], Juan Irure-Ventura[1], Rosalía Valero[2], Pilar García Berbel[3], Francisco Javier Freire[4], Marcos López-Hoyos[1], Juan Carlos Ruiz[2], Emilio Rodrigo*[2]

[1]Hospital Universitario Marqués de Valdecilla/IDIVAL, Immunology, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla/IDIVAL, Nephrology, Santander, Spain, [3]IDIVAL, Santander, Spain, [4]Hospital Universitario Marqués de Valdecilla/IDIVAL, Pathology, Santander, Spain

Background: Kidney transplantation (KTx) is usually monitored by measuring creatinine, proteinuria, immunosuppressive blood levels, specific donor antibodies and polyomavirus. However, the only way to detect the alloimmune damage is to perform a graft biopsy. Non-invasive monitoring of the alloimmune response could contribute to improving KTx results. donor-derived cell-free DNA (dd-cfDNA) is a new noninvasive biomarker of allograft injury related to rejection before clinical allograft dysfunction. We aim to analyze the role of this biomarker in detecting kidney graft damage and acute rejection in a cohort of KTx.
Methods: We carried out a prospective study including KTx performed in our unit throughout 2021. All acute rejections were biopsy proven (BPAR). "Troubled" graft was defined if the graft was suffering acute rejection, obstruction or graft infection. Blood samples were obtained at 1-month post-transplant. Cell free DNA was extracted from plasma using QIAamp Circulating Nucleic Acid Kit (Qiagen), amplified by using multiplex PCR with CareDX AlloSeq cfDNA kit and sequenced on a MiSeq sequencing instrument (Illumina, Inc.) to calculate the percentage of circulating dd-cfDNA.
Results: 36 KTx recipients were included with an age of 58 ± 11 years, 72% male. Mean 1-month dd-cfDNA was 0.86 ± 0.92%. Six (17%) patients suffered acute rejection before the second month. dd-cfDNA was significantly higher (0.49%, IQR 0.47% vs. 1.54%, IQR 1.56%, p = 0.002) in those patients with BPAR and in 5 patients with antibody-mediated rejection (0.50%, IQR 0.45% vs. 1.83%, IQR 1.33%, p = 0.001). dd-cfDNA discriminated those patients with BPAR (AUC-ROC 0.889, 95%CI 0.773-1.00, p = 0.003) (graph). Among 5 patients with dd-cfDNA above 1% without BPAR, 2 suffered hydronephrosis and required a nephrostomy tube or a bladder catheter and one of them developed a graft pyelonephritis. dd-cfDNA identified "troubled" graft (OR 37.96, 95%CI 3.13-460.23, p = 0.004) independently of renal function.
Conclusions: The determination of dd-cfDNA using Alloseq allows the identification of kidney graft damage, especially rejection, in a minimally invasive way independently of kidney function. Incorporating the determination of dd-cfDNA into the monitoring of KTx recipients offers different information from the markers traditionally used.



P434 AGILE DATA JOURNEY AND GOVERNANCE TO LEVERAGE DIGITAL TRANSFORMATION OF A KIDNEY TRANSPLANT CENTER IN COLOMBIA

Sergio Salcedo Herrera[1], Andrea García López[2], Juan García López[3], Jefferson Barbosa Salinas[3], Jessica Pinto Ramírez[1], Jhon Vélez Arebláez[3], Diego Hernández[3], Fernando Girón Luque*[4]

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Background: Kidney transplantation is a complex clinical service. The decision making of the organization requires the capture of large volumes of heterogeneous clinical data (structured and non-structured). We aim to apply a data journey model to achieve the centralization of patient data across a structured clinical governance process to undergo digital transformation in a kidney transplant service in Colombia.
Methods: We performed a cross-collaborative methodology bridging health informaticians and clinical domain experts using agile methodology (Scrum and SAFe). The data journey was applied through iterative discovery sessions to build a data governance strategy involving data definitions and unified repository for those definitions. That data governance strategy leverages correct data warehousing (Integrating data from multiple operational systems) and finally, having clean, unified, and standardized data allows the organization to analyze, report and visualize resulting structured data.
Results: A total of five health informaticians, three clinicians and two clinical researchers participated in the modeling agile sessions. We identified six service data sources involved in the transplant pathway pertaining to recipients, donors, follow-ups, laboratories, outcomes and providers. Data bases were uploaded and integrated in a data warehouse using data engineering tools such as spark and an HDFS/Hive-based cloud storage. The cleaning process was iterative and took approximately one year. There is a connection to the data warehouse used by researchers who are proficient in R language for doing descriptive and predictive analysis. This allowed self-consumption of information and facilitated the use of electronic health records for research purposes.
Conclusions: Data journey has been a key solution to improve interoperability. By using data journey modelling, we were able to visualize analytics to provide a meaningful assessment of current data (decision making) and to develop two algorithms: one to predict graft survival and one to classify the status of kidney allograft. These findings would translate to other areas of the organization to improve clinical governance process as the agile frameworks helped the organization to achieve these goals the fastest and high-quality way possible

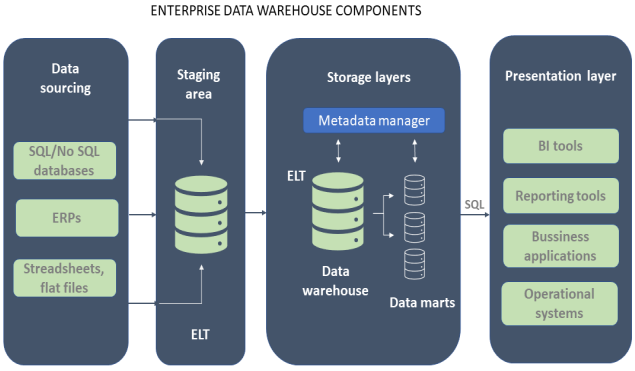

Figure 1. Data sources are all the data sources where raw data originates and/or is stored. Enterprise resource planning **(ERP)** refers to a type of software that organizations use to manage day-to-day business activities. Extract, load, transform **(ELT)** tools connect to all the source data and perform its extraction, transformation, and loading into a centralized storage system for easy access and analysis. The data is finally loaded into the storage space. **Metadata** is data about data. These are the explanations that give hints for users/administrators of what subject/domain this information relates to. **Data marts** are built specifically for a particular subject area, business function, or group of users. **Presentation layer:** The final building block comprises tools that give end users access to data. Also called the **BI interface**, this layer will serve as a dashboard for data visualization, business reporting, and pulling out separate pieces of information for such tasks as machine learning.

P435 EDUCATION ON DIGITAL TRANSFORMATION: A PRIORITY TO MAXIMIZE ITS BENEFITS AND USES. EXPERIENCE OF A SINGLE CENTER IN LATIN AMERICA

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Background: The digitalization of healthcare has been profound and significantly impacted current health systems. Even more, it is expected that digital transformation will become more influential and important in the future. For example, in kidney transplantation, several developments are implementing digital pathways for nephrological care and referral procedures, among others. However, to develop and apply these technologies, the education and training of the health workforce in digital competencies have to be a priority. Therefore, we aim to improve and empower the level of digital literacy among the health workforce and patients.
Methods: Since 2021, we have developed a collaborative and transdisciplinary education methodology through virtual lectures to develop digital and technology competencies in patients and the health workforce. Currently, we also have uploaded an educational platform that involves virtual lectures, knowledge assessment, and social deliberation.
Results: A total of 19 training sessions were held, 16 for the health workforce involving 299 professional attendance records and 3 for patients, including 222 renal transplant patients and families. Health workforce training topics included: digital education, digital transformation for enterprises, prediction, digital marketing, social networks, and point of care. And patient education was mainly about health systems changes, patients in the digital era, and vaccination for the transplant recipient.
Conclusions: Digital transformation of transplant care is real and rapidly evolving. Therefore, to maximize de potential benefits of digitalization, there is a need to have an equally rapid education aiming to prepare and train patients and professionals in the new technologies. Furthermore, we believe these results can be useful for other organizations to pursue the path of education in digital transformation.

P436 TECHNICAL FAILURE IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION: INCIDENCE AND PREDICTORS FROM THE LARGEST PORTUGUESE CENTER OVER 20-YEARS

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Background: Simultaneous pancreas-kidney transplantation (SPKT) is the best treatment for patients with diabetes mellitus and chronic kidney disease. Technical failure (TF) is defined as graft loss within 90 days of surgery due to postoperative surgical problems. SPKT results have improved, but TF remains high; pancreas graft (PG) thrombosis is a frequent severe complication (4.7-8.8%, in recent data). Donor and recipient factors have been associated with early PG thrombosis. The aim of this study is to describe our experience in SPKT regarding TF in the first 90 days, and to identify predictors for its occurrence.
Methods: Patients who had a SPKT between 2000 and 2022 were included. Donor and recipient characteristics and complications in the post-SPKT period were analysed.
Results: 263 SPKT were performed over these 22 years. The average recipient age was 35.5 years, 52% men; 73% were on hemodialysis. Twenty-six TF (9.9%) were documented at 90 days. Patients with TF were more frequently on peritoneal dialysis (PD) (p=0.044). Patients with TF had grafts from older donors (p=0.045); required prolonged hospitalization (28 (20-46) vs 16 (12-25) days, p<0.001) and needed more overall reinterventions (2.1±2.6 vs 0.3±0.8, p <0.001). They also had higher kidney graft (KG) loss (15% vs 2%, p=0.001) and higher overall 90-day mortality (19% vs 0%, p<0.001) Table 1 shows detailed data. In the multivariate analysis (excluding PG reinterventions as predictors), donor age ≥36 and previous PD were independent predictors for TF at 90 days (HR: 2.513, p=0.019 and HR: 2.503, p=0.021). After including PG reinterventions we identified as independent predictors of TF: reintervention for thrombosis (HR 32.751, p<0.001), or for PG leak (HR 22.655, p<0.001) and year of transplant 2000-2011 (HR 2.667, p=0.022).
Conclusions: Our population presented an incidence of TF similar to that reported by others and confirms PG loss as a severe event associated with mortality and KG loss at 90 days. Donor age ≥36 years and previous PD were independent predictors of TF, an outcome strongly associated with PG reinterventions, particularly if leak or thrombosis driven.

Characterization of recipients, donors, and technical failure				
	Total	No technical failure	Technical failure	*p*
Pancreas-kidney transplants, n (%)	263 (100%)	237 (90.1%)	26 (9.9)	
Recipient characteristics				
Age, mean ± SD	35.5±6.3	35.7±6.3	33.6±5.8	0.100
Gender (female), n (%)	126 (48)	112 (47)	14 (54)	0.523
Diabetes duration (years), mean ± SD	24.2±6.1	24.3±6.1	23.0±6.0	0.290
Previous renal replacement therapy				
Hemodialysis	192 (73)	177 (75)	15 (58)	**0.044**
Peritoneal dialysis	59 (22)	48 (20)	11 (42)	
Preemptive	12 (5)	12 (5)	0	
Months on dialysis, median (IQR)	21 (12-33)	21 (12-34)	26 (13-31)	0.957
Body mass index (Kg/m^2), mean ± SD	22.4±2.8	22.4±2.8	21.8±2.7	0.302
Diabetic retinopathy, n (%)				
No	4 (2)	3 (1)	1 (4)	0.497
Yes	209 (82)	189 (82)	20 (83)	
Yes, with amaurosis	42 (16)	39 (17)	3 (13)	
Neuropathy, n (%)	158 (64)	144 (65)	14 (58)	0.526
Ischemic heart disease, n (%)	23 (9)	20 (9)	3 (13)	0.499
Cerebrovascular disease, n (%)	7 (3)	7 (3)	0	1
Peripheric arterial disease, n (%)	42 (17)	36 (16)	6 (25)	0.277
Hypertension, n (%)	219 (84)	197 (84)	22 (85)	1
Smoking, n (%)	93 (36)	82 (35)	11 (42)	0.444
HgA1c, mean ± SD	8.5±1.6	8.4±1.6	8.7±1.8	0.565
Donor characteristics				
Donor age, mean ± SD	29.3±10.7	28.9±10.4	33.3±12.6	**0.045**
Donor age≥36, n (%)	85 (32)	71 (30)	14 (54)	**0.013**
Immunology				
MM A, mean ± SD	1.28±0.62	1.28±0.63	1.23±0.51	0.551
MM B, mean ± SD	1.62±0.56	1.61±0.56	1.69±0.55	0.433
MM DR, mean ± SD	1.36±0.63	1.37±0.63	1.31±0.62	0.602
Transplant year (2000-2011)	121 (46)	105 (44)	16 (62)	0.094
Total length of stay, (days) median (IQR)	16 (12-27)	16 (12-25)	28 (20-46)	**<0.001**
Intensive care unit stay, (days) median (IQR)	2 (1-3)	2 (1-2)	2 (2-5)	**0.001**
Surgical reinterventions				
Total reinterventions, n (%)	65 (25)	42 (18)	23 (88)	**<0.001**
Total reinterventions, mean ± SD	0.5±1.2	0.3±0.8	2.1±2.6	**<0.001**
Reinterventions global Pancreas (Px), n (%)	57 (6)	35 (15)	22 (85)	**<0.001**
Reinterventions thrombosis Px, n (%)	17 (6)	3 (1)	14 (54)	**<0.001**
Reinterventions bleeding Px, n (%)	26 (10)	20 (8)	6 (23)	**0.018**
Reinterventions leak Px, n (%)	4 (2)	0	4 (15)	**<0.001**
Reinterventions infection Px, n (%)	21 (8)	12 (5)	9 (35)	**<0.001**
Reinterventions other Px, n (%)	16 (6)	13 (5)	3 (12)	0.201
Reinterventions global Kidney (Kd), n (%)	12 (5)	9 (4)	3 (12)	0.103
Reinterventions thrombosis Kd, n (%)	6 (2)	3 (1)	3 (12)	**0.014**
Reinterventions bleeding Kd, n (%)	3 (1)	3 (1)	0	1
Reinterventions fistula Kd, n (%)	3 (1)	3 (1)	0	1
Kidney loss at 90 days, n (%)	6 (2)	2 (1)	4 (15)	**0.001**
Recipient death at 90 days, n (%)	5 (2)	0	5 (19)	**<0.001**

Table 1: Characterization of recipients, donors, and technical failure.

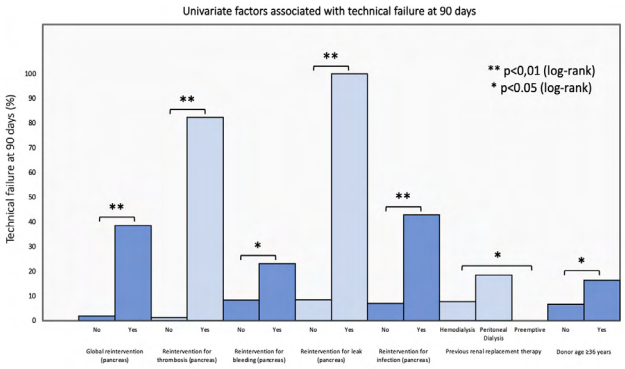

Figure 1: Univariate factors associated with technical failure at 90 days.

P437 SAFETY PROFILE OF SGLT2 INHIBITORS IN RENAL TRANSPLANT PATIENTS

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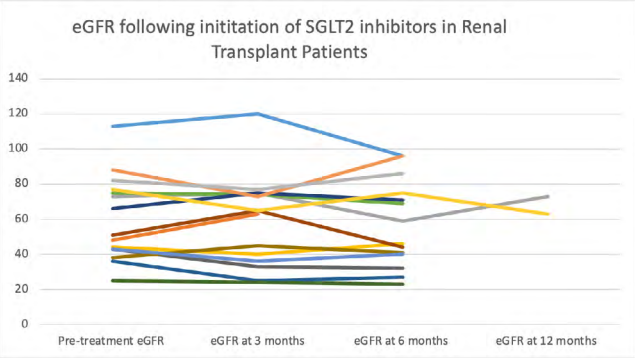
Background: SGLT2 Inhibitors (SGLT2is) are being recognised for their prognostic benefits in slowing progression of chronic kidney disease. These agents may work by reducing glomerular hypertension which is independent of their anti-glycaemic properties. However, SGLT2is increase urinary glucose excretion raising concerns of urinary tract infections (UTIs) which may preclude their use in transplanted patients taking immunosuppression. We aimed to explore the safety of SGLT2i initiation in patients with diabetes with a kidney transplant as this has yet to be determined.
Methods: From a database of 1494 transplant patients followed-up at our centre, a list of patients who received SGLT2is from the hospital pharmacy was obtained. A data extraction table was used to retrospectively collect information on clinical characteristics and treatment complications; renal function at baseline and at the following months post SGLT2 initiation: 1, 3, 6 and 12.
Results: 19 kidney transplant patients had SGLT2is prescribed, 3 of which did not initiate the prescribed treatment. Out of a total of 16 patients [mean age 60.1 years; 62% male] who initiated treatment, the median duration of SGLT2i treatment was 9 months (Table 1). 1 patient developed a UTI and Diabetic Ketoacidosis in the context of severe covid pneumonitis. A 2nd patient with a history of urethral stricture had to cease SGLT2is due to UTIs. There were no recorded genital fungal infections, rejection episode or any other diabetic related acute complications. Renal function remained stable following SGLT2i initiation (Figure 1).
Conclusions: There were three recorded complications, all of which occurred in the context of other clinical issues which may potentially confound results independent of SGLT2i use. Considering UTIs are common in kidney transplant population, comparison with a control group would help us understand if these are increased with SGLT2i treatment and if patient education about sick day rules can help reduce complications. Although our sample size was too small to evaluate any conclusive impact in kidney function, the eGFR did not appear to decline following SGLT2i initiation. Further large-scale multi-centre studies are needed to evaluate if there is a prognostic benefit for kidney transplant patients like the DAPA-CKD and EMPA-KIDNEY trials.

Table 1. Clinical characteristics of patients receiving SGLT2i

Demographics (n =16)	
Sex (%) male; female	62.5% (10/16); 37.5% (6/16)
Mean age (years)	60.1 (± 12.75)
Mean time since renal transplant (years)	8.31(± 5.58)
Cause of ESRF (%)	
• Diabetic Nephropathy	37.5 (6/16)
• Hypertensive Nephropathy	12.5 (2/16)
• Immune-mediated	31.3 (5/16)
• Inherited	12.5 (2/16)
Cause (unknown)	6.2 (1/16)
Median duration of SGLTis treatment (months)	9 (IQR 6-11)
Type of SGLT2i initiated (%)	
• Dapagliflozin	93 (15/16)
• Empagliflozin	16 (1/16)
% of patient also prescribed ACEi/ARBs	60 (9/15)
% of patients allergic prescribed ACEi/ARBs	6.3 (1/16)
Transplant Related Diabetes (%)	43.8 (7/16)
Pre-Transplant Diabetes (%)	56.2 (9/16)
Mean Duration of Diabetes (years)	
• Pre-Transplant Diabetes	21.87 (± 5.91)
• Transplant Related Diabetes	9.90 (± 7.15)
• Overall	13.30 (±8.75)

Figure 1: eGFR following initiation of SGLT2i in Renal Transplant Patients



P439 NURSING EXPERIENCE WITH TELEMEDICINE DURING THE COVID-19 PANDEMIC IN THE CARE OF PATIENTS AFTER LIVER TRANSPLANTATION

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Background: The concept of telemedicine is based on offering healthcare services in situations where distance is a critical factor, using telecommunication technologies to exchange necessary information. During the pandemic period, telemedicine was used for post-liver transplant outpatient appointments.
Methods: Since liver transplant patients are immunosuppressed and social distance was compulsory, during the COVID-19 pandemic telemedicine was used to assist patients, and descriptive and quantitative research was carried out to analyse the effect of telemedical appointments on patient care. All patients were scheduled for a face-to-face appointment and were screened by the nursing and medical team, , and checking their laboratory tests. Patients with laboratory alterations and/or clinical complaints were maintained in presential care, while those who did not present laboratory alterations and/or clinical complaints were assisted remotely (via telephone contact), and all documentation (drug prescriptions, exams requests and return) were carried out and delivered to be collected by the patient on a scheduled period.
Results: Telemedical appointments for liver transplant patients resulted in a cost reduction of approximately U$ 4000 per patient for the Brazilian government since no transport or accommodation were required. Besides, it maintained the same quality as presential appointments, as no significant adverse effects were perceived: from the 4112 appointments, only one patient developed lung neoplasia and another head-neck neoplasia. Furthermore, all the 32 patients who were infected by the SARS-COV-2 virus presented no severe damage and only four were hospitalized.
Conclusions: Conclusion: Through telemedicine, it was possible to maintain the same quality service without exposing already immunosuppressed patients, besides saving governmental capital. Therefore, telemedicine presented itself as a leverage and it is maintained as an outpatient care tool.

P440 PREDICTING INDEX FOR OUTCOMES AFTER DECEASED DONOR LIVER TRANSPLANT AFTER 1-YEAR POST-TRANSPLANT

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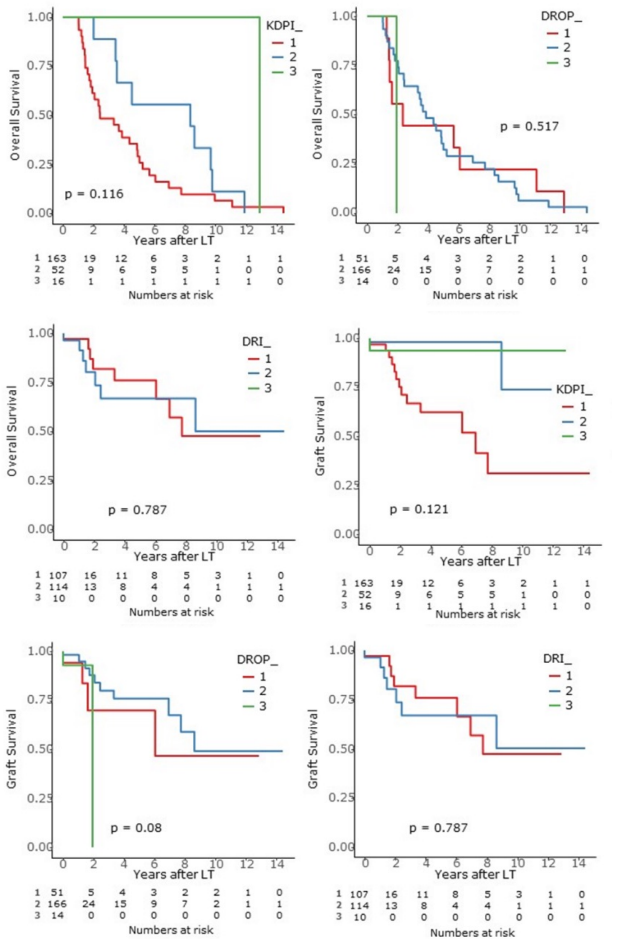
Background: The Donor Rejected Organ Pre-transplantation (DROP) Score, and the donor risk index (DRI) have been proposed for predicting graft and overall survival. These scores are calculated based on transplant-related variables. The kidney donor profile index (KDPI), which is calculated from donor variables, is suggested for predicting prognosis after kidney transplantation. Our study aims to compare the predicted graft survival and overall survival after deceased donor liver transplantation (DDLT).
Methods: This study analyzed data from transplant recipients who underwent DDLT at Samsung Medical Center between January 1st, 2000, and December 31st, 2020. Retransplantation, pediatric DDLT, dead patients within 1 year post-transplant, or follow-up loss patients were excluded. The group of recipients was stratified into three sub-classes according to the KDPI.
Results: A total of 231 DDLT cases were included. The numbers of KDPI grade 1, 2, and 3 were 163 (70.5%), 52 (22.5%), and 16 (6.9%). The proportion of esophageal varix bleeding in the KDPI grade I was less than in the KDPI grade II and III. KDPI was correlated with the donor rejected organ pre-transplantation (DROP) (P=0.018), but was not correlated with the donor risk index (DRI). Graft failure and death occurred in 20 (8.7%) and 41 (17.7%) patients. Time to graft failure increased with increasing KDPI (P < .001). The overall survival rate was significantly higher only in the low KDPI group than in the high KDPI group (p = 0.029). The other index scores were not showed significant results in overall survival rates: DROP (p=0.517), and DRI (p=0.842). In graft survival rates, all three index scores were not significant with DROP and DRI except KDPI (p=0.029).
Conclusions: Our study suggests that KDPI also is a useful index in predicting DDLT outcomes after 1-year post-transplant.



P442 DISCREPANCY BETWEEN PULMONARY ARTERY CATHETER AND CO-OXIMETRY VALUE OF MIXED VENOUS OXYGEN SATURATION DURING LIVER TRANSPLANTATION

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Background: Monitoring of tissue oxygenation is one of the most important goals in the critically-ill patients such as liver recipients. Pulmonary artery catheter (PAC) provides continuous monitoring of mixed venous oxygen saturation (SvO2) using fiberoptic reflectance spectrophotometry. Although the requirement of in-vivo calibration during liver transplantation was reported, there is no guideline about recalibration. We have observed significant drift of PAC SvO2 from reference co-oximetry value during liver transplantation. Therefore, we aimed to assess the incidence of significant discrepancy between PAC and co-oximetry values of SvO2, and the risk factors for the discrepancy.
Methods: This retrospective study included 54 recipients who underwent living donor liver transplantation at our institution between October 2021 and April 2022. PAC was inserted, and in-vivo calibration was conducted using co-oximetry value. We defined the significant discrepancy as the drift was ≥ 5% from the reference co-oximetry value at 1-hour after graft reperfusion. To assess the risk factors for the discrepancy, perioperative variables were compared between recipients with and without significant discrepancy. Receiver operating characteristic (ROC) curves were generated to evaluate the ability of perioperative variables to predict the occurrence of significant discrepancy.
Results: Significant discrepancy was observed in 25 of 54 recipients (46.3%). PAC SvO2 was higher than co-oximetry value in 51 of 54 total recipients, and 25 of 25 recipients of significant discrepancy. Among the perioperative variables, the changes of SvO2 in co-oximetry from the baseline to 1-hour after graft reperfusion was significantly greater in the recipients with significant discrepancy [median (IQR) -3.2 (-5.3, 0.35) vs. 2.5 (-0.45, 4.5), P = 0.001]. The area under the ROC curve of the changes of SvO2 in co-oximetry from the baseline to 1-hour after graft reperfusion was 0.76 (0.63−0.87) (P = 0.001).
Conclusions: PAC SvO2 significantly drifted from reference co-oximetry value in nearly half of the recipients after graft reperfusion during liver transplantation. Therefore, in-vivo recalibration is required for reliable measurement of PAC SvO2 during liver transplantation, and further study during other operation is required.

P445 THE EFFECT OF STEROID PULSE THERAPY FOR THE REDUCTION OF ACUTE REJECTION EPISODE IN SUBCLINICAL BORDERLINE CHANGES : AN OPEN-LABEL, RANDOMIZED TRIAL

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Background: Subclinical rejection (SCR) has been correlated with subsequent chronic allograft nephropathy and allograft dysfunction. SCR is known to be effective in steroid pulse therapy (SPT) in other studies. However, there is controversy about borderline change. The purpose of this study is to investigate the effect of early SPT for the reduction of acute rejection episode during the first year after kidney transplantation in the patients who show subclinical borderline changes at 2-week protocol biopsy.
Methods: This study was a randomized clinical study in which 17 recipients with stable kidney graft function and borderline changes in the 2-week protocol biopsy were enrolled. The recipients were divided into two groups depending on SPT. We investigated changes in Banff scores through protocol biopsy after 1 year.
Results: Recipients who underwent acute cellular rejection and borderline change within 1 year were 4 recipients (50%) in the Non SPT group and 5 recipients (55.6%) in the SPT group, and there was no difference between the two groups (p > 0.999). There was no difference between the two groups in the change of the Banff score between the 2-week and 1-year protocol biopsy. And there was no difference in the rates of opportunistic infections including cytomegalovirus (p = 0.471) and BK polyomavirus (p > 0.999). Also, there was no difference between the two groups with respect to creatinine and eGFR at 2-week to 3-year after surgery.
Conclusions: There was no difference in Banff score change, infection rate, and graft function between the two groups. In conclusion, we suggest that steroid pulse therapy is not essential for subclinical borderline change which is detected at 2-week protocol biopsy.

P447 IMMUNOLOGIC RESPONSE TO SARS-COV-2 VACCINATION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Pediatric population is at a lower risk of severe SARS-CoV-2 infection compared to adults. Nevertheless, transplant-related immunosuppression in pediatric kidney recipients increases their hazard compared to the general population. This systematic review aims to evaluate the efficacy of SARS-CoV-2 vaccines and determine risk factors of no seroconversion in pediatric and adolescent kidney transplant recipients.
Methods: PubMed-MEDLINE were searched for studies reporting the efficacy of Sars-CoV-2 vaccine in pediatric and adolescent (under 18 years of age) kidney transplant recipients. Meta-analysis was also performed using fixed and random effect models.
Results: A total of 7 studies including 254 patients were included. The random effect model demonstrated a 63% seroconversion rate (95%CI 0.5-0.76) following a two-dose schedule which increased to 85% (95%CI 0.76-0.93) after 3rd dose administration. Seronegativity was 10.5-fold higher (95%CI 2.32, 47.92) in patients under mycophenolate mofetil compared to azathioprine. Rituximab administration decreased the probability for serocoversion (OR 0.12, 95%CI 0.03-0.43). Mean glomerular filtration rate (GFR) was 9.25 ml/min/1.73m^2 lower (95%CI -16.37-2.13) in patients with no seroconversion. Seroconversion rate was lower in vaccinated compared to infected patients (OR 0.13, 95% CI 0.02-0.72).
Conclusions: Vaccination against Sars-Cov-2 in pediatric and adolescent kidney transplant recipients elicits humoral response and 3rd dose is advised as response rates augment following a third immunization. Previous rituximab administration and lower GFR reduces the likelihood for seroconversion. Moreover, seroconversion rate is more frequent in patients under antimetabolite therapy with azathioprine compared to mycophenolate mofetil.

P448 IMPACT OF NONSPECIFIC ALLOGRAFT BIOPSY FINDINGS IN SYMPTOMATIC KIDNEY TRANSPLANT RECIPIENTS

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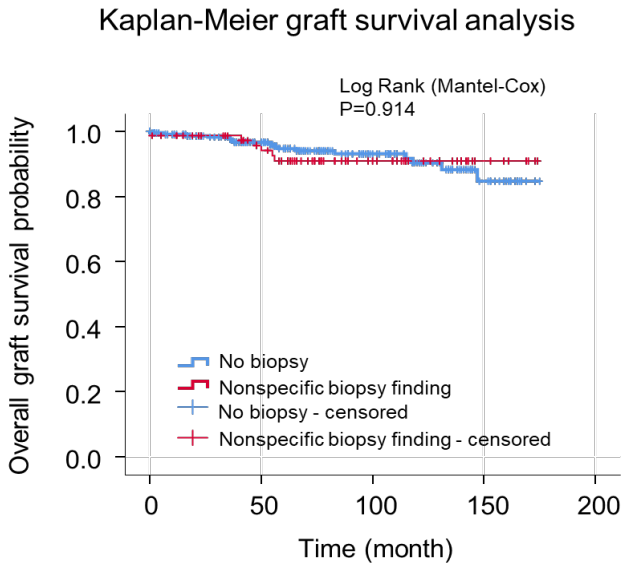
Background: An indication biopsy is indicated to diagnose the cause of allograft dysfunction. In indication biopsies, subclinical and borderline allograft findings may be fewer than in protocol biopsies. Nevertheless, we occasionally encounter ambiguous biopsy results in symptomatic kidney transplant recipients in practice. The allograft survival outcome in symptomatic recipients with nonspecific allograft biopsy findings remains unclear. The purpose of this study was to analyze the impact of nonspecific indication biopsy findings in symptomatic kidney transplant recipients.
Methods: We retrospectively collected records from 773 kidney transplant recipients between January 2008 and October 2021. The characteristics of transplant recipients with nonspecific allograft findings in the first indication biopsy were analyzed. Nonspecific allograft biopsy findings were defined as other biopsy findings excluding ABMR, TCMR, borderline rejection, CNI toxicity, infection, glomerulonephritis, and diabetic nephropathy. The graft outcome was compared between recipients who had never had an indication biopsy and those who had a first indication biopsy with nonspecific findings.
Results: Recipients with nonspecific allograft biopsy findings (n = 81) and those with no indication biopsy findings (n = 510) were studied. The causes of the indication biopsy were increased creatinine levels (48.2%), proteinuria (11%), both (18%), or unknown (14%). Following the first indication biopsy, 33.7% and 10.8% of them had second and third allograft biopsies, respectively. Around 30% of recipients with nonspecific indication biopsy findings also had nonspecific findings in the following biopsy. The graft survival in recipients with nonspecific indication biopsy findings was comparable to that in recipients who did not require the indication biopsy before matching (Log Rank P=0.931) and after propensity score matching (Log Rank P=0.914).
Conclusions: Even in symptomatic kidney transplant recipients, nonspecific allograft biopsy findings might not be a poor prognostic factor for allograft survival compared to recipients who did not require the indication biopsy.



P449 DELAYED GRAFT FUNCTION EFFECT ON T CELL SUBPOPULATIONS FOLLOWING RENAL TRANSPLANTATION

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Background: Delayed graft function (DGF) is marked by activation of both innate and adaptive immunity and may have long-term implications in the immune response to the kidney allograft. CD28null T lymphocytes (CD3CD28null) are terminally differentiated cells associated with cardiovascular diseases and are expanded in advanced chronic kidney disease.
Methods: In this prospective study, we included 105 patients who were transplanted and followed for up to 12 months. Patients were classified into 2 groups according to the presence of DGF. Cytometric analysis was performed on the day of transplantation and then at 3, 6, and 12 months posttransplant, to estimate the phenotype of T lymphocytes. Based on this analysis, T lymphocyte subtypes studied were: CD4, CD8, CD4CD28null, and CD8CD28null.
Results: DGF was recorded in 20 out of 105 patients (19%). One year after transplantation the patients retained good graft function (eGFR=64±19 ml/min/1.73m^2) with no differences between the two groups. The percentage of CD3CD28null lymphocytes was reduced in non-DGF patients at six (p=0.007) and twelve (p=0.010) months posttransplant while in DGF patients it remained steady. CD4/CD8 ratio was negatively associated with CD3CD28null percentage (p<0.001) at all time points and was reduced in DGF patients at 12 compared to 3 months after the transplantation (p=0.005) while in non-DGF patients it remained steady. Twelve months after transplantation, patients with non-DGF had lower CD3CD28null [13.5(16) vs 27.4(38) %, p=0.018] while DGF patients had lower CD4/CD8 ratio [1.1(1.2) vs 1.8(1.0), p=0.010].
Conclusions: One year after successful kidney transplantation, patients with DGF have a lower CD4/CD8 ratio which is combined with a stable high CD3CD28null percentage in T lymphocytes.

P450 HAPLOIDENTICAL HSCT WITH KIR GENOTYPE MISMATCHED: DIMINISHED RISK OF MORTALITY, DISEASE-FREE MORTALITY AND ACUTE GVHD

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Background: In allogeneic hematopoietic stem cell transplantation (HSCT), stem cells are ideally obtained from HLA- identical donors. However, it has been estimated that only 30% of patients could be transplanted with HLA-identical donors, so other alternatives such as haploidentical HSCT (hHSCT) have gained relevance. The major disadvantages with the use of haploidentical donors are an increased risk of graft rejection and graft versus host disease (GVHD). For this reason, it has been proposed to evaluate NK cell alloreactivity and its association with diverse HSCT outcomes according different KIR compatibility models.
Methods: We retrospectively analyzed 73 donor-recipient pairs with hHSCT at a single center between 2006 and 2018. Donors were first- or second-degree relatives with 3 to 5 allelic mismatches at all HLA loci. KIR typing was performed by PCR-SSO. To evaluate the KIR gene-gene (KIR G-G) model, we defined KIR A/A genotype by the absence of activator KIR (except *KIR2DS4*), and KIR B/x genotypes by the presence of one or more of the following genes: *KIR2DL5, 2DS1, 2DS2, 2DS3, 2DS5* or *3DS1*. We evaluated the association between KIR G-G model and overall survival, disease-free survival, non-related mortality, acute and chronic GvHD, and relapse. Survival analysis was carried out by Kaplan Meier method using the log rank test. Moreover, we employed Cox regression method and Competing risk analysis.
Results: The half of the follow-up time, where 50 % of the deaths occurred, was 47 months. Acute GVHD, chronic GVDH and relapse occurred in 38, 16 and 9 patients respectively. Of 73 evaluated pairs, 11 (15%) had KIR genotype mismatches (A/A donor into B/x recipient (6.8%), and B/x donor into A/A recipient (8.2%)).In patients with haploidentical donors, the recipients transplanted with KIR genotype mismatched donors had 77% less risk of mortality and 77% more likely to have disease-free survival (HR 0,23 (IC 95% 0.06 – 0.82), p=0.024); also, these patients had 73% less risk of acute GvHD (sHR 0.27 (IC95% 0.07 – 0.98), p=0.05).
Conclusions: These results allow us to suggest that the KIR G-G model could be an important tool to predict alloreactivity events associated with overall survival, free-disease survival and acute GVHD in patients with hHSCT. KIR genotyping could be a crucial selection criterion to choose the best donor.

P451 CIRCULATING IMMUNE CELL SUBSETS CORRELATE WITH INDICES OF LEFT VENTRICULAR FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS WITHOUT CARDIOVASCULAR DISEASE

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Background: Kidney transplant recipients (KTRs) carry a significant cardiovascular disease (CVD) burden. The relationship between immune system responses with heart failure is intricate. The aim of our cross-sectional study was to investigate correlations between blood levels of specific immune cells subsets with conventional and novel deformation indices of left ventricular (LV) function in KTRs.
Methods: 31 stable KTRs (mean age 58 ±9.28 years, 67% males) without CVD and 17 chronic kidney disease (CKD) stage 3 patients without CVD were enrolled. The peripheral blood immune cells, including CD14++CD16-, CD14++CD16+ and CD14+CD16++ monocytes, Natural Killer (NK) cells (CD3+CD16+56+), CD3-CD19+ B cells, CD3+CD4+ T cells, CD3+CD8+ T cells and T regulatory (Tregs) cells (CD4+CD25+ FoxP3+) were measured by flow cytometry. Left atrial volume index (LAVI), LV mass index (LVMI), E/E', global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), TWIST, UNTWIST were assessed by echocardiography.
Results: KTRs had a mean eGFR 58 +/-18 ml/min/1.73 m2 (CKD-EPI) and mean 24-hour proteinuria (PER) 707 +/-1185 mg/24h. B-cells, T-cells and CD8+ T cells counts correlated positively with eGFR ($p<0.05$). Increased non-classical CD14+CD16++ monocytes were associated with PER ($p<0.01$). An inverse correlation was found between classical CD14++CD16- monocytes and PER ($p<0.05$). Increased monocytes and pro-inflammatory CD14++CD16+ monocytes counts correlated positively with LAVI and E/E' respectively ($p<0.05$). Finally, increased NK cells levels were associated with more negative GCS values ($p<0.05$).
Conclusions: Alterations of immune cells subsets correlate with subclinical markers of LV dysfunction in KTRs with no established CVD and future research is required to further evaluate them as prognostic tools in KTRs.

Table 1.

	KTRs (No=31)	CKD (No=17)	P value
WBC (No/mm^3)	8675+/-2852	7060 +/-1671	0.003
Monocytes (No/mm^3)	629 +/-246	453 +/-144	0.000
CD14++ (No/mm^3)	517 +-/223	356 +/-137	0.000
CD14++ (%)	86 +/-8.3	79 +/-8.3	0.001
CD14+CD16++ (No/mm^3)	22 +/-14	31+/-16	0.008
CD14+CD16++ (%)	3.8+/-2.5	7.2+/-3.7	0.000
T lymphocytes (%)	81.4 +/-8.3	76.6 +/-8.4	0.011
NK cells (%)	13.4 +/-7.9	17.1 +/-7.8	0.039
Tregs (No/mm^3)	22 +/-13	38 +/-34	0.006
Tregs (%)	1.2 +/-0.75	2 +/-1.4	0.002

P452 EVALUATION OF A READY-TO-USE AND FULLY AUTOMATED REAL-TIME PCR TO DETECT 11 VIRUSES IN HUMAN SAMPLES

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Background: One of the challenges of clinical virology laboratories is to optimize the use of devices to diagnose the presence of viruses in different matrices, that can affect the health of the donated organ. Often, the available solutions allow to detect only one or few pathogens on the same device, leading to an excessive usage of space, resources, and operator time. The present study evaluated the performance of a fully automated solution, for the detection and quantification of Adenovirus (HAdV), Epstein Barr Virus (EBV), Poliomavirus BK (BKV) Herpes simplex virus 1 and 2 (HSV-1&2), human Herpes virus 6 (HHV-6), Herpes virus 7 (HHV-7) and Herpes virus 8 (HHV-8), Poliomavirus JC (JCV), Varicella-Zoster virus (VZV), Human parvovirus B19 (Parvo).
Methods: Human samples of plasma, blood, urine and swab were tested to evaluate the performance of STAT-NAT® SN200 kits for the quantification of HAdV, EBV, BKV, HSV-1, HSV-2, HHV-6, HHV -7, HHV-8, JCV, Parvo and VZV viruses, accordingly with the respective IFUs. The aim was to assess the analytical sensitivity (LoD, LoQ), linearity, precision and specificity on 22 pathogens, following the CLSI guidelines (Clinical and Laboratory Standards Institute). The DNA samples were extracted using SENTiNAT® X48 Pathomag Extraction kit. Extraction, set up and PCR amplification were performed on the fully automated, sample-to-results, SENTiNAT® 200 system. Combination of different assays were tested to assess the flexibility and multiparametric capability of the instrument.
Results: Summary of the analytical performances of all the tested STAT-NAT® SN200 kits is reported in table below. During the routine activities, SENTiNAT® 200 has been successfully used to a test a combination of STAT-NAT® SN200 kits to perform multi-parametric viral assays up to six targets from the same patient on different matrix simultaneously (e.g. blood, urine, plasma and swab), starting from the same eluate.
Conclusions: The combination of STAT-NAT® SN200 kits with the fully automated sample-to-results SENTiNAT®200 offers a flexible solution to detect and quantify a wide range of virus targets on different matrices in the same run, with sensitive, precise and reproducible results.

Target	Matrices	LOD	LOQ	Linearity	Specificity	Reproducibility %CV
HAdV	Whole Blood	1000 IU/mL	1000 IU/mL	$1.0X10^2$ - $2.0x10^8$ IU/mL	100%	<10%
	Plasma	750 IU/mL	750 IU/mL			
	Swab	400 IU/mL	400 IU/mL			
EBV	Whole Blood	450 IU/mL	750 IU/mL	$1.0X10^2$ - $1.0x10^6$ IU/mL	100%	<10%
	Plasma	195 IU/mL	200 IU/mL			
BKV	Plasma	190 IU/mL	200 IU/mL	$1.0X10^2$ - $1.0x10^8$ IU/mL	100%	<10%
	Urine	200 IU/mL	250 IU/mL			
HSV1	Whole Blood	750 cps/mL	750 cps/mL	$2.5X10^2$ - $1.0x10^7$ cps/mL	100%	<10%
	Plasma	400 cps/mL	450 cps/mL			
	Swab	300 cps/mL	300 cps/mL			
HSV2	Whole Blood	750 cps/mL	750 cps/mL	$2.0X10^2$ - $1.0x10^8$ IU/mL	100%	<10%
	Plasma	250 cps/mL	250 cps/mL			
	Swab	250 cps/mL	250 cps/mL			
HHV-6	Whole Blood	490 IU/mL	560 IU/mL	$5.0X10^1$ - $1.0x10^8$ IU/mL	100%	<10%
	Plasma	380 IU/mL	380 IU/mL			
HHV-7	Whole Blood	250 cps/mL	350 cps/mL	$1.0X10^2$ - $1.0x10^7$ cps/mL	100%	<10%
	Plasma	202 cps/mL	300 cps/mL			
HHV-8	Whole Blood	500 cps/mL	500 cps/mL	$2.0X10^2$ - $1.0x10^7$ cps/mL	100%	<10%
	Plasma	200 cps/mL	300 cps/mL			
Parvo	Whole Blood	600 IU/mL	750 IU/mL	$1x10^2$ to $1x10^9$ IU/mL	100%	<10%
	Plasma	180 IU/mL	250 IU/mL			
JVC	Whole Blood	500 IU/mL	750 IU/mL	$5.0X10^2$ - $1.0x10^7$ IU/mL	100%	<10%
	Plasma	500 IU/mL	600 IU/mL			
VZV	Whole Blood	500 cps/mL	600 cps/mL	$2.0X10^2$ - $1.0x10^7$ cps/mL	100%	<10%
	Plasma	250 cps/mL	350 cps/mL			
	Swab	250 cps/mL	350 cps/mL			

P453 IMMUNE CELL REPERTOIRE IN KIDNEY TRANSPLANT BIOPSIES CLASSIFIED AS ACUTE REJECTION

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Background: Diagnosis of kidney transplant (KTx) rejection is based on the pathology findings of a KTx biopsy according to the Banff Classification of Renal Allograft Pathology. Distinguishing between different types of KTx rejection when it is not a clear-cut case may be challenging due to the fact that the exact composition of the inflammatory cells can be difficult to comprehend and visualize on the same biopsy slide. Here we describe the feasibility of using a novel multiplex immunofluorescent panels on formalin fixed paraffin embedded (FFPE) KTx biopsies combined with digital image analysis to investigate the immune cell repertoire of different types of acute KTx rejection.
Methods: Two novel multiplex immunofluorescent panels were designed and performed on 76 KTx FFPE biopsies. Antibodies to panel 1: CD3 (T cells), CD8 (cytotoxic T cells) and, CD68 (macrophages) and panel 2: CD14, CD16, CD163 (mononuclear phagocytes) and CD56 (NK cells) were used. Three groups were compared: antibody-mediated rejection (AMR, n=25), acute T cell-mediated rejections (aTCMR, n=19), and acute tubular necrosis (ATN, n=32). Digital image analysis was performed using QuPath and data was analyzed using Graphpad Prism software.
Results: In both AMR and aTCMR, almost all immune cell subsets inflammatory cells were significantly more prevalent in both glomeruli and tubulointerstitium than in ATN cases with the exception of CD14+ and CD16+ cells in the glomeruli and, CD14+CD16+ and CD16+CD56+ cells in the tubulointerstitium. The tubulointerstitium of aTCMR showed a higher abundance of T cells compared to AMR (CD3+ and CD3+CD8+, p <0.05). No differences in glomerular T cells were seen. The glomeruli of AMR showed significantly more monocytes and macrophages than aTCMR (CD14+, CD16+, CD68+, CD163+ and, CD16+CD56+, p < 0.05).
Conclusions: Multiplex immunofluorescent panels are a feasible method to assess T cells, monocyte and macrophage subsets in KTx FFPE biopsies. Comparing rejection cases to ATN cases, we detected a stronger expansion of T cells and mononuclear phagocytes in both glomeruli and tubulointerstitium in rejection cases. Lastly, comparing AMR to aTCMR cases revealed that AMR is characterized by expansion of mononuclear phagocytes within the glomeruli, while TCMR is characterized by interstitial T cell infiltration.

P454 DEVELOPMENT OF A PARATHYROID CELL THERAPY ADAPTED FOR ALLO- AND XENO- TRANSPLANTATION FOR THE TREATMENT OF HYPOPARATHYROIDISM

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Background: Hypoparathyroidism is a threatening condition, mainly post-surgery, associated with calcium disorders. Allo-transplantation have been explored to prevent or treat hypoparathyroidism, but long-term results remain controversial as there is a lack of tools designed to evaluate the processing of parathyroids. The objective of our study is to propose useful tools adapted to allo- and xeno-transplantation.
Methods: Human parathyroid samples were obtained during parathyroid surgeries. Porcine parathyroids were harvested in Landrace Pigs. Digestion of parathyroids was performed using collagenase and parathyroid cells were cultured using DMEM-F12 medium. Functionality of the cells was assessed with perifusion studies, which exposed the cells to sequential flows of high or low-calcium media. Mice experiments involved parathyroids minced or digested and transplanted under the kidney capsule of c57bl/6 RAG2-KO mice, followed up until day 30. Levels of human parathormone in mice were measured with ELISA tests. Standard stainings were performed on grafts samples to determine grafts volumes. Red Sirius, collagen-1 and alpha-sma stainings were performed to estimate fibrosis.
Results: First we showed that both minced parathyroids from human or pigs could be efficiently transplanted under the kidney capsule of RAG2KO mice with persistent viable tissue at day 30 post-transplantation. Then we investigated if enzymatic digestion of human parathyroids was comparable to minced tissue. After digestion, human parathyroid cells could be cultured up to 4 days and showed a response in vitro to calcium stimuli. After transplantation into mice, digested parathyroids showed similar outcomes compared to minced parathyroids, with an increasing secretion of parathormone from day 0 to day 30. Even though digested parathyroid graft volumes were lower than minced ones, we found a significant higher percentage of fibrosis in minced parathyroids.
Conclusions: Porcine and Human parathyroids can be transplanted successfully under the kidney capsule of immune-incompetent mice. Enzymatic digestion of parathyroids is a reliable tool to process parathyroids before transplantation, which will be of help for future preclinical models.

P455 PRELIMINARY RESULTS OF INTRAOPERATIVE VASCULAR FLOW ASSESSMENT IN KIDNEY TRANSPLANTATION

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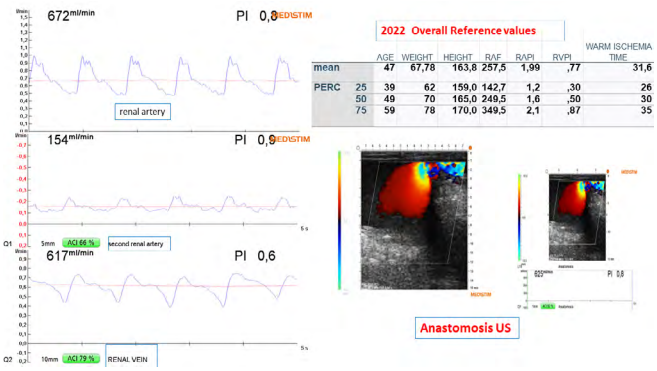
Background: The intra and early postoperative ultrasound (US) evaluation of the transplanted kidneys represents the most widespread, non-invasive, reliable method for the assessment of the renal allograft vascular and perfusion status. US with the evaluation of the resistance index (RI) is based on blood velocity and pressure, providing an indirect perfusion measurement and it has been shown to predict short-term allograft function. We aimed at focusing on flow measurements performed after the graft reperfusion and eventual associations with clinical features.
Methods: 96 flow measurements in thirty-three consecutive transplant patients (7 from living donors, 26 from deceased of which 4 following hypothermic machine perfusion) were prospectively recruited from May to December 2022. Assessment was performed with MiraQ system which combines US and flow measurements: surgical findings can be documented through L15 High-frequency US Probe that allows to assess morphology meanwhile transit time technology measures flow. This combined real-time assessment allows an early detection of vascular alterations and an immediate revision, if necessary (1 case in our series).
Results: In descriptive analysis, flow measurements distributions' shapes changed depending on the type of donor, with their skewness suggesting better values for living donors both in the arterial and venous flow measurements (-1.7/0.2; -1.5/-0.5 respectively). A propensity score matching renal venous RI, with its regressor of impact on the vascular stiffness and resistance, patient age and weight were included in an univariate general linear model, together with BMI, warm ischemia time and the type of donor (deceased vs living) and then in a logistic model testing differences between two groups categorized by arterial Renal Flow: median <249.5 (abnormal, n=52) and median ≥249.5 (normal, n=44) to identify peculiar and independent variables predictive impact. The preliminary results showed different significant predictive values for different types of kidney donors and independent significant values of warm ischemia times (P_f <0.005); the logistic model confirms, also in a categorical perspective, an impact for all the regressors, including the BMI
Conclusions: Data favor living donors flow outcomes (OR: 0.05; CI 0.06-0.8).



P456 FRACTION OF EXHALED NITRIC OXIDE IN LIVER TRANSPLANT RECIPIENTS AND MATCHED CONTROLS

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Background: Liver transplant (LT) recipients have an increased risk of pulmonary infections which may lead to inflammation and pulmonary damage. However, the burden of chronic pulmonary diseases in LT recipients is unknown. Fraction of exhaled nitric oxide (FeNO) is associated with eosinophilic airway inflammation and is an established airway biomarker. We aimed to investigate the prevalence of elevated FeNO in LT recipients and in matched controls from the general population.
Methods: FeNO was measured using NIOX Vero in LT from the Danish Comorbidity in Liver Transplant recipients (DACOLT) study and in age- and sex matched controls from the Copenhagen General Populations Study (CGPS). Study participants answered a questionnaire regarding smoking, history of pulmonary disease, and medication. Elevated FeNO was defined according to the American Thoracic Society with cut-off at ≥25 parts per billion (ppb) and ≥50 ppb. Levels <25 ppb indicate that airway inflammation is less likely and levels >50 indicates that inflammation is likely. We used linear and logistic regression models adjusted for age, sex, and current smoking to investigate potential differences in FeNO levels between LT recipients and controls.
Results: We included 272 LT recipients and 2137 controls (Table 1). LT recipients were slightly younger, but proportions of current smokers, self-reported asthma and COPD were comparable between the two groups. Median FeNO was higher in LT recipients (16.0 vs. 15.4, p<0.0001) and more LT recipients had FeNO ≥25 ppb (27.2% vs. 12.1%, p<0.0001) and ≥50 ppb (4.0% vs. 1.7%, p=0.02). In analyses adjusted for age, sex, and current smoking, FeNO was significantly higher in LT recipients with an estimated difference of 4.7 ppb (95% confidence interval (CI): 3.1-6.2, p<0.0001). Adjusted odds ratio for FeNO>25 ppb and >50 ppb in LT recipients was 2.99 (95%CI: 2.2-4.1, p<0.0001) and 2.61 (95%CI: 1.3-5.2, p=0.006), respectively.
Conclusions: LT recipients had significantly higher levels of FeNO when adjusted for age, sex, and current smoking. LT recipients had significantly higher odds for FeNO >25 ppb and >50 ppb compared to the general population. This suggests excess eosinophilic airway inflammation in LT recipients, and further studies are needed to clarify the impact of inflammation and burden of pulmonary diseases.

Table 1

	LT recipients n=272	Controls N=2137	p-value
Characteristics			
Sex (male), n (%)	159 (58.5)	1175 (55.0)	0.3
Age, years, median (IQR)	55 (46-64)	57 (49-65)	**0.0003**
LTX related variables			
Time since LTX years, median (IQR)	6.9 (2.8-12.0	NA	
Immunosuppressive medication		NA	
- Prednisolone, n (%)	132 (48.6)		
- Tacrolimus/ciclosporin, n (%)	224 (82.4)		
- Everolimus, n (%)	17 (6.3)		
- MMF, n (%)	176 (64.7)		
Smoking and self-reported respiratory morbidity			
Smoking status			
- Current, n (%)	35 (12.9)	304 (14.2)	0.6
- Previous, n (%)	82 (30.1)	836 (39.1)	**0.005**
Self-reported asthma, n (%)	18 (6.6)	150 (7.0)	0.9
Self-reported COPD	8 (2.9)	78 (3.6)	0.7
Pulmonary function measures			
FeNO >25 ppb, n (%)	74 (27.2)	259 (12.1)	**<0.0001**
FeNO >50 ppb, n (%)	11 (4.0)	37 (1.7)	**0.02**
FeNO (ppb), median (IQR)	16.0 (10.0-26.0)	15.4 (9.0-18.0)	**<0.0001**

P457 MODELLING CHANGES IN THE PHARMACOKINETICS OF TACROLIMUS DURING PREGNANCY AFTER KIDNEY TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

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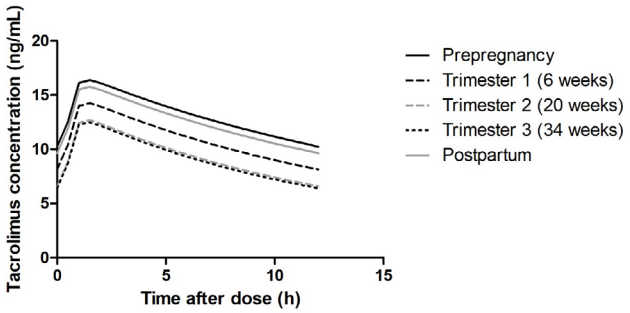
Background: Pregnancy after kidney transplantation (KT) is a realistic option but maintaining tacrolimus whole-blood pre-dose concentrations during pregnancy is complicated as physiological changes affect the pharmacokinetics of and hence exposure to tacrolimus. The aim of this study was to investigate the changes in tacrolimus whole-blood pre-dose concentrations throughout pregnancy in kidney transplant recipients and correlate these with covariates in a population pharmacokinetic (popPK) model.
Methods: Data of pregnant women using a twice-daily oral tacrolimus formulation after KT were retrospectively collected from six months before conception, throughout gestation, and up to six months postpartum. Pharmacokinetic analysis was performed using non-linear mixed effects modelling software (NONMEM). The final model was evaluated using goodness-of-fit plots, visual predictive checks and a bootstrap analysis.
Results: A total of 257 whole-blood tacrolimus pre-dose concentrations from 14 women who became pregnant after KT were included. Tacrolimus apparent clearance (CL/F) increased during pregnancy from 33.2 to 41.9 L/h, with the highest change observed in the first trimester. Haematocrit (delta objective function value (ΔOFV) -84.37) and gestational age (ΔOFV = -83.40) were negatively correlated with CL/F (p-value <0.01). These covariates explained 45% of the inter-individual and 82% of the inter-occasion variability on CL/F. Simulated whole-blood tacrolimus pre-dose concentrations, with the gestational age correlated to mean haematocrit values of that period, show a clear distinction between non-pregnant state and pregnancy on CL/F (Figure 1). A rapid decrease in tacrolimus concentrations occurred during the first trimester, which decreased a bit further during the second trimester and stayed stable during the last trimester. This change rapidly disappeared postpartum.
Conclusions: Gestational age and haematocrit impact the exposure to tacrolimus during pregnancy. To maintain target whole-blood tacrolimus pre-dose concentrations during pregnancy, a dose increase is suggested. This popPK model may be used in the future for tacrolimus dose adjustments in pregnant kidney transplant recipients.



P458 PERSON-CENTERED APPROACH IN DESIGNING A LEAN LIVING DONOR KIDNEY TRANSPLANT PATH: ADD VALUE OF IMPROVEMENT TOOLS

Fabiana Rubba*[1], Gianluca Rompianesi[2], Anna Borrelli[3], Silvia Campanile[2], Teresa Trunfio[4], Oriana Barbieri[3], Giovanni Improta[1], Roberto Troisi[2], Maria Triassi[1]

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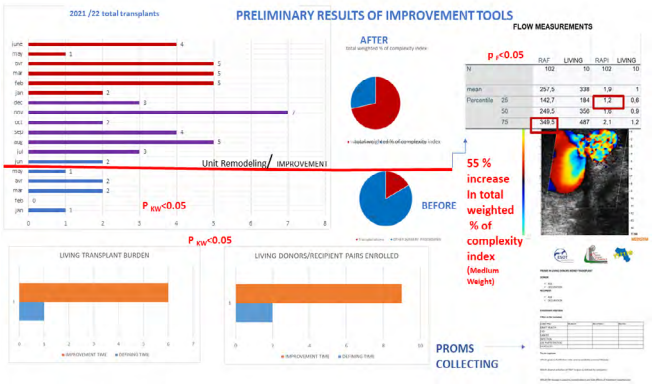
Background: Benchmark and collecting data methods play key roles in quality flow improvement and from a public health perspective, they may serve to inform preventative strategy development and health infrastructure planning. Lean Six Sigma approach combines the principles of Lean Production for the distinction of value-added activities from non-value-added ones, with tools including value flow map, flowchart about speed, continuity of flow and work in progress, with the methodological rigor for the reduction of variability. Define, measure, analyze, improve and control are the 5 clinical areas of DMAIC, which is part of lean Six Sigma methodology. Through collecting person centered perceptions of hospital inpatients, we can identify areas for both improvement and refinement in the hospital admission process. Patient-reported outcomes (PROs) that define Likert's scores of life participation, medication adherence, disease symptoms, and side effects may have crucial impact in the context of kidney transplantation.
Methods: We implement the DMAIC in Federico II Kidney Transplant program to construct a person centered living donor transplant path. The definition, measurement and analysis phases involve the evaluation of the historical scenario (Define Time) in the contextual layout and the assessment of the outcome's variables thereby. A single center reference cohort of 33 transplants and a National Benchmark cohort of 80996 patients were considered as reference category. The improvement phase concerns main quality interventions:
A prospective database including donor and recipient outcomes and also quality functional measurements A collecting flow for PROS centered both on donor and recipient concerning symptoms and side effects
Results: Main results include significant increase in total transplantations, in living donors and in enrolled donors with consequent 55% increase in DRG's transplantation total weighted percentage of complexity index; the time that occurs between the enrolment and surgery was shortened from 60 to 30 days and flow measurements for living donor recipients were positioned in the best quartiles of single centre range.
Conclusions: Future perspectives include long term data assessment challenging findings from the designed path also with the Benchmark cohort



P460 THE PROGNOSTIC VALUE OF LYMPHOCYTE SUBSETS IN ANTIBODY RESPONSE AFTER SARS-COV2 VACCINATION IN DIALYSIS PATIENTS AND KIDNEY TRANSPLANT RECIPIENTS

Ioannis Mallioras*[1], Christos Georgopoulos[1], Anila Duni[1;2], Georgios Markopoulos[3], Haralampos Pappas[1;2], Efthymios Pappas[4], Vasileios Koutlas[2], Eirini Tzalavra[2], Gerasimos Baxevanos[5], Georgios Katagis[6], Konstantina Gartzonika[6], Georgios Vartholomatos[3], Michalis Mitsis[2], Eirini Christaki[7], Haralampos Milionis[7], Evangelia Dounousi[2;8]

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Background: The immune responses to SARS-COV-2 vaccination remain under study in hemodialysis (HD) patients and kidney transplant recipients (KTR)s in the setting of the immunosuppressed milieu. The aim of our prospective study (ClinicalTrials.gov, NCT04932876) was to determine the predictive value of lymphocyte subpopulations in the production of antibodies (Ab) against SARS-CoV-2 after the second vaccine dose.
Methods: The study cohort included 34 HD patients and 54 KTRs who received two doses of the BNT162b2 (Pfizer–BioNTech). Lymphocyte subsets, including B cells, CD4+ and CD8+ T cells, naïve and memory T lymphocytes were analyzed by flow cytometry (FC) before vaccination (T0), before the 2nd dose (T1), 2 weeks after the 2nd dose (T2). Exclusion criteria included previous infection by SARS-CoV2 and infection by SARS-CoV2 during study follow-up. The anti-SARS-CoV2 Ab response was assessed by the ARCHITECT IgG II Quant test (Abbott). Titers >50 arbitrary units (AU)/ml were considered positive. A multiple linear regression model was applied separately to the two subgroups of patients.
Results: The mean age of KTRs and HD patients was 58.5 and 68.5 years respectively. In KTRs, the populations of CD19+ lymphocytes, CD3+CD16+56+ cells and CD4+CD45RO lymphocytes can predict antibody formation (p-ANOVA<0.001) based on the multiple regression model: Ab=4869+519*CD19-226*CD3+CD16+56-139*CD4+CD45RO. In HD patients the populations of CD19+ lymphocytes, CD45RA+CD45RO lymphocytes, CD4 to CD8 ratio, CD3-CD16+56+ cells and CD4+CD45RO lymphocytes can predict Ab formation (p-ANOVA<0.001) based on the multiple regression model: Ab=20267+835.3*CD19-286*CD45RA+CD45RO-375.2*CD4+CD45RO+851*CD4/CD8-187.3*CD3-CD16+56+. The two regression models explain the variation of the dependent variable (Ab), according to the adjusted index, at a rate of 24% and 67% respectively. The 2 models were analyzed for residual autocorrelation (DW statistic >DU>DL). No multicollinearity was observed (All VIF< 1).
Conclusions: Quantification of lymphocyte subsets appears to have a significant prognostic value regarding development of Ab after vaccination against SARS-CoV-2, especially in KTRs. There are significant differences in lymphocyte subsets related to Ab production between HD patients and KTRs.

P461 NATURAL KILLER CELLS BEFORE KIDNEY TRANSPLANTATION INVOLVED WITH OPPORTUNISTIC INFECTION

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Background: Longitudinal analysis has revealed strong links between the proportion of lymphocytes cells and acute rejection (AR), opportunistic infection (OI) or presence of DSA after kidney transplantation (KT). Lymphocytes profile at the time of KT associated with such complications have not been studied.
Methods: We conducted a longitudinal study to analyze lymphocytes subsets and NK cells at the time of first isolated KT before any immunosuppressive treatment from 01/2016 to 12/2018 and no exposure to anti-CD20 treatment. Within 24 months after KT, first event occurring defined groups: acute rejection (AR), opportunistic infection (OI) and OI-AR-free (control group). B cells subpopulations were determined as follows: B total (CD19+), naïve B cells (CD27- IgD+), switched memory (CD27+ IgD-), non switched memory (CD27+ IgD+), double negative (CD27-IgD-), B transitional (CD24high CD38high) and plasmablast (CD24-CD38highCD27high). T cells subpopulations were defined by T CD3+, T CD3+CD4+, T CD3+CD8+ and NK cells as CD56+(CD16+/-).
Results: Among 422 patients included, blood sample was not available in 139

(33%). Both groups were similar at the time of transplantation and within 24 months after. Among the 283 patients included in analysis, 44 (15.5%) belonged to AR group, 49 (17.3%) to OI group and 190 to control group (Table 1). Age was significantly higher in OI group (58.5 (±12.3) vs. 53.2 (±14.1) years; P=0.047). All B and T lymphocytes subsets were similar in the three groups. AR group experimented significantly lower pre transplant NK cells, absolute number, and proportion, than OI group (p=0.003) and control group (P=0.002) (Figure 1). Patients with DSA pre transplant and AR had similar level of lymphocytes subsets and NK cells than those with no AR.
Conclusions: Our study suggested that pretransplant NK cells could be associated with AR and OI within the 24 months after KT. Kinetics of different cells subsets within 3 and 12 months after KT analysis is in progress. NK cells subsets need to be further analyzed.

P462 PREVALENCE OF PERIPHERAL ARTERY DISEASE IN LIVER TRANSPLANT RECIPIENTS

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Background: Cardiovascular diseases have emerged as a leading cause of morbidity and mortality in liver transplant (LT) recipients. Peripheral artery disease (PAD) is the third leading cause of atherosclerotic cardiovascular disease following coronary heart disease and stroke. However, the prevalence of PAD and the role of traditional cardiovascular risk factors and immunosuppression in PAD pathogenesis in LT recipients is unexplored. Therefore, we investigated the prevalence of PAD in LT recipients and in sex- and age matched controls and investigated the role of traditional risk factors and transplantation related factors in PAD in LT recipients.
Methods: The Danish Comorbidity in Liver Transplant Recipients (DACOLT) study is an ongoing prospective, national cohort study. Controls were matched by age and sex and included from the Copenhagen General Population Study. All participants underwent physical examinations including measurement of the ankle-brachial index (ABI). PAD was defined as ABI<0.9. We calculated the prevalence of PAD and investigated the association of potential risk factors using a logistic regression model adjusted for age, sex and smoking.
Results: 496 LT recipients and 2382 controls were included in the study. Median age was 55.5 years and 54.8% of the population were male. Median time since LT was 6.8 years (IQR: 2.8-13.4). There was no difference in the prevalence of PAD between the two groups (5.3% in LT recipients vs. 5.8% in controls, p=0.697). In adjusted logistic regression analyses for the whole group, hypertension and never vs. current smoking was associated with PAD (aOR 1.98 (95% CI: 1.40-2.81), p=<0.001 and aOR 0.51 (95% CI: 0.31-0.82) p=0.006), respectively. Liver transplantation was not found to be associated with PAD in adjusted logistic regression analysis and no association with transplantation related factors were identified.
Conclusions: In preliminary analyses, we found a comparable prevalence of PAD in LT recipients and population controls. Furthermore, LT was not associated with PAD in adjusted regression analysis. Further analyses are planned including analyses of the association between PAD and immunosuppressive drugs as well as other traditional- and transplantation related factors. All data has been collected.

Table 1: Logistic regression analysis for Peripheral Artery Disease for the whole group

	aOR [95% confidence interval]	p-value
Liver transplantation (yes vs. no)	1.01 (0.65-1.56),	0.959
Age (per decade older)	1.02 (0.91-1.16)	0.717
Sex (male vs. female)	1.12 (0.80-1.55)	0.514
Hypertension (yes vs. no)	**1.98 (1.40-2.81)**	**<0.001**
Smoking (Never vs. current	**0.51 (0.31-0.82)**	**0.006**
BMI (per 1 increase)	1.00 (0.96-1.04)	0.960

Adjusted for age, sex and smoking.
Abbreviation: BMI, body mass index.
Hypertension is defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg.

P463 RIGHT KIDNEY LIVING DONOR TRANSPLANTATION WITH LESSER ASYMMETRIC SPLIT RENAL FUNCTION: TWO CASE REPORTS

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Background: The number of end stage renal disease patients continues to grow in South Korea. Because of the discrepancy between increase in ESRD patients and kidney donations, transplantation with expanded criteria donors is gradually being implemented.
Methods: We present two cases of renal transplantation with lesser asymmetric split renal function that did not fall under the expanded criteria, but were performed as an opportunity to expand the indications for kidney donation
Results: For case 1, a 67-year-old woman underwent ABO-identical living related kidney transplantation from her 42-year-old son on May 2022. For case 2, a 42-year-old man underwent ABO-compatible living unrelated kidney transplantation from his 40-year-old wife on February 2022. In preoperative 99mTc-DTPA renal scan for donor evaluation, the results showed asymmetric split renal function. Scaled glomerular filtration rate of donors were 96.91ml/min/1.73 m ^{2} in case 1 and 165.81ml/min/1.73 m ^{2} in case 2. The left to right ratios of donor kidney split renal function were 62:38 in case 1 and 60:40 in case 2. Laparoscopic right donor nephrectomy was performed for the safety of donor. For renal vein elongation, we obtained right gonadal vein for case 1 and right ovarian vein for case 2. The vein grafts were reconstructed as circular wide tubes for right renal vein lengthening. Elongated right renal veins were anastomosed to each of the recipient's right external iliac vein with end-to-side fashion. Then we performed end-to-side anastomosis of the allograft right renal artery to each of the recipient's right external iliac artery. For case 1, recipient underwent hemodialysis for 45days due to delayed graft function. 6months after transplantation, allograft function of both recipients was acceptable.
Conclusions: Short term outcome of our cases shows lesser asymmetric split renal function may be additional option of the expanded criteria of living donor kidney transplantation.

P464 EVALUATION OF THE PROTECTIVE EFFECT OF ALKALINE PHOSPHATASE AGAINST ISCHAEMIA AND REPERFUSION INJURY IN PORCINE KIDNEYS

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Background: Kidney transplantation has been established worldwide as the last treatment for end-stage renal failure. However, ischemia-reperfusion injury (IRI) inevitably occurs during kidney transplantation. The most severe form of IRI leads to delayed graft failure, which is an important cause of morbidity and mortality after renal transplantation. A promising novel therapy strategy is the enzyme alkaline phosphatase (AP). Clinical and experimental evidences described great effect of AP therapy in modulate the inflammatory response in sepsis-associated acute kidney injury. Here we investigated the protective effect of bovine intestinal alkaline phosphatase (BiAP) on IRI and renal function in porcine kidneys.
Methods: Sixteen viable porcine kidneys (n = 8/group) were obtained from a slaughterhouse. All kidneys were submitted to 30 min of warm ischemia, 24h of oxygenated hypothermic machine perfusion (HMP), and 4h of normothermic machine perfusion (NMP). BiAP was added at the beginning of each step in the AP group. Non-treated kidneys (C) were used as controls. Biopsies and samples were taken to assess the renal injury.
Results: Kidneys treated with BiAP presented higher HMP flow (C:8.6± 2.9; AP 17.4±3.4 ml/min/100g; P=0.0313). In parallel, the treated group showed higher values in ATP concentration in renal biopsies after NMP (C: 21.74±9.362; AP36.88 ±11.99 *µmol/g protein; P= 0.014*). Regarding tissue damage, treated kidneys presented lower values to ASAT (C:704.2±580.6; AP:449.9±317.8 U/L, P=0.0625) and LDH (C:918.6±681.2; AP:638.6±371.8 U/L, P=0.0625).
Conclusions: Preliminaries data presented here suggest a protective effect of BiAP, preserving renal microcirculation, cellular metabolic activity and consequently avoiding tissue damage. Once AP was developed as an anti-inflammatory sepsis therapy, further analysis focusing on inflammatory parameters can elucidate the protective mechanism of the BiAP against IRI in kidneys.

P465 AMBULATORY BLOOD PRESSURE MONITORING PRIOR TO KIDNEY DONATION

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Background: In kidney transplantation, the *requirements* for organ *donation* has been extended to older donors or those with a history of cardiovascular disease that previously have been considered as contraindications. This study aims to determine the interest of ambulatory blood pressure monitoring (ABPM) prior to kidney donation.
Methods: It is a descriptive retrospective study of 15 living kidney donors who underwent casual clinic and ABPM.
Results: In our series of 105 living donor, in 90 among them, the hemodynamic evaluation of kidney donors was limited to clinic blood pressure levels. The remaining 15 donors underwent ABPM. Subjects were between the ages of 48 and 56, with a mean of body mass index of 26,5 kg/m² [22 -29,5 kg/m²]. The clinic systolic blood pressure (SBP) average was 138,5 mmHg [114 – 150] (table1). For 10 cases with clinic BP the ABPM was used to diagnose high blood pressure. The diagnosis of hypertension was rejected in 5 patient aged <50 y.o with a clinic BP at 140/90 mmhg and an ABPM daytime BP <135/85 mmHg and also In 2 patient aged > 50 y.o with normal BP in clinic BP measurement .The ABPM was used to check the blood pressure controle in 2 patients whom were treated by calcium channel blocker associated to an angiotensin II receptor antagonists in one case and confirmed a well-controlled hypertension assessed by ABPM <130/85 mmHg under treatment but one of them had a non-dipper hypertension. they had nephrectomy for successful kidney transplantation in the recipient and simple operative follow-up for the donor.
Conclusions: ABPM reveals white coat effect hypertension and confirm well- controlled hypertension. it should be more frequently used before and after kidney donation. the Amsterdam Forum recommend the use of an ABPM considers that, if donors whose blood pressure exceeds 140/90 mmHg should be generally challenged, some candidates over 50y.o whose hypertension is easily controlled without visceral repercussions may to be considered as donors.

Table1: Ambulatory blood pressure monitoring prior to kidney donation in 15 patient

Clinic SBP, mm Hg	140+/-13,2
Clinic DBP, mm Hg	90+/-8,1
Average 24-hour SBP, mm Hg	114+/-12,29
Average 24-hour day time SBP, mm Hg	109+/- 9,88
Average 24-hour night time SBP, mm Hg	115 +/- 14,2
day/night %	10,4+/- 8,9

P468 LUNG FUNCTION AFTER THORACO-ABDOMINAL NORMOTHERMIC REGIONAL PERFUSION IN A PORCINE DCD MODEL

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Background: Thoraco-Abdominal Normothermic Regional Perfusion (TA-NRP) is a relatively new method to assess potential donor organs in vivo. This platform enables in situ reperfusion of both thoracic and abdominal donor organs with oxygenated blood in donation after circulatory death (DCD) settings. Our purpose was to investigate the lung function during and after TA-NRP in a porcine DCD model while simultaneously monitoring the effect of low and high oxygenation on donor cardiac function.
Methods: Danish landrace pigs (80 kg) underwent 15 minutes anoxic circulatory arrest after disconnecting from mechanical ventilation. Subsequentially, resuscitation was initiated with TA-NRP through central cannulation. The animals received either high oxygen (FiO2 1.0, decreased to 0.6 post TA-NRP) or low oxygen (FiO2 0.21, increased to 0.40 during and after TA-NRP). Thereafter, 180 min of assessment post TA-NRP was followed. Blood gases, inflammatory cytokines and 8-isoprostane as oxidative stress marker were measured. Ventilation parameters were recorded. Tissue samples were taken from the ventral side for histological analysis and wet/dry weight ratio.
Results: In total 15/19 animals (7/9 in the low and 8/10 in the high oxygen group) were able to wean from TA-NRP. PaO_2 was significantly higher during TA-NRP and after 180 min in the high oxygen group compared to baseline. In both groups the PaO_2 remained acceptable and stable after TA-NRP. However, peak airway pressure was significantly increased and dynamic compliance significantly decreased during and post TA-NRP, independent of oxygen strategy. A higher trend in pro-inflammatory cytokines was seen in the high oxygen group. No differences were found in 8-isoprostane levels, histological scores and wet/dry weight ratio.
Conclusions: Lungs in both low and high oxygen groups maintained a stable and acceptable oxygenation capacity post TA-NRP. However, dynamic compliance decreased and peak airway pressure increased suggesting that TA-NRP is affecting the donor lung function which needs to be further investigated. No significant differences were observed in pro-inflammatory cytokines, oxidative stress, histological scores and oedema development. Further studies are necessary to determine lung function after transplantation.

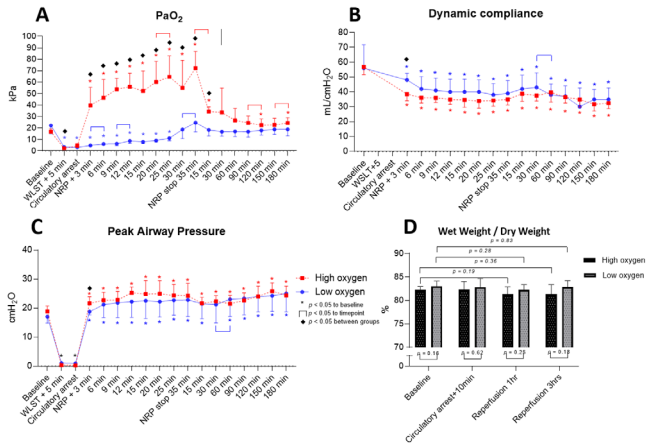

Figure 1. Ventilation parameters from baseline till 180 min after TA-NRP. A: PaO_2, B: Dynamic compliance, C: Peak airway pressure and D:Wet weight/Dry weight of the tissue samples. WLST = Withdrawal of life sustaining treatment, NRP = normothermic regional perfusion.

P471 LEARNING FROM VIGILANCE – THE INSTRUCTIVE VALUE OF THE NOTIFY LIBRARY

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Background: Since 2012, the Notify Library (https://www.notifylibrary.org) collects scientific literature related to different types of adverse occurrences associated with the clinical use of blood, organs, tissues and cells (Medical Products of Human Origin, MPHO). The scope of the Library is to support the sharing of published vigilance information for educational purposes by making available the existing knowledge on serious adverse events and reactions in transfusion and transplantation.
Methods: Each record in the Notify Library can be linked with one or multiple references. The record inclusion criteria are that it has been reliably documented in a published article or official vigilance reporting system and that it has instructive value for the fields of transfusion and transplantation. The selection and review of references for publication is performed by international experts who collaborate in 5 topic-specific editorial groups: infection transmission, malignancy transmission, living-donor reactions, process-related incidents, and other clinical complications. The aim of this communication is to provide an overview of the Notify Library and promote its use among the European Transplant community.
Results: The Notify Library contains 1848 didactic records quoting 2742 published references. Analyzing the database content by MPHO type, 44% of records (809/1848) were related to organs (kidney, 338; liver, 248; lung, 75; heart, 53; combined/multivisceral, 26; pancreas, 14; other/unspecified, 55), 20% (370/1848) to blood and blood components, 16% (301/1848) to hematopoietic progenitor cells, 14% (266/1848) to tissues and 6% (102/1848) to other MPHO. Of the 809 records that involve organs, 640 were categorized as “Harm to a recipient” (infection transmission, 333; malignancy transmission,270; immunological complications, 20; non infectious-non malignant transmissions, 13; other, 4), 101 as “Harm to donor” and 68 as “Risk of harm” (including 36 cases of donor disease without documented transmission in the recipient).
Conclusions: Notify Library is the first open-access, searchable database of systematically identified reports of disease transmission and other adverse occurrences arising from the donation and clinical application of MPHO.

P474 HISTOLOGICAL ANALYSIS OF EXPRESSION OF AT1R, ETAR AND ADHESION MOLECULES IN PEDIATRIC KIDNEY TRANSPLANT PROTOCOL BIOPSIES

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Background: Antibody-mediated rejection (AMR) is the major cause of premature kidney transplant failure. The role of alloantibodies against Human Leukocyte Antigens (HLA) in mediating AMR has been of primary interest in transplantation. However, there is evidence that non-HLA autoantibodies have a role in the involvement in AMR. Auto and allo antibodies against angiotensin II receptor 1 (AT1R) and endothelin A receptor (ETAR) have been associated with poor allograft outcomes in renal transplantation. Nevertheless, evidence for routine tests remain insufficient, especially in the pediatric field.
Methods: In our pediatric renal transplant cohort was performed ELISA assay of anti-AT1R and anti-ETAR antibodies. From these patients, we selected 12 transplant recipients with at least protocols biopsies and antibodies dosage at 6 and 24 months after transplantation. Six patients had high levels of anti-AT1R and anti-ETAR antibodies (>40 U/mL) and six were negative (<17 U /mL). Immunohistochemistry was performed on patient's tissue biopsies to evaluate the expression of AT1R and ETAR receptors and adhesion molecules iCAM-1 and VCAM-1.
Results: Our analysis showed that there is no difference between AT1R and ETAR receptors expression in the presence or absence of circulating antibodies. In contrast, iCAM-1 and VCAM-1 expression was statistically significant in the presence of circulating antibodies at 24 months after transplant.
Conclusions: In our cohort, the presence of anti-AT1R and anti-ETAR antibodies does not seem to influence the expression of their receptors in the transplanted organ. However, anti-AT1R and anti-ETAR antibodies are associated with an increase of iCAM-1 and VCAM-1 expression in the graft. This preliminary study has some limitations, such as the low number of patients and a follow-up time which could be insufficient to observe the manifestation of a chronic change on biopsy. However, the increase in adhesion molecules could prove to be an event that anticipates the development of histological damage. Thus, increasing the cohort and extending long-term observation would help to better understand the impact of anti-AT1R and anti-ETAR antibodies after transplantation.

P475 SUCCESSFUL DESENSITIZATION WITH IMLIFIDASE AND DARATUMUAB IN A HIGHLY IMMUNIZED, CROSS-MATCH POSITIVE LIVING-DONOR RE-TRANSPLANT RECIPIENT

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Background: Transplantation of highly sensitized patients remains a major obstacle. Imlifidase is currently the only approved therapy for desensitization treatment of highly sensitized adult kidney transplant patients with a positive crossmatch (XM) against available deceased donors, while it is not approved for the use in living kidney transplantation.
Methods: We report as case of a successful AB0-incompatible (AB0i) living kidney transplantation in a highly sensitized, B and T cell CDC XM-positive patient with systemic lupus erythematosus (SLE) and secondary antiphospholipid syndrome (APS) with multiple thrombosis, previous kidney transplantation with graft loss 5 years ago due to venous thrombosis in the graft vein and extremely limited vascular access for dialysis.
Results: We (pre-) treated the patient with rituximab, Anti-thymocyte globulin, intravenous immunoglobulin imlifidase, and daratumumab besides standard immunosuppression (Figure 1A). Surgical procedure of living donor kidney transplantation (donor: mother, 68y) was uneventful, however, the patient remained anuric until day 28 after transplantation with subsequent increase of diuresis. Since then, creatinine levels declined to a baseline creatinine of 1.9 mg/dl (Figure 1B). Histopathologically, the picture of acute tubular necrosis was present in biopsies on day 7 and 14 with no signs of rejection (Figure 1C). All IgG antibodies were sensitive to imlifidase treatment and, so far, remained low under daratumumab treatment and standard immunosupression. Besides donor-specific antibodies (Figure 1D) anti-dsDNA antibodies and antiphospholipid antibodies, were cleaved, too. Anti-CD38 treatment affected mainly peripheral NK-cell numbers. Interestingly, despite anti-CD20 and anti-CD38 treatment, the patient was still able to generate peripheral plasmablasts (Figure 1F,G).
Conclusions: In this case, we successfully used a novel combined treatment strategy for a highly immunized patient with the combination of daratumumab and imlifidase. Besides controlling alloantibodies also autoantibodies such as anti-phospholipid antibodies were removed which makes this therapy an option for patients with catastrophic APS.

Figure 1A

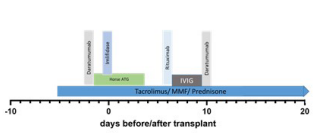


Figure 1B

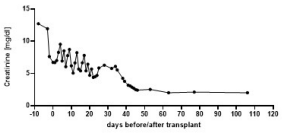


Figure 1C

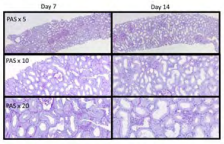


Figure 1D

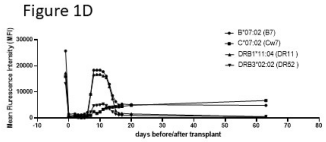


Figure 1E

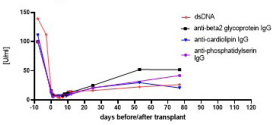


Figure 1F

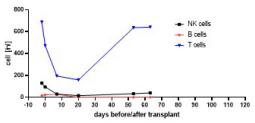
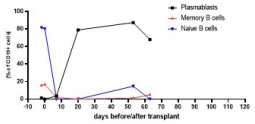


Figure 1G



P476 IMPLANTABLE CARDIOVERTER DEFIBRILLATORS AND PREVENTION OF SUDDEN CARDIAC DEATH IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Sudden cardiac death (SCD) is the leading cause of death among ESRD and dialysis patients. Cardiovascular diseases are the leading cause of death among kidney transplant recipients (KTR). Implantation of a cardioverter defibrillator (ICD) is the first-line treatment option for prevention of SCD. Data on ICD in patients with chronic kidney disease is scarce. To the best of our knowledge there is no data in the literature on KTR with ICD and here we present our experience.
Methods: We retrospectively analysed medical records of patients receiving kidney transplant between December 1999 and December 2021. Characteristics and outcomes of patients with ICD defibrillator were investigated.
Results: Of 1689 patients who received kidney alograft 9 patients underwent ICD implantation (0.53%), 8 males. The cause of ESRD was unknown in 2 patients, ADPKD in 2 patients, 2 had tubulointerstitial nephritis while nephroangiosclerosis, vesicoureteral reflux and Balcan endemic nephropathy were the cause of ESRD in one pateint each. Mean dialysis vintage prior kidney transplantation was 3.3 years (0.7-8.5). Average age at the time of transplantation was 53.4 years (42.7-66.6). Indication for ICD implantation was primary prevention of SCD in 5 patients while 4 patients had ICD in secondary prevention. Mean time of ICD implantation after transplantation was 8.2 years (1.9-16.4), while female patient had ICD implanted 2.9 years prior kidney transplantation. Average age at the time of ICD implantation was 60.4 years (49-69.4). At the time of ICD implantation all patients had reduced kidney graft function with average eGFR 38 ml/min/1.73 m^2 . During average of 4.1 years of follow up (0.6-7.2) graft function remained stable in all patients. One patient died 5 years after ICD implantation due to severe COVID.
Conclusions: KTR are specific category of CKD patients with increased cardiovascular risk. If there is an indication these patients should be considered candidates for ICD implantation prior or after kidney transplantation. Further studies are needed to prevent exclusion of kidney transplant recipients from this important and life-saving procedure.

P478 HLA-DQ MISMATCHING AND RENAL TRANSPLANT OUTCOMES IN THE UK

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Background: The aim of our study was to assess the effect of HLA-DQ mismatches on renal transplant outcomes, in terms of acute rejection episodes and death censored graft survival among the UK population.
Methods: All renal transplant patients registered in the NHSBT database from 2007 till 2020 were retrospectively reviewed. Patients were followed up till June 2022. Patients with missing data about their HLA-DQ mismatched were excluded. Data about recipient demographics, transplant factors (HLA mismatches, cold ischemia time, number of previous transplants, type of induction and maintenance immunotherapy), and donor factors (demographics, donor type for living and deceased transplant). Acute rejection at 3 months follow-up was defines as clinically suspected or biopsy-proven rejection. Death censored graft survival was defined as the need of maintenance dialysis post-transplant. Logistic and cox regression analysis were used.
Results: 18,898 deceased donor transplant and 12,340 living donor transplant patients were included in the analysis. Among the deceased transplants, HLA-DQ mismatch was significantly associated with higher risk of acute rejection episodes (2-HLA-DQ :OR=1.39; 95%CI=1.10 to 1.75; P value<0.01). This relationship remained significant even among patients with 0-HLA-DR mismatch (2-HLA-DQ :OR=1.66, 95%CI=1.05 to 2.58, P =0.02 ;and 1-HLA-DQ :OR=1.21, 95%CI=1.03 to 1.48,P=0.04). However, HLA-DQ mismatch was not associated with death censored graft survival (P<0.05). Among the living transplants, HLA-DQ mismatch was significantly associated with higher risk of acute rejection episodes (one or two HLA-DQ :OR=1.32; 95%CI=1.07 to 1.62; P value<0.01). This relationship remained significant even among patients with 0-HLA-DR mismatch (one or two HLA-DQ :OR=1.97; 95%CI=1.39 to 2.08; P value<0.01). However, HLA-DQ mismatch was not associated with death censored graft survival (P<0.05).
Conclusions: HLA-DQ mismatching is associated with higher risk of early acute rejection among deceased and living transplant patients, independent of HLA-DR mismatch. However, it not associated with worse graft survival.

P479 HIGHEST RESPONSE RATES OF VECTOR CONTAINING REGIMENS AFTER FOUR DOSES OF COVID-19 VACCINES IN RENAL TRANSPLANT RECIPIENTS

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Background: Homologous dual-dose vaccination with vector (V) or mRNA (R) based vaccines is insufficient in renal transplant recipients (RTx), whereas heterologous vector/mRNA vaccination – like in immunocompetent individuals – induces stronger humoral and cellular immunity. It is not known so far, if and to which extent a heterologous regimen accomplished with third or fourth vaccination may lead to improved immunogenicity in former low-responders.
Methods: Whole blood samples of 46 RTx after homologous or heterologous dual-dose vaccination (VV, VR, RR) were analyzed after second, third and fourth vaccination. Patients with prior vector containing regimen received mRNA vaccines (VVRR, VRRR); patients after initial homologous mRNA vaccination were either maintained at the mRNA regimen (RRRR) or received subsequent heterologous V/R vaccination (RRVR). Spike-specific IgG, neutralizing antibody activity as well as quantity, phenotype and functionality of spike-specific CD4 and CD8 T cells were analyzed 7-42 days after the respective vaccinations.
Results: In all vector containing regimens, an increase of antibody responders was detectable after third and fourth vaccination (VVRR 62.5%, VRRR 50%, RRVR 66.7%). T-cell response rates were higher already after second vaccination after a heterologous regimen and further increased after third and fourth vaccination (VVRR 87.5%, VRRR 88.9%, RRVR 55.6%). In contrast, the response rates for both IgG (45.5%) and T cells (45.5%) remained low after third homologous mRNA vaccination with no further increase after the fourth. When analyzing the combined response of IgG and/or T cells, response rates were highest in vector containing regimens (100% after VVRR, 94.4% after VRRR, 77.8% after RRVR), and lowest after RRRR vaccination (54.4%). The groups did not show any differences in T-cell reactivity after polyclonal stimulation supporting that the detected effects were vaccine specific.
Conclusions: Vector containing regimens led to highest response rates after four vaccinations. A heterologous vector/mRNA combination applied as third and fourth vaccination seems superior to a mere mRNA based four-dose regimen in previous non-responders.

P480 DIAGNOSTIC POTENTIAL OF SEQUENCING BASED T CELL ANALYSIS IN RENAL TRANSPLANT PATIENT WITH ACUTE COVID-19 AND GRAFT FAILURE

Ulrik Stervbo[1], Jan Zapka[1], Bodo Hoelzer[1], Julia Kurek[1], Moritz Anft[1], Adrian-Atila-Nicolas Doevelaar[1], Timm H. Westhoff[1], Nina Babel*[1;2]

[1]Marien Hospital, Center for translational medicine, Herne, Germany, [2]Charité Campus Virchow Clinic, Berlin, Germany

Background: Kidney transplantation is associated with an increased risk of severe COVID-19 disease. The focal nature of infections make false negative results with common histology possible, which in turn could lead to a flawed diagnosis and treatment. Utilizing the entire biopsy may alleviate the problem but is impractical with the current histological technology. Here we present a sequencing based evaluation of kidney infiltrating T cell receptors (TCR) in two cases of kidney transplant patients, who suffered impaired kidney function during an acute SARS-CoV-2 infection.
Methods: The possible role of cellular immunity towards SARS-CoV-2 infected kidney cells was assessed through AIRR-seq by next generation sequencing of the TCR of whole biopsies and SARC-CoV-2 specific T cells of the peripheral blood. SARC-CoV-2 specific T cells were isolated from peripheral blood by overnight stimulation with an overlapping peptide pool of SARS-CoV-2 S-protein (Wuhan variant) and subsequent isolation by MACS for CD154+ and CD137+ T cells. One kidney transplant donor was a living relative, which enabled us to setup a mixed lymphocyte reaction to further evaluate acute rejection, as a cause of decreased kidney function.
Results: From patient 1 we obtained $1.7x10^7$ reads from the S-protein specific T-cells, and $2.5x10^6$ reads from the biopsy. Of these, we identified 127,310 distinct clonotypes in the peripheral blood, but 0 in the kidney biopsy. This lack of T cell infiltration was confirmed by conventional histology, and exclude a T cell driven etiology. From patient 2 we obtained $9.8x10^6$ reads from the kidney biopsy, $9.5x10^6$ reads from the S-protein specific T-cells, and $5.7x10^6$ reads from the mixed lymphocyte reaction. This translated into 104,760, 24,743, and 5,312 distinct clonotypes, respectively. Here, 11.1% of the repertoire of the kidney infiltrating T cells were identical to S-protein specific T-cells in the periphery, and only 3.12% of the repertoire was identical to donor reactive TCRs.
Conclusions: AIRR-Seq of whole biopsies is a method to evaluate T cell infiltration and the specificity of these infiltrating T cells. We find that one patient had an infiltration of predominantly SARS-CoV-2 specific T cells, indicating SARS-CoV-2 as a leading cause of the kidney function deterioration.

P481 ENDOVASCULAR TREATMENT OF RESISTANT RENO-VASCULAR HYPERTENSION IN A PATIENT WITH MIDDLE AORTIC SYNDROME (CLINICAL CASE)

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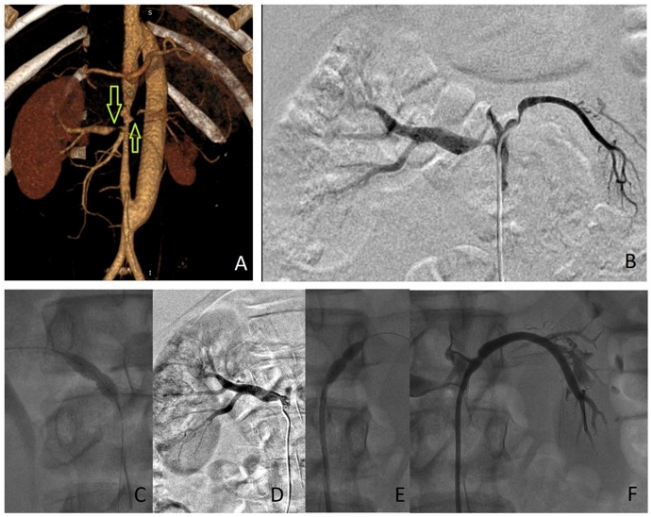
Background: Middle aortic syndrome (MAS) is a very rare condition generated by segmental narrowing of distal descending thoracic or the abdominal aorta. It is often associated with renal artery stenosis and resistant renovascular hypertension. We present a clinical case of surgical correction of a severe refractory renovascular hypertension in a child with middle aortic syndrome who was admitted to our clinic as a potential kidney recipient.
Methods: The patient was a 13 y.o. boy after aorto-aortic bypass grafting with recurrence of resistant vasorenal hypertension who came to Shumakov center to decide on further treatment tactics. He was considered to be a potential kidney transplant recipient. His height was 159 cm; weight was 57.4 kg. Heart rate at rest 102/min. Blood pressure measured on the right hand was 184/96, on the left hand 190/100. He had stenotic lesions of both renal arteries, a progressive decline of the left kidney function and volume. was admitted to our clinic as a potential kidney recipient. We decided on an intravascular approach instead. We performed balloon vasodilation with stenting of the inferior pole left kidney artery, and the right renal artery. The lesions of the renal arteries and the stages of the intervention are shown in Figure 1.
Results: Control examination was performed 4 months after stenting. It showed reduction of the arterial hypertension (average blood pressure in the daytime was 142.6 mm Hg, average DBP during the daytime was 79.5 mm Hg, average blood pressure at night was 111.3/61.5 mm Hg. And LV hypertrophy (LVMI (S) decreased from 163.8 g/m2 to 159.7 g/m2). Dopplerography of the renal arteries showed improvement of velocimetric indicators: an increased peak (PSV) and diastolic (EDV) velocities and normalization of the resistance index values at all levels (Tab. 1). After the examination, we were able to reduce the antihypertensive therapy.
Conclusions: Hypoplasia of the abdominal aorta is a rare pathology with undefined etiology. Surgical intervention in the form of an aorto-aortic bypass is an important stage of treatment. In case of vasorenal arterial hypertension recurrence, caused by the progression of the renal arteries stenosis, endovascular correction can be considered a safe and effective method.

Figure 1



Tab. 1

Fig.1 a) CT angiography performed after aorto-aortic bypass surgery showing hypoplasia of the abdominal aorta and stenosis of both renal arteries. b) angiography showing renal arteries stenosis. c, e) renal arteries stenting. d, f) results of renal arteries angioplasty

	Peak systolic velocity (PSV) m/s / diastolic velocity (EDV) / resistance index					
	Baseline		After aorto-aortic bypass grafting and reimplantation of the left renal artery into the graft		After balloon vasodilatation with stenting of the inferior pole left kidney artery, and the right renal artery	
	Right	Left	Right	Left	Right	Left
Renal arthery	1,04/0,23/0,78	0,97/0,33/0,66	0,42/0,20/0,52	unable to measure	0,68/0,29/0,57	0,6/0,17/0,7
Segmental arteries	0,41/0,15/0,64	0,25/0,09/0,6	0,30/0,17/0,42	0,24/0,12/0,5	0,42/0,18/0,57	0,34/0,15/0.7
Interlobar arteries	0,14/0,09/0,34	0,17/0,09/0,48	0,19/0,12 0,37	0,18/0,12 0,33	0,26/0,14/0,46	0,24/0,11/0,55

Table. 1 Intrarenal ECHO-doppler velocimetric indices.

P482 LONGITUDINAL ANALYSIS OF PERIPHERAL BLOOD IMMUNE CELL SUBSETS IN KIDNEY TRANSPLANT RECIPIENTS AND CLINICAL CORRELATIONS – A PROSPECTIVE STUDY

Anila Duni[1;2], Athanasios Kitsos[2;3], Georgios Markopoulos[4], Vasileios Koutlas[2], Eirini Tzalavra[2], Vasileios Tatsis[2], John Alekos[3], Louiza Gkika[3], Gerasimos Baxevanos[5], Haralampos Pappas[2;3], Georgios Vartholomatos[4], Michalis Mitsis[2], Evangelia Dounousi*[2;3]

[1]University Hospital of Ioannina, Department of Nephrology, Ioannina, Greece, [2]University Hospital of Ioannina, Department of Surgery and Kidney Transplant Unit, Ioannina, Greece, [1]University Hospital of Ioannina, Department of Nephrology, Ioannina, Greece, [4]University Hospital of Ioannina, Laboratory of Hematology - Unit of Molecular Biology, Ioannina, Greece, [5]Hatzikosta General Hospital of Ioannina, Internal Medicine Department, Ioannina, Greece

Background: There are little data regarding the clinical value of regular monitoring of immune cells phenotypes in the peripheral blood of kidney transplant recipients (KTRs). The aim of our study was a longitudinal follow-up analysis of immune cell subtypes in the peripheral blood of KTRs and potential clinical correlations.
Methods: 48 stable KTRs were enrolled in this observational, prospective study. Patients were prospectively followed for 12 months. Exclusion criteria were history of acute rejection, cardiovascular disease (CVD), malignancy, autoimmunity and active or chronic infections before study enrollment or during follow-up. The peripheral blood immune cell subsets CD14++CD16-, CD14++CD16+ and CD14+CD16++ absolute values and percentages out of total monocytes and NK cells (CD3+CD16+56+), CD3-CD19+ B lymphocytes, CD3+ CD4+ T cells, CD3+CD8+ T cells and Tregs (CD4+CD25+ FoxP3+) absolute values and percentages out of total lymphocytes were measured by flow cytometry at baseline (T0) and after 12 months (T1). Clinical and laboratory parameters were recorded at T0 and T1.
Results: The final cohort included 40 KTRs (mean age 58 ±9.28 years, 26 males, 17 patients on cyclosporine and 23 patients on tacrolimus). During follow up, the mean eGFR (CKD-EPI) declined from 58 ±17 to 53 ±18ml/min/1.73 m2 (p= 0.004). There was a decrease in total monocytes (648±241/μL versus 537 ±194/μL, p=0.01) and total lymphocytes (2115 ±127/μL versus 1925±724/μL, p=0.04). The classical CD14++CD16- monocytes increased at T1 (533±224/μL) compared to T0 (451±185/μL) (p=0.04). The rest immune cell subsets did not show any significant changes. A larger increase of the intermediate CD14++CD16+ monocytes counts from T0 to T1 correlated with a greater eGFR decline during follow-up (ρ = -0.339, p=0.04). No significant changes were observed in spot urine protein to creatinine ratio (UPCR), inflammatory markers (CRP, ESR) or calcineurin inhibitors blood levels between T0 and T1.
Conclusions: Our results suggest that increased yearly graft function loss might be associated with more marked augmentation of the pro-inflammatory CD14++CD16+monocytes counts. Future studies with longer follow-up are required to specify the role of regular monitoring of immune cells subsets as potential prognostic biomarkers in KTRs.

P483 RESULTS OF NORMOTHERMIC REGIONAL PERFUSION IN CONTROLLED DONATION AFTER CIRCULATORY DEATH PROVIDED BY A MOBILE ECMO TEAM ACROSS THE REGION OF MADRID

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Background: The use of Abdominal normothermic regional perfusion (A-NRP) in controlled donation after circulatory death (cDCD) is recommend in preference to in situ cooling and rapid procurement (1B). This procedure requires experience and the availability of ECMO. In order to provide support with A-NRP in centers with cDCD programs but without ECMO access, the region of Madrid created a A-NRP team. Our center, with ECMO experience, is a part of a one week-on/one week-off roster.
Objective: to describe the experience of our center as part of the Mobile ECMO team since the program begun.
Methods: Retrospective study (Apr 2017-Dec 2022). We included all Mobile ECMO team outings. We studied demographic data, ICU length of stay and the reasons for withdrawal of life-sustaining treatments (WLST) of the donors. Number of organs evaluated and the reasons for discard. ECMO run and complications related with ECMO cannulation.
Results: During the period studied our ECMO Mobile team was mobilized 41 times to ten different hospitals. A-NRP was successfully performed in 37 cases. Of the 37 utilized donors 21 (59%) were male with mean age of 58 ± 14 years. The reasons for WLST were anoxic encephalopathy following cardiac arrest (n=17, 46%), catastrophic brain injury after ischemic/hemorrhagic cerebrovascular event or traumatic brain injury (n=16, 43%), terminal respiratory illness (n=3, 8%) and one case after euthanasia. Mean ICU length of stay was 9 ± 8 days. Cannulation problems were reported in 15 cases (40%) with 4 hemorrhagic complications during vessels cannulation and 11 events of non-progression of the aortic balloon that needed surgical cross clamp of the aorta before A-NRP. Mean warm ischemia times were 15 ± 6 minutes. Mean duration of the A-NRP was 82 ± 27 minutes. Of the 64 kidneys, 32 livers and 11 lungs evaluated, 58 kidneys, 18 livers and 7 lungs were implanted. The main reason for discard was unfavorable visual assessment and surgical complications and only in one case because of prolonged warm ischemia time.
Conclusions: The establishment of a Mobile ECMO team is feasible across the region of Madrid and it allows to all potential cDCD donors be evaluated for A-NRP. Cannulation problems are common but in most of the cases the A-NRP is possible, that emphasized the fact that experience team is essential to achieve good results.

P484 IMPACT OF CONVERSION OF TWICE-DAILY TACROLIMUS TO ONCE-DAILY EXTENDED-RELEASE MELTDOSE TACROLIMUS ON CELLULAR IMMUNITY

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Background: LCP-Tacro [LCPT], a novel once-daily, extended-release formulation of tacrolimus, has a reduced C_{max} with comparable AUC exposure, requiring a ~30% dose reduction in contrast to immediate-release tacrolimus (IR-Tac). Once-daily LCPT in de novo kidney transplantation has a comparable efficacy and safety profile to that of IR-Tac with advantages in bioavailability and absorption. The present investigation intends to analyse the effects of conversion from IR-Tac to LCPT on phenotype and function of T-cell and B-cells.
Methods: 20 kidney transplant patients treated by triple standard immunosuppression with a stable graft function undergoing a switch from IR-Tac to LCPT were included in this observational prospective study. We analysed peripheral blood of the patients before and 4 and 8 weeks after IR-Tac to LCPT conversion using multi-parameter flow cytometry. We measured the main immune cell types and performed an in-depth characterization of B cell, dendritic cell (DC) and T cells including regulatory T cell (Treg). Additionally, we analysed antigenic responsivity of T cells by assessing third-party antigen (Tetanus)-reactive T cells, which could be analyzed by restimulation with tetanus vaccine (TD).
Results: Overall, we found no significant alterations following LCPT conversion for the most immune cell populations with a few cell populations showing quantitative increase. Thus, 4 weeks after conversion, more lymphocytes and regulatory T cells could be measured in the patients. These differences were borderline significant (p= 0.051 and p=0.08 respectively). Furthermore, we found significantly more regulatory T cells with a naïve phenotype ($CD45RA^+CCR7^+$). These alterations did not change again 8 weeks after conversion.
Conclusions: Here, we demonstrate first insights into the immune system changes occurred under IR-Tac to LCPT conversion therapy in kidney transplant patients. While phenotypic and functional characteristics of the most T and B cell populations did not change following conversion to the Tac dose sparing regime, we could observe an increase in the number of regulatory T cells in peripheral blood following IR-Tac to LCTP conversion, which might additionally contribute to the overall immunosuppressive effect.

P485 PERFORMANCE OF DIFFERENT ESTIMATED GLOMERULAR FILTRATION RATE EQUATIONS IN PREDICTING END-STAGE KIDNEY DISEASE EARLY AFTER LIVER TRANSPLANTATION

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Background: Kidney dysfunction is common after liver transplantation (LT), but postoperative end-stage kidney disease (ESKD) is difficult to predict. The aim of this study was to evaluate the risk of ESKD after LT and the predictive ability of various estimated glomerular filtration rate (eGFR) equations.
Methods: This single-center study included patients undergoing primary LT 2006-2020. We calculated 10 different eGFR equations, based on plasma creatinine and/or cystatin C measured just before LT, and assessed their predictive ability using area under receiver operating curve (AUC).
Results: Among 556 LT patients with a median follow-up of 5.0 years (IQR 2.0-8.5), 20 developed ESKD during follow-up, 7 of them within 1-year post-LT. Six of these 7 suffered from major perioperative complications. The GFR assessment in liver disease (GRAIL) formula (AUC 0.71) and the Royal Free Hospital (RFH) equation (AUC 0.70) performed best in predicting ESKD within 1 year. AUCs for cystatin C-based eGFR equations ranged from 0.65-0.66. Depending on the eGFR equation used, ESKD incidence within 1-year was 3.4-16.7% at pre-LT eGFR-values <30 mL/min, 0.5-3.1% at eGFR 30-60 mL/min, and 0.6-1.2% at eGFR ≥60 mL/min.
Conclusions: ESKD within 1-year post-LT was uncommon even in patients with severe pre-operative kidney dysfunction, and extremely rare in patients unaffected by major perioperative complications. ESKD could not be reliably predicted by pre-LT eGFR. Cystatin C-based eGFR equations failed to predict ESKD better than creatinine-based ones.

Figure 1. Positive predictive values (PPVs) for end-stage kidney disease (ESKD) within first year after liver transplantation stratified by estimated glomerular filtration rate (eGFR) subgroups.

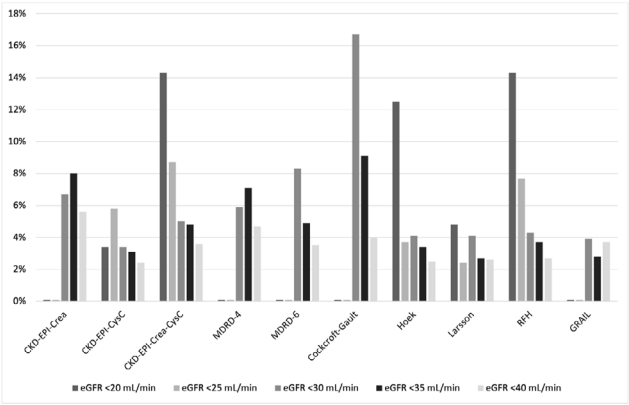

Table 1. Area-under-the-curve (AUC) values with 95% confidence intervals (Cis) for various estimated glomerular filtration rate (eGFR) equations for end-stage kidney disease (ESKD) within the first post-transplant year, and for need for post-operative kidney-replacement therapy.

	ESKD <1 year	Post-operative kidney replacement therapy
eGFR equation	AUC (95 % CI)	AUC (95 % CI)
CKD-EPI-Crea	0.592 (0.339 - 0.844)	0.673 (0.616 - 0.730)
CKD-EPI-CysC	0.652 (0.426 - 0.878)	0.721 (0.668 - 0.774)
CKD-EPI-Crea-CysC	0.631 (0.392 - 0.870)	0.712 (0.658 - 0.766)
Cockcroft-Gault	0.537 (0.283 - 0.790)	0.600 (0.536 - 0.663)
MDRD-4	0.611 (0.380 - 0.790)	0.673 (0.616 - 0.729)
MDRD-6	0.640 (0.433 - 0.847)	0.702 (0.650 - 0.755)
Hoek	0.655 (0.442 - 0.867)	0.727 (0.675 - 0.779)
Larsson	0.655 (0.442 - 0.867)	0.727 (0.675 - 0.779)
RFH cirrhosis GFR	0.695 (0.517 - 0.873)	0.707 (0.655 - 0.760)
GRAIL	0.709 (0.525 - 0.893)	0.694 (0.638 - 0.749)

P486 NOVEL ANTIBODIES TO TARGET THE MEMBRANE ATTACK COMPLEX IN TREATING KIDNEY ISCHAEMIA REPERFUSION INJURY

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Background: Complement is a potent driver of inflammation in many disease processes including Ischaemia Reperfusion Injury (IRI). The cytotoxic and pro-inflammatory membrane attack complex (MAC) is the major pathological effector of the complement cascade. This direct pathological role of MAC makes it an attractive therapeutic target. Eculizumab, an anti-C5 monoclonal antibody (mAb), is one drug that has transformed patient outcome in renal diseases, but its considerable cost makes it untenable for common use. We have developed and patented a novel mAb (anti-C7) that targets MAC downstream of C5, and have shown it to be efficient in reducing inflammation in rodent models of myasthenia gravis. The aim of this study was to test whether this novel anti-C7 mAb could reduce injury in a rat Kidney IRI model.
Methods: Adult male Lewis rats were injected with anti-C7 mAb 2H2 or D1.3 isotype IgG control (n=6 each). A midline laparotomy was performed; pedicles of both kidneys were clamped for 45mins; Kidney tissue was retrieved at 48h. Paraffin sections were made and sectioned for H&E and immunohistochemistry. Blood was taken for measurement of serum creatinine and complement lytic activity pre-op and at 48h.
Results: Anti-C7 mAb treated kidneys showed (i) Less histological damage (reduced EGTI score; assessing the architecture of the endothelium, tubules, glomeruli and interstitium within the renal cortex); (ii) Reduced serum creatinine at 48h; (iii) Complete inhibition of complement haemolytic Activity and reduced terminal complement components (TCC) in serum at 48h; and (iv) Markedly reduced TCC deposition on immunohistochemistry analysis.
Conclusions: MAC can be successfully targeted downstream of C5 (through inhibition of the C7/C5b-7 complex) by this novel anti-C7 mAb. Targeting MAC-intermediates has potential as an innovative therapeutic approach in treating kidney IRI and improving transplant outcomes. Moreover, this approach is potentially more cost effective than other anti-MAC therapeutics such as eculizumab

P488 STRONGEST IMMUNOGENICITY OF HETEROLOGOUS COVID-19 VECTOR/MRNA VACCINATION IN COMPARISON TO HOMOLOGOUS REGIMENS IN KIDNEY AND LUNG RECIPIENTS

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Background: Dual-dose mRNA vaccination proved insufficient in the induction of antiviral immunity in transplant patients. Based on our observation of increased immunogenicity after heterologous vector/mRNA vaccination in immunocompetent individuals, the impact of heterologous vaccination was analyzed after transplantation in comparison to homologous regimens. In addition, vaccine-induced immune responses were compared between renal and lung transplant recipients (RTx/LTx) and respective transplant candidates on the waiting list.
Methods: Blood samples of 252 transplant recipients (169 RTx, 83 LTx) and 41 waitlist patients were recruited. Analysis of spike-specific IgG, neutralizing antibody activity as well as of spike-specific CD4 and CD8 T cells was performed 14 days after heterologous vector/mRNA vaccination or after vaccination with homologous regimens.
Results: Overall, response rates were highest in the group of waitlist patients. Comparison of the different vaccine regimens revealed significant differences in IgG and T-cell levels in all patient groups. Despite different levels of immunosuppression, the immunogenicity profile was similar in RTx and LTx. In both groups, heterologous vaccination not only induced higher amounts of IgG (NTx p=0.027; LTx p=0.006) and T cells (CD4 NTx p=0.003; LTx p=0.017; CD8 NTx p=0.004, LTx p=0.004), but also led to significantly higher response rates than homologous regimens. Regarding antibodies, 47.8% of RTx and 70% of LTx showed vaccine-induced reactivity after heterologous vaccination whereas only 24.5-25% reacted to homologous vaccination. Similarly, heterologous vaccination induced spike-specific CD4 and CD8 T cells in 63% and 50% of RTx and 60% and 50% of LTx, respectively with only 12.3-41.7% being positive for CD4 and 7.7-33.3% for CD8 T cells after a homologous regimen.
Conclusions: The heterologous vector/mRNA vaccination was superior to homologous regimens in inducing both antibodies and T cells. Additionally, the higher percentage of T-cell responders indicates that immunogenicity of the vaccines is underestimated when considering antibodies alone.

P489 IMPACT OF IMMUNOSSUPRESSION WITHDRAWAL IN DONOR(HLA)-SPECIFIC MEMORY B CELL RESPONSES IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

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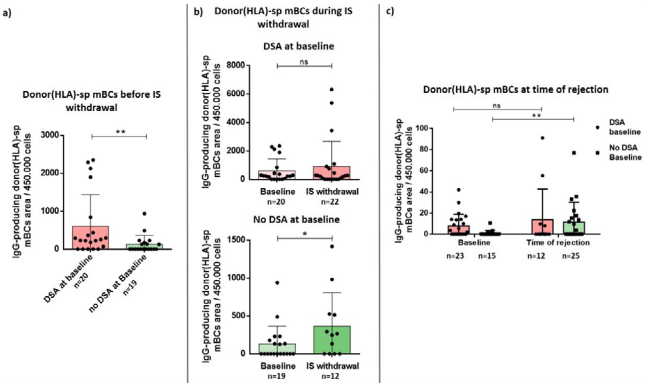
Background: To generate allograft tolerance and avoid long-term immunosuppression (IS) is key to good health and quality of life in pediatric liver transplant recipients. Despite this, IS withdrawal may activate humoral alloimmune responses that may ultimately cause rejection. Tracking donor(HLA)-specific (d-sp) memory B cells (mBCs) besides DSA may guide safe IS withdrawal by identifying early anti-donor alloimmune activation.
Methods: 48 pediatric liver transplant recipients participating in a complete IS withdrawal trial (iWITH, NCT01638559) with serial PBMC samples obtained during IS withdrawal were assessed for the presence of d-sp mBC frequencies and DSA. D-sp mBCs responses were characterized using a novel HLA-specific B-cell Fluorospot assay at baseline, prior to, during and after (months 3, 6, 9, and 12) IS withdrawal as well as at time of rejection. HLA-sp mBC counts were given as means of surface spot area (mm2) per 450,000 seeded, polyclonally expanded mBC.
Results: At baseline, patients with DSA exhibited higher frequencies of mBCs than patients without DSA (604.5 ± 185.4 vs 129.4 ± 53.8,p=0.009, respectively) (Fig 1a). Interestingly, frequencies of d-sp mBCs increased during IS withdrawal in all patients (604.5 ± 185.4 vs 911 ±376.6, p=0.77, respectively), but most in those without detectable DSA at baseline (129.4 ± 234.7 vs 364.8 ± 442.3, p=0.05, respectively) (Fig1b). Notably, at the time of allograft rejection, high frequencies of d-sp mBc were detected in the majority of patients, suggesting a role in driving allograft rejection in patients undergoing IS withdrawal (Fig 1c).
Conclusions: A wide range of donor(HLA)-specific mBC frequencies may be detected in peripheral blood in pediatric liver transplant recipients with DSA, and seem to appear over time during IS withdrawal. Thus, tracking donor(HLA)-sp mBc may identify transplant recipients not capable of maintaining a quiescent anti-donor alloimmune response as IS is reduced.



P491 THE CLINICAL RELEVANCE OF BONE MARROW BIOPSY IN SOLID ORGAN TRANSPLANT RECIPIENTS

Rafał Staros[1], Bartosz Foroncewicz[1], Agnieszka Kołkowska-Leśniak[2], Bogna Ziarkiewicz-Wróblewska[3], Emilia Knioła[1], Paulina Nazaruk[1], Ignacy Tkaczyk[1], Leszek Pączek[1;4], Krzysztof Mucha*[1;4]

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Background: Solid organ transplant recipients are at an increased risk of hematological disorders compared to the general population, owing to immunosuppression (IS) and viral diseases. Bone marrow trephine biopsy (BMB) remains a reference technique in hematological diagnostics. We aimed to identify the most common BMB indications and results in kidney (KTRs) and liver transplant recipients (LTRs) and to identify the population at risk of hematological pathology based upon patients' IS, complete blood count (CBC) and blood biochemical assays (BCHEM).
Methods: In this retrospective study we enrolled all adult KTRs and LTRs, who underwent BMB between 01.2008 and 05.2021. The collected data included patient clinical characteristics, BMB indications and results, CBC, BCHEM and IS at 3 months post-Tx and at the time of BMB. Only first-time biopsies were used for analysis.
Results: We identified 77 (3.45%) out of 2235 KTRs and 103 (8.06%) out of 1278 LTRs, who underwent a total of 180 BMB due to 21 clinical indications. In LTRs the most frequent were leukopenia (17.5%), dysproteinemia (17.5%) and thrombocytopenia (14.6%), whereas in KTRs: anemia (33.8%), dysproteinemia (15.6%) and leukopenia (14.3%). PTLD was diagnosed in 2.6% of KTRs' and 9.7% LTRs' BMBs. MDS was more frequent in KTRs (5.2%) than LTRs (1.9%). Plasmacytic dyscrasia (PD: multiple myeloma and MGUS) was diagnosed only in KTRs (1.3% and 5.2% respectively). A quarter of KTRs' BMB and a third of LTRs' showed normal bone marrow. We compared the results of CBC, BCHEM and IS between patients with and without abnormalities in BMB and found that KTRs with normal BMB had lower steroid (GCS) doses at 3 months post-Tx (p=0.024), higher RBC (p=0.03) and HCT (p=0.011) at the time of BMB. LTRs with normal BMB had lower cyclosporin (CsA) doses (p=0.03) at 3 months post-Tx as well as lower GCS doses (p=0.031) at the time of BMB, and a lower decrease in tacrolimus (TAC) through concentrations over time (3 months post-Tx to BMB) compared to LTRs with abnormal BMB.
Conclusions: The two most important assays leading to BMB are CBC and blood protein electrophoresis. Up to a third of BMB in KTRs and LTRs will show no pathology. PTLD was more frequent in LTRs; MDS and PD in KTRs. Higher GCS and CsA doses as well as labile TAC through concentrations might be associated with abnormal BMB findings.

P493 HIGH INCIDENCE AND VIRAL LOAD OF HHV-6A IN A MULTI-CENTRE KIDNEY TRANSPLANT COHORT

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Background: Human herpesvirus 6 (HHV-6) is a common opportunistic pathogen in kidney transplant recipients. Two different variants of HHV-6, HHV-6A and HHV-6B, have been identified, of which the latter seems to be dominant. However, it is unclear whether they increase the likelihood of other viral reactivations.
Methods: We characterized a multi-centre cohort of 93 patients along nine study visits for viral load. We tested for the following viruses: HHV-6A and HHV-6B, the herpesviruses cytomegalovirus (CMV) and Epstein-Barr virus (EBV) and the polyomavirus BK (BKV).
Results: We detected HHV-6A viral load in 48 (51.6%) patients, while the incidence of HHV-6B was much lower, being detected in 7 (7.5%) patients. The incidence of HHV-6A was higher than of BKV, CMV and EBV. HHV-6A also demonstrated higher viral loads than the rest of viruses. There was a strong but non-significant association between HHV-6A and HHV-6B as co-infection (P=0.112), whereas no increased incidence of other viruses among patients with HHV-6A reactivation was observed. There was no negative effect of high HHV-6A (>10,000 copies/mL) load on markers of renal graft and hepatic function or blood count twelve months post-transplant.
Conclusions: In contrast to previously published data, our results show a clear dominance of HHV-6A in peripheral blood when compared to HHV-6B, with higher incidence and viral load levels. Despite the high HHV-6A loads observed, we did not identify any negative effects on posttransplant outcome.

P494 CYCLOSPORINE STIMULATES MITOCHONDRIAL RESPIRATION OF PORCINE PRECISION-CUT NUTRIENT-SUPPLIED KIDNEY SLICES, A PILOT STUDY

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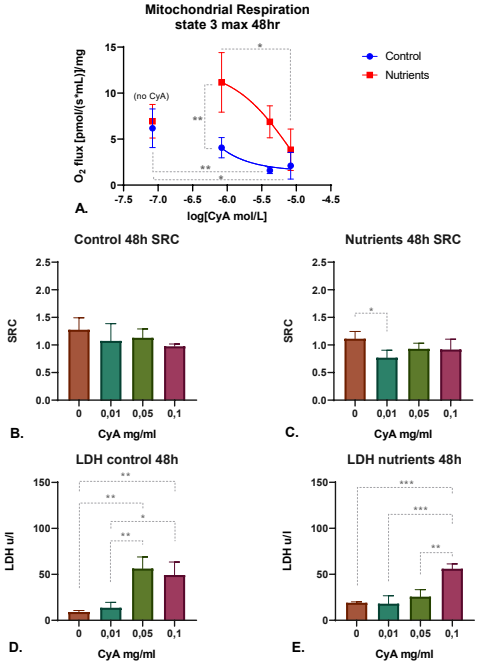
The optimal nutrient-rich perfusion solution for preserving mitochondria during normothermic machine perfusion (NMP) is unknown. To study prolonged normothermic preservation, we developed a precision-cut kidney slice (PCKS) model. A limitation of the model for metabolic studies is that the slices do not use their full energy-producing capacity because of the lack of renal physiological function such as reabsorption, which is present during NMP. Cyclosporine (CyA) can partly uncouple mitochondrial respiration, thus we hypothesized that the addition of CyA can challenge renal tubules by increasing their metabolic activity. In this pilot study, we aimed at finding the CyA concentration that is able to decrease spare respiratory capacity (SRC), which can make the PCKS model a better representative of NMP.Porcine kidneys *(n=3)* were obtained from a local slaughterhouse. After 30 minutes of warm ischemia, they were placed in oxygenated Hypothermic Machine Perfusion (HMP) for 3 hours. Next, cortical kidney slices were made in a Krumdieck slicer and then placed into an oxygenated incubator at 37°C. The basic incubation medium was Dulbecco's Modified Eagle Medium (DMEM) without glucose and pyruvate. The Nutrients group included glucose, glutamine and fatty acids and the Control group had no nutrients. Both groups had four subgroups, one without CyA and three with different concentrations (0,01mg/ml, 0,05mg/ml, 0,1mg/ml). Every 24 hours, slices and incubation medium were sampled for O_2 consumption, measured using the Oxygraph-2k, and LDH analysis. After 48 hours, the PCKS incubated in the nutrient-containing medium showed a dose-dependent response in mitochondrial respiration. The dose of 0,01mg/ml CyA resulted in higher state 3 mitochondrial respiration *(Figure 1A)*. In line with this finding, this 0,01mg/ml CyA group had a significantly lower SRC than slices without CyA, in the nutrient group *(Figure 1C)*. LDH, as general injury marker, was also significantly lower in PCKS incubated with the lowest dose of CyA, independent of the incubation medium *(Figure 1D,E)*. CyA supplementation can stimulate PCKS respiration in a dose-dependent manner. The optimal concentration to achieve stimulation is 0,01mg/ml, due to its effect of higher mitochondrial respiration, lower SRC and lower toxicity compared to higher dosages.

Table 1

Contents \ Groups	Control	Control + CyA			Nutrients	Nutrients + CyA		
Glucose (2mg/mL)					+	+	+	+
Fatty acids (1,5mg/mL)					+	+	+	+
Glutamine (2mM)					+	+	+	+
Cyclosporine (CyA mg/ml*)		0,01	0,05	0,1		0,01	0,05	0,1

*0,1mg/ml = 8,3*10⁻⁴mol/L CyA

Figure 1



P495 TRANSEUROPEAN EDUCATIONAL INITIATIVE IN ORGAN DONATION AND TRANSPLANTATION

Chloe Balleste*[1], Francesca D'angelo[2], Aleksandra Rudak[1], Eva Steina[3], Ricardo Casaroli Marano[2]

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Background: The shortage of organs for transplant observed in each European Union (EU) member state has been the main challenge to address in organ transplantation (OT). Transeuropean Educational initiative in Organ Donation and Transplantation (TEODOR) is a 36-month Erasmus+ project funded by the European Commission which aims at designing an innovative training program on organ donation (OD) and OT for physicians and healthcare personnel from Latvia, Czech Republic and Lithuania. The training was designed to improve technical and non-technical competencies required for better clinical performance and patient outcome, and boost best practice exchange among countries, with the aim of enhancing OD and OT activities.
Methods: The course was addressed to Key Donation Professionals and Key Transplantation Professionals as a strategy to engage all the main stakeholders involved in the process of OD and OT. The educational intervention is student-centered and adapted to adult-learning for life-long results. This was achieved through a multilevel (from awareness to high level) and blended methodology (online and face-to-face). The first level comprised microlearning capsules and webinar on the most important concepts of OD and OT. The second level contained online self-guided learning modules. The third level will involve local seminars and a face-to-face trans-national seminar.
Results: A total of 75 participants were expected to be trained by the end of the course. Additionally, more than 12 trainers from the beneficiary countries would be trained to continue conducting the training after this project. We also expect to have prospective study in the three beneficiary partner countries and scientific publications.
Conclusions: The impact and potential longer-term benefits of TEODOR will be observable at different societal and professional levels, including individual, healthcare professionals, and decision makers. At European level, we expect TEODOR to create better compliance with the EU recommendations and best practice exchange among Baltic, Southern, Central and Northern European healthcare professionals to improve OD and OT practices and education. At national level, we expect it to positively impact national agencies on development of organ exchange programs.

P496 OPPOSITE EFFECTS IN FRACTIONAL DONOR-DERIVED CELL-FREE DNA FROM URINE AND PLASMA IN KIDNEY RECIPIENTS? RESULTS FROM A PILOT STUDY

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Background: Close monitoring of kidney allograft recipients is of high relevance for a timely detection of allograft injury and rejection. Limited sensitivity and specificity of current blood and urine-based biomarkers can delay the suspicion of an allograft injury as well as the biopsy needed for diagnosis confirmation. Donor-derived cell-free DNA (dd-cfDNA) in plasma has been shown to indicate kidney allograft injury. Our aim was to perform a pilot investigation of urinary dd-cfDNA as a potential new, non-invasive biomarker for allograft monitoring in kidney recipients.
Methods: Blood and urine samples from kidney transplant recipients (n = 93) were obtained at regular clinic visits. Droplet digital PCR was performed using mismatched HLA alleles between recipient and donor, based on which the absolute (cp/mL) and relative (%dd-cfDNA) quantities of dd-cfDNA were determined. Adjusting for dependency of dd-cfDNA on time after transplantation, correlations with clinical and biochemical parameters were assessed.
Results: In samples from patients with biopsy-proven allograft injury, when compared to samples from stable recipients, significantly increased dd-cfDNA cp/mL ($p = 0.002$) and %dd-cfDNA ($p = 0.032$) in plasma was found, whereas the %dd-cfDNA in urine was significantly decreased ($p = 0.016$). Similarly, recipients of deceased donor organs showed significantly increased %dd-cfDNA values in plasma compared to living donor recipients ($p = 0.049$), whereas the opposite was seen in urine ($p = 0.026$). Additionally, higher %dd-cfDNA was observed in urine from male recipients ($p = 0.003$). Finally, while no correlation was found between leucocyte counts and dd-cfDNA in blood, there was a significant negative correlation between %dd-cfDNA and increased leucocyte counts in urine ($p = 0.002$).
Conclusions: Interestingly, our pilot study on dd-cfDNA in kidney allograft recipients identified contrary tendencies of urinary %dd-cfDNA compared to %dd-cfDNA in plasma. Dd-cfDNA measured in urine, which as a sample material originated from direct filtration through the kidneys, could therefore give additional insight into the condition of the allograft. However, the findings from our pilot study require replication in a larger cohort.

P497 URINARY BIOMARKERS IN A LIVING DONOR KIDNEY TRANSPLANTATION COHORT – PREDICTIVE VALUE ON EARLY AND LONG-TERM GRAFT FUNCTION

Julia Huisman[1;2], Nora Spraakman*[2], Jeroen Koomen[2], Marrit Talsma[2], Robert Pol[1], Stefan Berger[3], Henri Leuvenink[1], Michel Struys[2;4], Gertrude Nieuwenhuijs-Moeke[2]

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Background: Early non-invasive detection and prediction of graft function after kidney transplantation is essential since interventions might prevent further deterioration. The aim of this study is to analyze the dynamics and predictive value of four urinary biomarkers Kidney Injury Molecule-1 (KIM-1), Heart-type Fatty Acid Binding Protein (H-FABP), N-Acetyl-β-D-Glucosaminidase (NAG) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) in a living donor kidney transplantation (LDKT) cohort.
Methods: Biomarkers were measured up to 9 days after transplantation of 57 recipients participating in the VAPOR-1 trial.
Results: Dynamics of KIM-1, NAG, NGAL and H-FABP significantly changed over the course of 9 days after transplantation. KIM-1 at day 1 and NAG at day 2 after transplantation were significant predictors for estimated glomerular filtration rate (eGFR) at various timepoints after transplantation with a positive estimate ($P<0.05$), whereas NGAL and NAG at day 1 after transplantation were negative significant predictors ($P<0.05$). Multivariable analysis models for eGFR outcome improved after addition of these biomarker levels. Several donor, recipient and transplantation factors significantly affected the baseline of urinary biomarkers.
Conclusions: In conclusion, urinary biomarkers are of added value for prediction of graft outcome, but influencing factors like timing of measurement and transplantation factors need to be considered.

P499 MULTIMODAL REMOTE HOME-MONITORING OF LUNG TRANSPLANT RECIPIENTS DURING COVID-19 VACCINATIONS: PILOT STUDY OF COVIDA DESK

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Background: Remote patient monitoring (RPM) of vital signs and symptoms for lung transplant recipients (LTRs) has become increasingly relevant in many situations. Nevertheless, RPM research integrating multisensory home-monitoring in LTRs is scarce. We developed a novel multisensory home-monitoring device and tested it in the context of COVID-19 vaccinations. We hypothesize that multisensory RPM and smartphone-based questionnaire feedback on signs and symptoms will be well accepted among LTRs. To assess the usability and acceptability of a remote monitoring system consisting of wearable devices, including home spirometry and a smartphone-based questionnaire application for symptom and vital sign monitoring using wearable devices, during the first and second SARS-CoV-2 vaccination.
Methods: Observational usability pilot study for 6 weeks of home-monitoring with the COVIDA Desk for LTRs. During the first week after the vaccination, intensive monitoring was performed by recording data on physical activity, spirometry, temperature, pulse-oximetry and self-reported symptoms, signs and additional measurements. During subsequent days, the number of monitoring assessments was reduced. LTRs reported on their perceptions of the usability of the monitoring device through a purpose-designed questionnaire.
Results: Ten LTRs planning to receive the first COVID-19 vaccinations were recruited. For the intensive monitoring study phase LTRs recorded symptoms, signs and additional measurements. The most frequent adverse events reported were local pain, fatigue, sleep disturbance and headache. The duration of these symptoms was 5-8 days post-vaccination. Adherence to the main monitoring devices was high. LTRs rated usability as high. The majority were willing to continue monitoring.
Conclusions: The COVIDA Desk showed favorable technical performance and was well-accepted by the LTRs during the vaccination phase of the pandemic. The feasibility of the RPM system deployment was proven by the rapid recruitment uptake, technical performance (i.e., low number of errors), favorable user experience questionnaire and detailed individual user feedback.

P500 COVID-19: ROLE OF RESILIENCE ON THE PSYCHOLOGICAL IMPACT OF LOCKDOWN IN LIVER TRANSPLANT TRANSITIONAL CANDIDATES AND RECIPIENTS

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Background: The coronavirus disease 2019 (COVID-19) pandemic and the necessary spreading control measures implemented by the governments have induced drastic changes in daily life. The reduction in mobility and strict social contact limitations are posing a great challenge, particularly for the adolescents. The purpose of this study is to investigate the psychological and emotional impact of lockdown and their relationship with resilience, on adolescents and young adults listed for liver transplant or liver transplant recipient.
Methods: Social and demographic variables of subjects (n = 66) were collected and the analyses were based on the Depression Anxiety and Stress Scales (DASS-21), and Connor-Davidson Resilience Scale (CD-RISC 25), exploring the following areas: emotional states of depression, anxiety and stress; and resilience factors. A correlation between the measured degrees of depression/anxiety and resilience was evaluated by Pearson's correlation coefficient and linear regression models.
Results: The results showed a significant correlation between subscales: DASS depression/anxiety (r2= .62) depression/stress (r2= .65) CD-RISC commitment/optimism (r2= .71). The total score of DAAS depression/anxiety/stress scales significantly diminished at the increasing of CD-RISC total score. The inverse correlation between CD-RISC and DAAS seems to refer to the subscale of the relationship between DAAS depression and CD-RISC (β=-0.33, p=0.006).
Conclusions: Our findings suggest that resilience can be a protective factor for adolescent liver transplant recipients and liver transplant candidates in mitigating the onset of negative psychological symptoms correlated with the pandemic.

P501 RISK AND PROGNOSTIC FACTORS FOR POST-TRANSPLANTATION LYMPHOPROLIFERATIVE DISEASE IN SOLID ORGAN TRANSPLANT RECIPIENTS – A POLISH MULTICENTER STUDY

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Background: Post-transplantation lymphoproliferative disorder (PTLD) is a potentially fatal complication of transplantation (Tx). In solid organ transplant recipients, the risk of disease development is associated with graft type and is lowest for kidney (KTR), intermediate for liver (LTR) and high for lung (LngTR) transplant recipients. The aim of this study was to investigate the factors contributing to the development and treatment outcomes of PTLD and compare their impact on KTRs, LTRs and LngTRs.
Methods: In this study we included all KTRs, LTRs and LngTRs diagnosed with PTLD at four transplantation centres in Poland between 2002 and 2022. Data were collected from the patients' medical records: immunosuppression (IS), viral infections, PTLD type, treatment and outcomes. Mann-Whitney U-test was used to assess the differences in group composition, and univariate Cox regression was used to determine the impact of variables upon PTLD time of onset and patient survival.
Results: We identified 31 KTRs, 31 LTRs and 5 LngTRs who fulfilled the inclusion criteria. PTLD was diagnosed in 1.51% of 331 LngTRs and, among the patients of the center leading this study, in 22 (0.82%) out of 2699 KTRs and 29 (2.03%) out of 1386 LTRs. Two thirds of the patients were male, the median age at first Tx was 39 years. KTRs and LTRs differed in IS treatment: more KTRs used steroids (GCS, p=0.042) and cyclosporin (CsA, p=0.001), more LTRs used tacrolimus (TAC, p<0.001) and antiCD25 induction (p=0.003). LTRs developed PTLD earlier than KTRs (53 months vs 141 months, p=0.004). All of LngTx recipients were diagnosed <12 months after Tx and 80% had detectable EBV and CMV DNA. The groups did not significantly differ in the type of PTLD treatment. TAC had the opposite effect on PTLD time of onset in KTRs (HR=2.92, 95%CI 1.35-6.34, p=0.007) and LTRs (HR=0.18, 95%CI 0.04-0.89, p=0.036). Patient survival was longer in patients who were treated with anti-CD20 monotherapy (HR=0.28, 95%CI 0.08-0.96, p=0.042) and surgically (HR=0.33, 95%CI 0.12-0.91, p=0.031).
Conclusions: LTRs develop PTLD significantly earlier than KTRs, and time of disease onset is associated with TAC use. The dominance of early PTLD in LngTx and high rates of EBV and CMV infection are a consequence of younger age at Tx. Surgical treatment and anti-CD20 monotherapy improve patients' survival.

P502 LUNG PRESERVATION AT 4°C TO 8°C WITH A NOVEL LUNG STORAGE DEVICE: FIRST EUROPEAN EXPERIENCE

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Background: Lung preservation at 4°C to 8°C has recently been recommended as the optimal storage temperature to minimize lung injury between procurement and implantation (versus the usually accepted 0°C to 4°C). We describe herein the first European experience of lung preservation at 4°C to 8°C, using a novel lung storage device.
Methods: Two patients underwent a bilateral lung transplantation (LTx) in 11/2022 and 01/2023. Donor lungs were preserved in the Paragonix LUNGguard cooler. LUNGguard storage details, total ischemia time, and early postoperative outcome are described. Written informed consent for reporting was obtained.
Results: Patient 1 is a 55-year-old male with idiopathic pulmonary fibrosis, who underwent a high-urgent bilateral LTx (no extracorporeal life support (ECLS)) with donor lungs from a 44-year-old female (donation after circulatory death type III). Average LUNGguard temperature was 6.9°C, and preservation and total ischemia times were 270/451 minutes (right lung) and 404/557 minutes (left lung). Primary graft dysfunction (PGD) at 0/24/48/72h was 0/0/0/0. Postoperative course was uneventful, and the patient was discharged 19 days post-transplant. Patient 2 is a 15-year-old girl with cystic fibrosis, who underwent a bilateral lobar LTx (no ECLS) with donor lungs from a 37-year-old male (donation after brain death). The lung grafts were stored overnight in the LUNGguard at an average temperature of 5.9°C, with preservation and total ischemia times of 476/686 minutes (right lung) and 680/869 minutes (left lung). PGD at 0/24/48/72h was 2/1/0/0. Similar to patient 1, postoperative course was uneventful and the patient was discharged 26 days post-transplant.
Conclusions: Despite high-risk recipient and donor profile, and long ischemia times, lung preservation at 4°C to 8°C in the LUNGguard device seems safe and feasible, and has the potential to postpone LTx to day-time. Larger cohort and longer-term outcome are needed to confirm these promising observations.

P503 PUSHING THE BOUNDARIES OF DELISTING UNACCEPTABLE HLA IN HIGHLY SENSITISED PATIENTS IN CONTEXT OF NOVEL DESENSITISATION - USING C1Q ASSAY

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Background: Identifying HLA-specific antibodies in patients prior to kidney transplant is an established risk stratification tool toward improved outcome. The varied pathogenicity of HLA antibodies by their levels or functional characteristics is established in retrospective studies. Their use in the clinical practice of delisting is slowly evolving. As a centre with interest in HLA incompatible transplantation, we are exploring other ways to push the boundaries to improve transplantation opportunities. This study aims to show the utility of the C1q assay in improving the probability of transplant.
Methods: Current samples from 15 wait-listed highly sensitised patients (HSPs) with existing HLA IgG SAB results were selected and re-tested using the OneLambaTM C1qScreen to detect C1q-binding antibodies. We used the NHSBT matchability calculator and estimated chance of transplant tools (http://odt.nhs.uk/pdf/NHSBT_Tools.pdf) to assess the impact of delisting C1q negative specificities. Statistics were calculated using GraphPad Quickcalcs.
Results: Calculated reaction frequency (cRF) defined by IgG HLA-specific antibodies was (MFI ≥ 2000) -100% (n=9), 99% (n=2), 98% (n=2), 96% (n=1) and 93% (n=1).). The overall change in opportunity by listing only C1q-binding HLA antibodies as unacceptable is shown in table 1. This produced drop in cRF (p=0.057) and matchability points (p=0.008). As a result, there was a predicted increase in the offer rate (p=0.053) and 1-year estimated chance of transplant (p=0.029) compared to listing total HLA antibodies. Patients that demonstrated an increased chance of transplant showed a 3 to 5 fold increase.
Conclusions: This study shows a strong potential improvement in transplant opportunities for HSPs by selectively listing preformed C1q-binding HLA antibodies instead of total IgG HLA-antibodies. This approach may push the boundaries of delisting in the context of novel desensitisation on the deceased donor waiting list and virtual crossmatch process.

Table 1: Differences in output after applying C1q assay based delisting (compared with IgG SAB assay)

Output	Mean (range)	Median (IQR)
cRF reduction	12% (0-96%)	4% (0.5-15%)
Matchability point reduction	1.07 (0-5)	1 (0-1.5)
Increase in offer rate (n:10000)	54.45 (0-3820)	77 (30-694)
Increase chance of transplant	5% (0-21%)	0% (0-10%)

P505 EFFECT OF (MICRO)THROMBI IN DONOR LUNGS ON LUNG FUNCTION DURING EX VIVO LUNG PERFUSION AND POST-OPERATIVE OUTCOMES

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Background: All donor lungs contain to a greater or lesser extent thrombi. Therefore, we hypothesize that thrombi remaining in donor lungs may play an important role in initial impaired lung function. Our purpose was to investigate the correlation between coagulation- and fibrinolytic markers, lung function during Ex Vivo Lung Perfusion (EVLP) and outcomes after lung transplantation (LTx) of initially discarded and standard criteria human donor lungs.
Methods: EVLP was performed with n=8 standard criteria (logistical indication) and n=11 initially discarded (medical indication) donor lungs. LTx was followed if standard EVLP acceptance criteria were met. D-dimer, urokinase Plasminogen Activator Receptor (uPAR), Plasminogen Activator Inhibitor-1 (PAI-1) and Prothrombin Fragment 1+2 (F1+2) were measured in the perfusate after 90 and 180 min. Lung function during EVLP, Primary Graft Dysfunction (PGD) and Chronic Lung Allograft Dysfunction (CLAD) score were recorded.
Results: Post EVLP, 7/8 and 9/11 donor lungs with logistical and medical indication respectively were transplanted. A significant increase between 90 min and 180 min was observed in both groups in terms of uPAR, PAI-1 and D-dimer levels (A, B and C). F1+2 levels remained stable over time (D). Between groups PAI-1 at 90 min and D-dimer at 90 and 180 min were significantly higher in the medical group than in the logistical group. In both groups, no significant correlations were observed at 180 min between the venous pO_2, pulmonary vascular resistance, dynamic compliance, PGD 72h post-LTx and CLAD.
Conclusions: Increased uPAR, PAI-1 and D-dimer levels indicating (micro) thrombi during EVLP did not seem to be correlated with adverse EVLP parameters and negative clinical outcomes. Interestingly, significant higher D-dimer levels in initially discarded donor lungs may indicate the presence of more thrombi. Further studies and increasing sample size may be required to investigate potential correlations.

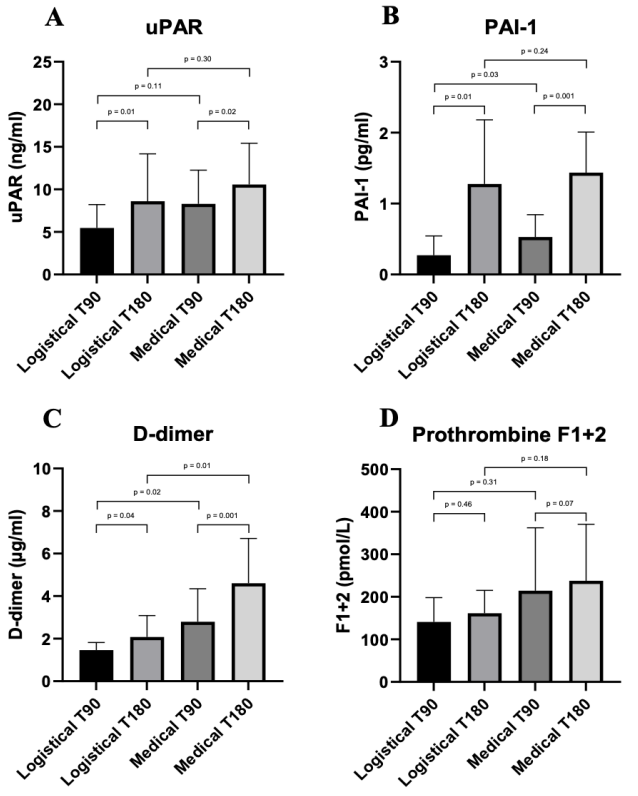

Figure 1. Perfusate measurements after 90 and 180 min EVLP of human donor lungs with logistical or medical indication for EVLP. A: Urokinase Plasminogen Activator Receptor, B: Plasminogen Activator Inhibitor-1, C: D-dimer and D: Prothrombin Fragment 1+2.

P506 DONOR QUALITY OF LIFE AND PSYCHOSOCIAL OUTCOMES AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Living donor kidney transplantation (LDKT) is the treatment of choice for end-stage renal disease. Data regarding the post-donation welfare of donors is paramount to further improve and promote LDKT. This study aimed to analyse factors relating to donors' experiences and how these impact their perceived quality of life and other psychosocial outcomes.
Methods: A systematic literature search of Pubmed, EMBASE and MEDLINE was conducted using relevant keywords and MeSH terms. This was supplemented by snowballing and a grey literature search. Data was collected on discrete donor outcomes such as health-related quality of life (HrQOL), and psychosocial outcomes which encompass donor mental and physical health, financial burden, attitudes towards donation, and their relationships with the recipients.
Results: 27 studies (2017 – 2023) were analysed including 7746 donors. 60% of studies used a validated HrQOL questionnaire tool. Generally, physical utility scores in donors remained comparable to the general population. 6 studies suggested challenges to mental health post-donation influenced by several pre-disposing factors, though 4 studies demonstrated the opposite, where improvements to psychological quality of life (QOL) were seen. Most studies showed that recovery for donors had no interference with activities of daily living. A small subset of donors met criteria for chronic post-surgical pain and persistent clinical fatigue. These patients tended to show dissatisfaction with the donation, in contrast to the general donor cohort. Positive relationships between donors and recipients were demonstrated. However, it was shown that a proportion of donors experienced economic losses related to donation.
Conclusions: LDKT is generally very well perceived by donors and does not affect their welfare. However, adverse effects on donor mental QOL, chronic pain, and economic status can be experienced by a minority of patients. Further research is required to identify and mitigate predictors of adverse effects on donor wellbeing post-LDKT.

P507 MEASUREMENT OF THE IMMUNOSUPPRESSANT POSSESSION RATIO BY CLINICAL PHARMACISTS CAPTURES A NON-ADHERENCE ASSOCIATED WITH ANTIBODY-MEDIATED REJECTION

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Background: Transplant physicians do not yet have a quantifiable and objective method for measuring non-adherence to immunosuppressants. Our objective was to test the feasibility of calculating an immunosuppressant possession ratio (IPR) in order to quantify the level of non-adherence at the time of antibody mediated rejection (ABMR).
Methods: IPR was calculated in a non-interventional prospective cohort of 91 kidney transplant recipients (KTR) using the following formula: number of pills collected at the pharmacy / number of pills prescribed over the study period × 100. In a retrospective cohort of 451 kidney transplant biopsies, we performed a case-control study to compare the 6-month IPRs between 26 cases of ABMR and 26 matched controls, with interstitial fibrosis and tubular atrophy (IFTA).
Results: We were able to calculate a real-time IPR in the 91 patients of the prospective cohort. Patients with an IPR<90% had more frequently a tacrolimus through level coefficient of variation >30% than patients with an IPR=100% (66.7% *vs* 29.4%, p=0.05). They were also more frequently non-adherent to outpatient visits (66.7% *vs* 23.2%, p=0.01). In the case-control study, patients with ABMR had lower 6-month IPRs than patients with IFTA (76.5% *vs* 99.5%, p<0.001). In the 26 KTRs with ABMR, non-adherence was more often diagnosed by a 6-months IPR<90% than by clinical suspicion (19 *vs* 8, p=0.02).
Conclusions: IPR is an objective and quantifiable tool which improves the diagnosis of non-adherence in KTRs with ABMR.

P509 POST-TRANSPLANT DIABETES MELLITUS IN KIDNEY TRANSPLANT PATIENTS – ONE CENTRE PILOT, PROSPECTIVE STUDY

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Background: Background: Post-transplant diabetes mellitus (PTDM) is a frequent metabolic complication after organ transplantation and is associated with increased risk of graft failure, cardiovascular disease, mortality and infections. Identification of PTDM risk factors is important for prevention strategies, risk stratification and management of the immunosuppressive protocol.
Methods: We prospectively analysed risk factors and clinical consequences of PTDM in patients after kidney transplantation performed in our centre between 2016 and 2022, in the group of 129 consecutive transplant recipient without diabetes before transplantation (M79, F51), mean age 47,6 years. Diabetes was defined as the requirement of pharmacotherapy at least 3 months after transplantation or was based on the oral glucose tolerance test (OGTT). Time of observation was 3-78 months.
Results: The incidence of PTDM was 21,5% (28/130). Patients who developed PTDM were older (p=0,015), had a higher Charlson comorbidity index (p=0,038) and a higher BMI (p=0,04). None of the factors was an independent risk factor for PTDM. The mean fasting glucose level before transplantation was statistically significantly higher in the group of patients that later developed diabetes (p=0,017). No difference in sex, method and time of dialysis, number of mismatches, ischaemic time, frequency of acute rejection, delayed kidney function, reoperation and kidney graft function and also in the baseline serum level of insulin, homocysteine, uric acid, C-peptide, albumin, lipid profile, HOMA-IR, QUICKI, were found. Kaplan-Meier survival curves of patients and grafts with and without PTDM did not differ. Tacrolimus was a part of the immunosuppressive scheme in 89% of PTDM patients and in 78% of nonPTDM patients (p>0.05).
Conclusions: Risk factors for the development of PTDM after KTX are older age, higher comorbidity and BMI. General risk factors for diabetes appear to be more important for the development of PTDM than those associated with transplantation. Simple indicators such as blood glucose levels and HBA1c indicate an increased risk of PTDM.

P510 PREVALENCE AND RISK FACTORS FOR ARTERIAL HYPERTENSION IN LIVER TRANSPLANT RECIPIENTS

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Background: Hypertension is more prevalent in liver transplant (LT) recipients than in the general population. Furthermore, hypertension is an important risk factor for cardiovascular diseases, which are a leading cause of mortality in LT recipients. Therefore, in this study, we aimed to investigate the prevalence of and risk factors for hypertension in LT recipients.
Methods: LT recipients were included from the Danish Comorbidity in Liver Transplant recipients (DACOLT) study[4]. Participants underwent a physical examination including measurements of height, weight, and blood pressure (BP), and answered a thorough questionnaire regarding lifestyle. Additionally, data on medication and LT-specific variables were obtained from reviews of medical charts. Hypertension was defined according to Joint National Committee guidelines as a systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg and/or use of antihypertensive medication. We investigated risk factors associated with hypertension using a logistic regression model adjusting for age, sex, and BMI.
Results: We included 498 LT recipients in the study, and of these, 305 (61%) had hypertension. Among the participants with hypertension, 157 (51%) had a measured blood pressure fulfilling the definition of hypertension at the physical examination, and 229 patients (75%) received antihypertensive treatment. In a model adjusted for age, sex, and BMI, hypertension was associated with age (aOR 1.81 [1.56;2.10], per decade, p<0.001), male sex (aOR 1.50 [1.00;2.25], p=0.049), and BMI ≥30 (aOR 2.36 [1.34;4.15], p=0.003), Table 1. Other risk factors including smoking, time since liver transplantation, and use of certain immunosuppressants were not associated with hypertension.
Conclusions: We found a high prevalence of hypertension in LT recipients, and we found hypertension to be associated with age, male sex, and obesity. Furthermore, we found a high percentage of participants with measured hypertension but no antihypertensive treatment, suggesting increased attention on hypertension in LT recipients could be beneficial.

Table 1: Risk factors associated with hypertension

	OR [95% CI]	*p*-value
Age, per decade	1.81 [1.56;2.10]	**<0.001**
Male sex	1.50 [1.00;2.25]	**0.049**
BMI		
BMI 20-24.9	*Reference*	
BMI 25-29.9	0.98 [0.62;1.54	0.924
BMI≥30	2.36 [1.34;4.15]	**0.003**
Physical activity		
Inactive	*Reference*	
Moderately inactive	0.69 [0.26;1.83]	0.456
Moderately active	0.45 [0.17;1.20]	0.110
Very active	0.45 [0.14;1.39]	0.163
Smoking status		
Never smoker	*Reference*	
Current smoker	1.42 [0.72;2.80]	0.311
Previous smoker	0.95 [0.59;1.53]	0.840
Transplant related variables		
Ever rejection	1.32 [0.69;2.52]	0.399
Time since liver transplantation, per decade	1.18 [0.90;1.54]	0.223
Ciclosporin vs. Tacrolimus	2.18 [0.94;5.04]	0.069
Everolimus vs. Tacrolimus	1.51 [0.62;3.66]	0.366
Mycophenolic acid vs azathioprin	1.44 [0.75;2.77]	0.273

Tested in a logistic regression model adjusting for age, sex and BMI

P511 KIDNEY TRANSPLANT IN HIGHLY SENSITIZED PATIENT: IMLIFIDASE DESENSITIZATION, C1Q-BINDING DELISTING AND TIMELY TREATMENT OF ANTIBODY-MEDIATED REJECTION

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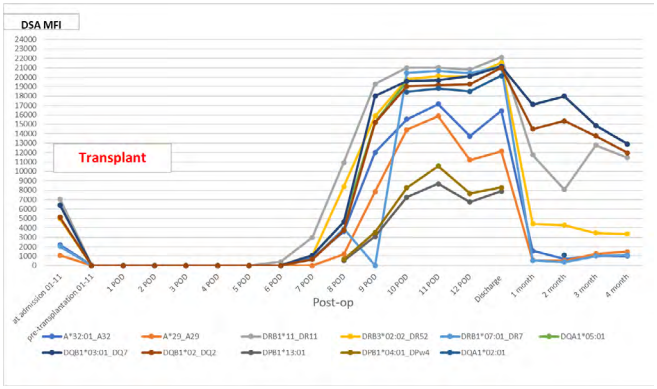
Background: Imlifidase is a new strategy to desensitize high immunological risk recipients of a deceased donor kidney transplant (KT). The preliminary results from clinical studies show good efficacy in converting positive to negative crossmatch (XM), but the incidence of acute antibody-mediated rejection (AMR) requires management optimization as well as a proper selection of donor and recipient.
Methods: A 43 year-old (yo) woman, highly sensitized (cPRA 100%), with lack of vascular access, was selected to receive desensitization with Imlifidase prior to KT using as a delisting criteria the C1q binding donor-specific antibodies (DSAs). A 63 yo male donor was allocated despite the presence of 8 DSAs (all C1q negative, MFI range 4000-22000), resulting in negative cytotoxic XM. On post-operative day (POD) 4, thymoglobulin was administrated for 3 consecutive days (1.5 mg/kg) and Rituximab (1 g) on POD 7. Immunosuppression regimen was high dose methylprednisone, tacrolimus and MMF.
Results: Two hours after Imlifidase injection (0,25 mg/kg), DSAs became undetectable and remained absent until day 6. Postoperatively, diuresis restored promptly with 88umol/L s-creatinine at day 7. DSA monitoring showed a steep rebound (Fig 1) on POD 8, when the patient presented with fever and became rapidly anuric. On the same day, a graft biopsy was performed, showing strong C4d positivity and neutrophil capillaritis, confirming the clinical diagnosis of AMR. Treatment with Eculizumab started, obtaining a prompt improvement of renal function. Plasmapheresis for 3 consecutive days, IVIG (2 g/kg) and 3 additional doses of Thymoglobulin (1.5 mg/kg) were given. Patient was discharged on POD 14, under Eculizumab bi-weekly treatment. Two months later, she became SARS-Cov 2 positive, although asymptomatic. Four months after KT, s-creatinine remains good (150umol/L), despite the persistence of high MFI DSAs which showed a significant rebound during viral infection.
Conclusions: Desensitization with Imlifidase in high immunological risk recipients facilitates access to KT, but it's not the only key for successful outcome. C1q-binding DSA delisting strategy and a very timely treatment of AMR including Eculizumab enabled to achieve optimal results and should be considered when approaching 100% cPRA candidates.

Fig.1: DSAs monitoring



P515 THE EFFECT OF STEM CELL-DERIVED EXTRACELLULAR VESICLES ON ISCHEMIA REPERFUSION INJURY IN SOLID ORGAN TRANSPLANTATION: A SYSTEMATIC REVIEW

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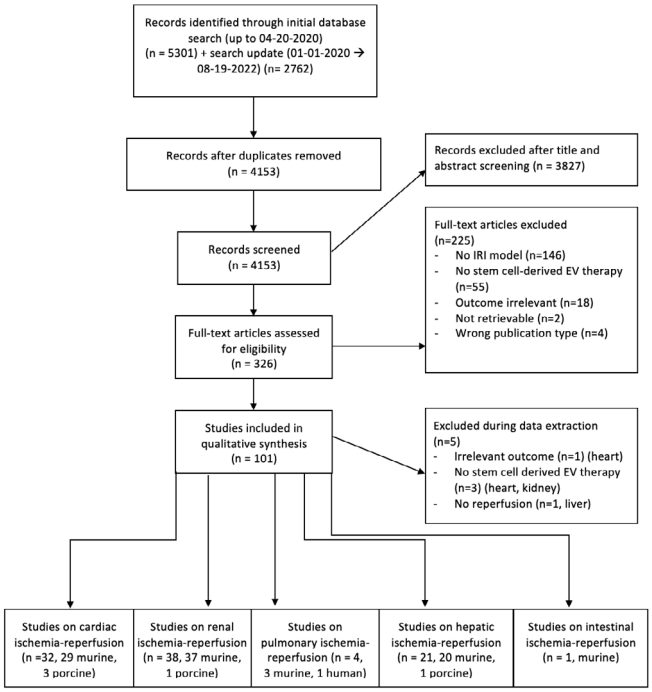
Introduction: Stem cell-derived extracellular vesicles (SC-EV) are paracrine mediators involved in tissue repair, regeneration, and immunomodulation. Protective effects of SC-EV against ischemia-reperfusion injury (IRI), still a major hurdle to the success of solid organ transplantation, have been reported. We conducted a systematic review to study the evidence of SC-EV therapy in experimental models of heart, lung, liver, kidney and intestinal IRI and transplantation.
Methods: PubMed, Embase and Web of Science were searched for studies on SC-EV therapy for cardiac, renal, hepatic, pulmonary and intestinal IRI until August 19th, 2022. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) and the SYstematic Review Center for Laboratory animal Experiments (SYRCLE) guidelines for the systematic reporting of animal studies were followed.
Results: 4153 unique articles were identified, of which 96 after screening and data extraction were included (figure 1). All included studies (heart=32, lung=4, liver=21, kidney=38, intestine=1) reported improved organ injury or function. SC-EVs exerted protective effects that were observed across all organs. First, they displayed anti-inflammatory effects as shown by reduced expression of pro-inflammatory cytokines and oxidative stress. Secondly, SC-EV exerted immunomodulatory capacities by reducing leukocyte infiltration and stimulating autophagy. Third, pro-regenerative effects were observed through increased proliferation and angiogenesis, and reduced apoptosis. Overall reporting quality as assessed by SYRCLE's risk-of-bias tool was poor.
Conclusion: This systematic review shows that SC-EVs reduces IRI in heart, kidney, liver, lungs and intestine. Before translation into humans, studies on optimal dosage, timing and stem cell sources are warranted in addition to the ability to produce sufficient quantities to treat human-size organs.

Figure 1. PRISMA Flow Diagram on the results of the systematic literature search



P516 THE IMPACT OF COORDINATION OF RENAL AND PANCREATIC ORGAN DONATION AND TRANSPLANTATION ON COLD ISCHEMIA TIME - EXPERIENCE OF THE CENTRE

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Background: The results of the analyzed publications and the research conducted in our clinic, "cold ischemia time" (CIT) <8h is an important predictor of good graft function and lower number complications. The study analyzed cold ischemia time depending on the type of transport, the experience of the surgical team and other important factors.
Methods: The aim of the study was to identify the factors that can shorten CIT to the greatest extent. The work analyzes the coordination of organ donations: pancreas and kidney with pancreas in the years 2015-2023. 124 coordination actions completed with transplantation were evaluated. All organ donation coordinations were divided into those where CIT > 8h and those where CIT < 8h. Variables analyzed in the thesis: 1. distance of the donor hospital from the transplantation center (>200km/<200km) 2. type of transportation of the procurement team (collection at the transplant center/vehicular transport/air transport) 3. transport time of the team harvesting organs for transplantation (<1h/2-4h/>5h) 4. experience of the organ harvesting surgeon (advanced/intermediate)
Results:

	CIT <8h N=82	CIT>8h N=42
the distance of the donor hospital from the transplant center	>200km-22 % <200 km -78%	>200km-71 % <200 km -29%
type of transport of the transplant team	organ donation at a transplant center - 51% wheeled transport - 44% air transport - 5%	organ donation at a transplant center- 0% wheeled transport - 100% air transport - 0%
transport time of the transplant team	<1h-48% 2-4h – 39% >5h-13%	<1h-0% 2-4h – 61% >5h-39%
organ transplant team operator experience (advanced/intermediate)	Advanced -72%, Intermediate- 28%	Advanced -61%, Intermediate- 39%

Conclusions: The process variable that was most significant in speeding up the procurement-transplantation process was the distance of the donor hospital from the transplantation center. Organ donations made in a transplant center or at a distance of up to 200 km (up to 1.5 h of transport) or using air transport significantly shorten the cold ischemia time. Another factor affecting the CIT was the experience of harvesting the surgeon.

P517 EXTRACELLULAR MATRIX - KEY COMPONENT IN THE PRODUCTION OF FUNCTIONAL AND PHYSIOLOGICALLY STABLE ARTIFICIAL PANCREATIC ISLETS USING THE INKJET METHOD

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Background: There are clinical trials using stem cell-derived β cells as an innovative and future-proof solution for the treatment of T1D. These cells are expected to replace the non-functioning islets. For this it's necessary to create their 3D conformations, which has been proven in in vitro studies. Attention should also be paid to the possibility of clinical application. The process of transplanting cluster β-cells, even from 3D culture, into the portal vein carries a high risk of damage, lack of functionality, as well as the risk of an undetermined final location of the cells. The aim of this experiment was to assess the viability and functionality of β cells in artificial 3D bioprinted inkjet pancreatic islets (PI).
Methods: INS-1E cells were used in the study. Two bioinks were used as the encapsulation carrier: 2% Methacrylated hyaluronic acid (HAMA)+20% Methacrylated gelatin (GelMa) with LAP (GROUP:H-G_INS); 2% HAMA+20% GelMa+-dECM with LAP (GROUP:ECM_INS). The control group was 2D culture. Cell functionality was assessed in the GSIS test and viability by the FDA/PI test. Test sample contained 3.5 million β cells.
Results: After 21 days, the encapsulated cells were shown to be virtually 100% viable. Dead cells were visible only in the control samples (no more than 15%). Cells suspended in the tested variants of hydrogels retained a stable structure. On day 2 of the experiment, there was no difference in cell activity. Groups of encapsulated cells showed significantly improved functionality from day 7 onwards. Both groups showed over 30% higher functionality compared to the control group. On the 14th day of the experiment, cells suspended in bioink with dECM showed a definite superiority in response to the administered glucose. Compared to the control group, the increase was over 50% (p=0.0005), and with the H-G_INS over 30% (p=0.0073). Day 21-also showed a functional advantage in the ECM_INS, almost 30% higher activity compared to the control group (p=0.0040).
Conclusions: dECM a 3D conformation is a key component for maintaining the proper functionality of β cells. In addition, the developed bioink composition and the method used enable the production of stable 3D structures that can be transplanted in a stable and safe manner without disintegrating in physiological temperature conditions.

P518 HEALTHCARE WORKERS AND ADMINISTRATIVE STAFF PERCEPTION OF ORGAN DONATION IN TWO HOSPITALS

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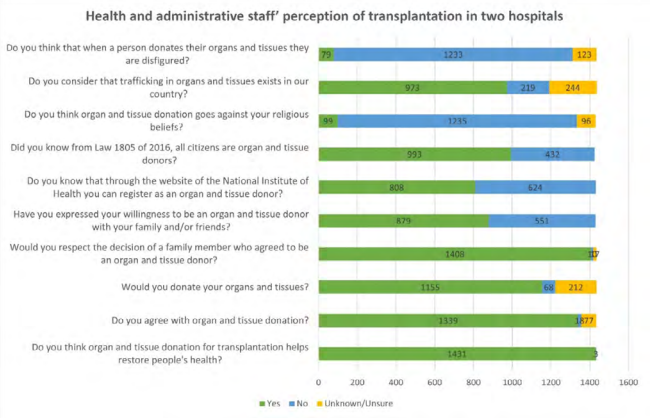
Background: Organ transplantation has become a worldwide practice, bringing patients a more prolonged, and improving their quality of life. However, patients die due to a short number of donors; therefore, donation education and awareness represent a challenge. We aim to evaluate the perception of donation of the institutions promoting donation and life (INSPROVIDA) education program in two transplant centres.
Methods: Cross-sectional study in two hospitals through virtual surveying, a test was applied to health and administrative staff between March 2022 and April 2023. The survey included 12 questions and we evaluated donation-related myths, knowledge, religious beliefs and law.
Results: Total population were 5100 workers, the sample included 1436 respondents (28.1%), mean age was 34.3 years, 74.7% were female in one of the centers, 34.9% were nursery technicians and participants worked more frequently in the Emergency department (14.3%). When asked about organ trafficking nearly 67.7% believed it exists. When asked about our country's laws on organ donation the vast 69.1% did not know them and 56.2% were not familiar with the National Institute of Health donation registry. Also, 61.2% of the sample had not expressed their willingness to be organ donors with their family and/or friends.
Conclusions: Health and administrative staff's perception of donation in two hospitals showed the role of education programs. Our results demonstrated myths still are present and such phenomena might impact donation rates. There is a need to promote health education focused on organ donation since there is a lot of unawareness of the regulations and procedures for its implementation.

Table 1. Sociodemographic characteristics of health and administrative staff in two hospitals.

Characteristic	n (%)
Age	34.3 mean ±9.9 years
Female	1073 (74.7%)
Profession	
Nursery technician	138 (34.9%)
Registered nurse	100 (25.3%)
Administrative staff	91 (23.1%)
Physician	35 (8.8%)
Other healthcare providers	25 (6.3%)
Healthcare technician	6 (1.5%)
Service	
Other	181 (17.3%)
Emergency department	149 (14.3%)
Surgical clinics	125 (12.1%)
Other administrative areas	124 (11.9%)
Critical Care	104 (9.9%)
Medical Clinics	99 (9.5%)
Safety	57 (5.4%)
Sexual and reproductive health	51 (4.9%)
Palliative care and religious support	38 (3.6%)
Cardiocirculatory care	30 (2.8%)
Cleaning	21 (2.0%)
Radiology	20 (1.9%)
Clinical laboratory	14 (1.3%)
Transport staff	14 (1.3%)
Outpatient care	9 (0.8%)
Medical education and research	3 (0.2%)
Buffet	2 (0.1%)
Religion	
Catholic Christians	810 (77.8%)
None	84 (8.1%)
Evangelical or Protestant Christians	60 (5.7%)
Other religions	27 (2.5%)
Non-attached believers	26 (2.5%)
Atheist or agnostic	22 (2.1%)
Jehovah's Witnesses	7 (0.7%)
Mormons	2 (0.1%)
Muslims	2 (0.1%)
Jews	1 (0.1%)

Figure 1. Health and administrative staff' perception of organ donation in two hospitals.



P519 THE MANY FACES OF HUMAN HERPES VIRUS 8 (HHV 8) DISEASE: CASE REPORT OF A PAEDIATRIC LIVER TRANSPLANT RECIPIENT

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Background: HHV 8 is endemic in South Africa with a seroprevelence of 48% and its role in the pathogenesis of Kaposi's sarcoma (KS) well-established. In immune compromised patients, infection can result in both KS and severe complications including haemophagocytic lymphohistiocytosis (HLH). We describe a case of primary infection, KS and HLH - a constellation of complications of HHV-8 infection not previously described in a paediatric liver transplant recipient.
Methods: Descriptive Case Study
Results: Our 2yr old patient presented with a febrile illness, deranged liver enzymes and cholestasis 4 months post-transplant. Investigation and intervention was conducted for all possible sources during which biopsy of the liver raised concern for possible vascular complications. A gastroscope was conducted to screen for varices during which an incidental finding of a vascular lesion in the stomach was discovered. Histological examination of the specimen returned as KS in the context of a positive serum HHV8 polymerase chain reaction (PCR). Subsequent lymph node biopsy confirmed disseminated KS for which chemotherapy was commenced. No sustained clinical improvement was observed. Repeat liver biopsy identified damage to the bile duct epithelium and the formation of bile lakes. On a review of the literature and results, the clinical presentation was consistent with primary HHV8 infection and Foscarnet was started. Clinical severity precluded the use of Rituximab. The fever remained refractory with 5/8 HLH criteria having developed. Treatment with high dose methylprednisone and Tocilizumab was commenced followed by an immediate clinical improvement. Ferritin and soluble interleukin 2 remained elevated and HHV 8 serum PCR positivity persisted, therefore Rituximab and Cidofovir were commenced for the ultimate clearance of HHV8 infection and treatment of HLH in addition to chemotherapy.
Conclusions: HHV 8 disease remains a credible threat to children undergoing liver transplantation. Testing of donor status and access to quantification could be valuable tools in transplant patients.. This case highlights the multiple facets of HHV8 and its life threatening complications to be considered in HHV8 infection in transplant.

P520 COMPARATIVE ANALYSIS OF INCOMPATIBLE ABO VS INCOMPATIBLE HLA LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Kidney transplant is the best therapy that can be offered to patients with advanced chronic kidney disease (ACKD). One of the main transplant challenges is to achieve a balance between the level of immunosuppression against the increase in complications. Assumed risks are greater in groups of patients that need desensitization in the case of living donor kidney transplantation ABO incompatible (ABOi) and HLA incompatible (HLAi). Our objective was to compare the results of Living Donor Kidney Transplantation ABOi vs HLAi.
Methods: We carried out a study of Living Donor Kidney Transplantation ABOi (n=61) and HLAi (n=27) from 2008 to 2021. Patients' age ranged between 53 +/- 12 (ABOi) and 50 +/- 11 (HLAi). Donor waiting times for both groups were 19.4 +/- 18.8 months and 86.8 +/- 87.6 months, respectively. Incompatibility rates were 4.1 +/- 1.5 in ABOi vs 3.7 +/- 1.1 in HLAi. Follow-up, measured in months, was 66 +/- 41 (ABOi) vs 78 +/- 56 (HLAi).
Results: Sessions of plasmaferesis/inmunoadsortion were 6.5 +/- 3.6 in ABOi vs 8.9 +/- 2.7 in HLAi. Incompatibility HLA was 4.2 +/- 1.6 in ABO vs 3.7 in 1.1 HLAi (p=003). Immunosuppression with Basiliximab was 54% (within the ABOi group) and 45% (HLAi group); meanwhile, immunosuppression due to Thymoglobulin was 5% (ABOi) and 14% (HLAi) (p=0.3). The incidence of acute rejection was 11.5 % for ABOi (cellular rejection 86% and 14 % mixed rejections) vs 17.2 % for HLAi (cellular rejection 60%, antibody-mediated rejection 40%) (p=0.5). Patient survival rate was 95% in ABOi vs 86% HLAi (p=0.2), while the survival rate of allograft was 91.8% in ABOi vs 64.3 % in HLAi (p=0.09). Both groups presented similar rates of CMV infection, 25% ABOi vs 29% HLAi (p=0.6), compared to 11.6% BK infection in ABOi and no cases in HLAi (p=0.06).
Conclusions: Kidney transplantation from a living donor using desensitization techniques is an effective option for patients with ACKD, resulting in high patient and allograft survival rates. Compared to the ABOi group, there are higher complications associated with patients in the HLAi group due to the greater complexity of the transplant and the degree of immunosuppression.

P521 GENE EXPRESSION ANALYSIS AND HISTOLOGICAL DIAGNOSIS OF TRANSPLANT BIOPSIES TAKEN AT THE TIME OF DONOR-SPECIFIC ANTIBODY DETECTION

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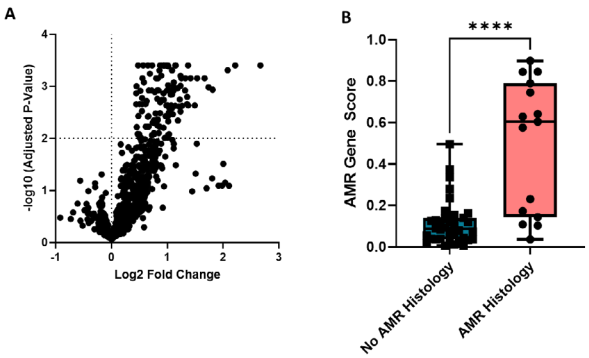
Background: The presence of donor specific antibodies (DSA) is a major risk factor for antibody-mediated rejection (AMR) and transplant loss. Only a proportion of patients with DSA, however, have histological features of rejection on transplant biopsy. We aimed to investigate the early histological and molecular features of rejection in a cohort of patients screened prospectively for DSA from the time of transplant, and to determine whether gene expression studies could identify sub-pathologic AMR.
Methods: Patients transplanted in our centre between 2019 and 2021 were screened for the development of DSA. All patients who developed a *de novo* DSA were offered a transplant biopsy. Biopsies were analysed using the Banff Classification for Allograft Pathology and gene expression analysis of 758 genes using the Banff Human Organ Transplant panel was performed.
Results: Out of 570 consecutive transplant recipients 14.4% developed a DSA of whom 51 (62%) underwent transplant biopsy. 29.4% biopsies had histological features of active AMR (either partially or completely fulfilling the Banff Diagnostic Criteria) and 25.4% had features of Borderline or T-Cell Mediated rejection (TCMR). The majority of biopsies (52.9%) showed no histological features of rejection. Differential gene expression analysis showed significant differences between biopsies with and without AMR (Figure 1A). A molecular AMR Gene Score developed in a previous retrospective cohort of indication transplant biopsies was significantly (P<0.0001) different between these 2 groups (Figure 1B). Previous sensitisation, DSA Class and Mean Fluorescence Intensity (MFI) were not associated with the development of histological features of AMR in the DSA-positive cohort, whilst a high AMR Gene Score at biopsy was strongly associated with histological AMR.
Conclusions: Patients without histological features of rejection at the time of de novo DSA detection do not have an elevated AMR molecular score. Further study is needed to identify whether molecular or histological features of AMR at the time of DSA detection are associated with subsequent episodes of rejection or allograft loss.

Figure 1



P522 SOCIAL SUPPORT AND EDUCATION REINFORCEMENT MODIFIABLE FACTORS FOR NON-COMPLIANCE IN RENAL TRANSPLANT RECIPIENTS. RESULTS OF A CROSS-SECTIONAL STUDY

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Background: In renal transplant recipients, compliance with medical therapy is vital. Non-adherence is considered a main risk factor for graft failure. Most literature defines adherence as self-based immunosuppression compliance but does not consider other relevant factors such as consult and procedures compliance. Therefore, this study aims to describe adherence prevalence in our patients and the factors related to non-compliance.

Methods: This cross-sectional study included 1030 renal transplant patients between January 2019 and July 2021. Sociodemographic, clinical, and adherence-related variables were obtained based on clinical records and a semi-structured interview done by the mental health group. A bivariate followed a descriptive analysis. A forward logistic regression was performed for non-compliance.

Results: Patients had a median of 47 years, and 58.1% were male. Non-adherence was presented in 30.7%, immunosuppression non-compliance in 25.9%, and low immunosuppression blood levels in 15.7% of patients. The non-adherence patients were younger, with a higher prevalence of males, single, transplanted for other transplant groups, had a longer time after transplantation, psychopathological diagnosis, and more reinforcement education by only nursing. Older age and multidisciplinary reinforcement education were protective factors. On the other hand, poor social support, psychopathology diagnosis, and longer time after transplant presented as non-adherence risk factors.

Conclusions: Non-compliance is wider than medication non-compliance and is presented in approximately one-third of renal transplant recipients. Therefore, there is a need to consider the related factors in the health follow-up and encourage future research in modifiable factors interventions, such as social support and education reinforcement interventions, aiming to increase compliance and achieve better outcomes for renal transplant patients.

Table 1. Characterization and multivariate analisys for non-compliance. aComparison by Mann-Withney U test. bComparison by chi-square test *Statistically significant result p<0.05 †First 3 months post-transplant follow

Variables	Total (N=1030)	Non-compliant (n=317)	Compliant (n=713)	P-value	Non-adjusted OR for non-compliance (CI 95%)	Adjusted OR for compliance red model (CI 95
Age in years, median [IQR]	47 [36-58]	44 [34-56]	48 [37-59]	0.002*a	0.98 (0.97-0.99)	0.97 (0.96-0.9
Sex, n(%)				0.174 b		
Feminine	427 (41.5)	121 (38.2)	306 (42.9)		reference	
Masculine	603 (58.5)	196 (61.8)	407 (57.1)		1.21 (0.92-1.59)	
Marital status, n(%)				0.001*b		
Single	319 (31)	117 (36.9)	202 (28.3)		reference	
Stable marital union	581 (56.4)	152 (47.9)	429 (60.2)		0.61 (0.45-0.82)	
Dissolved marital union	58 (5.6)	17 (5.4)	41 (5.8)		0.71 (0.38-1.29)	
Underage	17 (1.7)	9 (2.8)	8 (1.1)		1.94 (0.72-5.30)	
Other	55 (5.3)	22 (6.9)	33 (4.6)		1.15 (0.63-2.05)	
Transplant group, n(%)				<0.001*b		
Colombiana de Trasplantes	701 (68.1)	173 (54.6)	528 (74.1)		reference	
Another group	329 (31.9)	144 (45.4)	185 (25.9)		2.37 (1.80-3.13)	
Follow-up time, n(%)				<0.001*b		
Between 0 and 12 months	134 (13.0)	22 (6.9)	112 (15.7)		reference	reference
Between 13 and 60 months	419 (40.7)	112 (35.3)	307 (43.1)		1.83 (1.12-3.10)	1.51 (0.87-2.72
61 months or more	477 (46.3)	183 (57.7)	294 (41.2)		3.14 (1.95-5.25)	2.38 (1.35-4.36
Number of transplant, n(%)				0.379b		
First	1002 (97.3)	311 (98.1)	691 (96.9)		reference	
Second or more	28 (2.7)	6 (1.9)	22 (3.1)		0.60 (0.22-1.42)	
Donor type, n(%)				0.170 b		
Cadaveric	712 (69.1)	229 (72.2)	483 (67.7)		reference	
Living	318 (30.9)	88 (27.8)	230 (32.3)		0.80 (0.60-1.07)	
Early anxiogenic events†, n(%)				0.555 b		
No	594 (57.7)	178 (56.2)	416 (58.3)		reference	
Yes	436 (42.3)	139 (43.8)	297 (41.7)		1.09 (0.83-1.42)	
Support network†, n(%)				0.010*b		
Functional	889 (86.3)	259 (81.7)	630 (88.4)		reference	reference
Poor	103 (10.0)	40 (12.6)	63 (8.8)		1.54 (1.00- 2.34)	2.09 (1.26-3.4
Inadequate	38 (3.7)	18 (5.7)	20 (2.8)		2.18 (1.12-4.21)	2.31 (1.07-4.9
Education reinforcement†, n(%)				<0.001*b		
Nursing	559 (54.3)	220 (69.4)	339 (47.5)		reference	reference
Nursing and psychology	471 (45.7)	97 (30.6)	374 (52.5)		0.40 (0.30-0.53)	0.36 (0.25-0.5
Psychopathology, n(%)				<0.001*b		
No	652 (63.3)	123 (38.8)	529 (74.2)		reference	
Yes	378 (36.7)	194 (61.2)	184 (25.8)		4.53 (3.42-6.02)	
Psychopathological diagnosis, n(%)				<0.001*b		
Affective Disorder	115 (11.2)	54 (17.0)	61 (8.6)		3.80 (2.51-5.77)	3.71 (2.39-5.7
Personality disorder	70 (6.8)	50 (15.8)	20 (2.8)		10.75 (6.26-19.09)	11.56 (6.45-21.
Adaptive disorder	43 (4.2)	8 (2.5)	35 (4.9)		0.98 (0.41-2.06)	1.07 (0.43-2.3
Mental retardation and other developmental disorders	32 (3.1)	20 (6.3)	12 (1.7)		7.16 (3.45-15.47)	5.50 (2.52-12.4
Dementia and organic disorders	15 (1.5)	13 (4.1)	2 (0.3)		27.95 (7.59-180.27)	49.53 (12.52-33
Other	103 (10.0)	49 (15.5)	54 (7.6)		3.90 (2.52-6.02)	3.64 (2.29-5.7
No psychopathological diagnosis	652 (63.3)	123 (38.8)	529 (74.2)		reference	reference

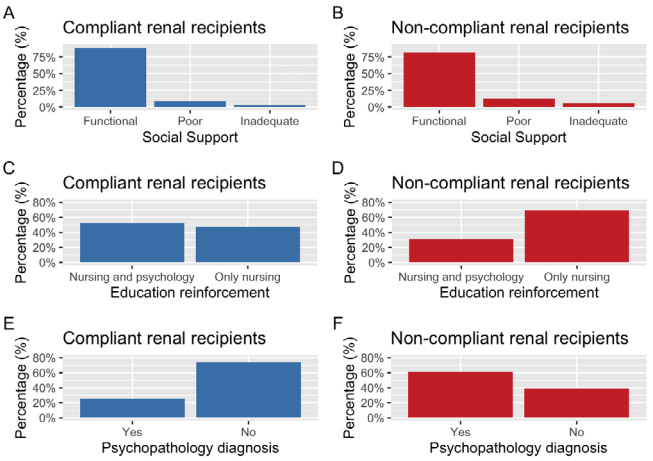

Figure 1. Relative frequencies comparison between compliant and non-compliant patients. a. Social support in compliant renal recipients; b. Social support in non- compliant renal recipients; c. Education reinforcement in compliant renal recipients; d. Education reinforcement in non- compliant renal recipients; e. Psychopathology diagnosis in compliant renal recipients; f. Psychopathology diagnosis in non- compliant renal recipients.

P523 A POLICY OF VERY SHORT PRESERVATION TIME IMPROVES THE RESULTS OF SIMULTANEOUS KIDNEY-PANCREAS TRANSPLANTATION FROM EXTENDED CRITERIA DONORS

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Background: According to the International Pancreas Transplantation Registry (IPTR), the risk of pancreas graft loss from early technical failure (TF) is significantly increased by preservation time (PT) ≥ 12 h, donor age ≥ 30 years, donor and recipient BMI ≥ 30 kg/m2, cardio/cerebrovascular (CCV) death of donors and donation after circulatory death (DCD). With the current shortage of grafts, we decided from 2015 to expand the criteria of grafts regarding donor age and CCV death but aimed to achieve a very short PT (< 8 h).
Methods: We analyzed our cohort of 105 simultaneous pancreas-kidney transplantations performed for type I diabetes between July 2015 and December 2022. The characteristics of recipients and donors, the rate of TF, as well as graft and patient survivals were compared to the IPTR 2022 data.
Results: Median age of donors was 36 years and 65.7% of them were older than 30. The main cause of death was CCV (57%). Median donor BMI was 23 kg/m2 and none had a BMI ≥ 30 kg/m2. DCD donors accounted for 3.8% of cases. Recipient median age and BMI were 40 years (IQR 33-45) and 23 kg/m2 (22-27). All transplantations were performed with systemic venous and enteric pancreatic drainage. Median PT was 397 min (334-455). In only 14% of cases, PT was greater than 8 but lower than 9 hours. 7 patients lost their pancreatic graft (6.7%) in the first 3 months from TF: vein thrombosis (2.9%), pancreatitis (2.9%) and enteric anastomotic leak (0.9%). Risk factors of TF were donor age ≥ 42, DCD donors, donor/recipient sex mismatch, and donor CCV death. All the TF occurred after transplantation from donors ≥ 42 years and deceased of CCV. At 1- 3- and 5-year post-transplant, graft and patient survivals were 88.6% 87.6% and 86.7%, and 97.1% 96.1% and 95.2%. Compared to the IPTR, we observed in our cohort similar graft and patient survivals, rates of technical failure (6.7% versus 5.5%), despite a significantly lower PT, an older donor age and a higher frequency of donor CCV death (Table).
Conclusions: In the context of shortage of pancreas grafts, a policy of very short preservation time (<8h) affords the use of expanded criteria grafts with similar results, compared to standard transplants. With such a policy, grafts from donors aged 30-42 years and/or deceased from cardiovascular death may be considered suitable for transplantation.

	IPTR 2022 (n=3982)	Present study (n=105)	p
Donor age ≥ 30 years, n (%)	862 (21.6)	69 (65.7)	<0.0001
Cardio/cerebrovascular death of donors, n (%)	690 (18.0)	60 (57.1)	<0.0001
Preservation time ≥ 12h, n (%)	1113 (29)	0(0)	<0.0001
In PT with enteric drainage	(3397)	(105)	
Pancreas technical failure n (%)	187 (5.5%)	7 (6.7%)	0.61
Cause of graft loss n (%)			
Vein thrombosis	126 (3.7)	3(2.9)	
Pancreatitis	7 (0.2)	3(2.9)	
Anastomotic leak	14 (0.4)	1(0.9)	
Bleeding	10 (0.3)	0	
Infection	17 (0.5)	0	
Other	14 (0.4)	0	

P525 THROMBOTIC MICROANGIOPATHY AFTER ABO INCOMPATIBLE KIDNEY TRANSPLANTATION: ASSESSMENT OF ANTI-A ANTIBODIES BY LUMINEX SINGLE ANTIGEN ASSAY

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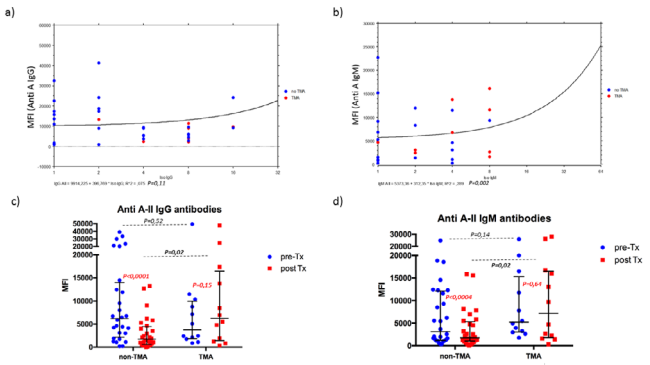
Background: Although long-term graft survival is comparable to that of ABO-compatible renal transplantation, the risk of humoral rejection following ABO incompatible (ABOi) transplantation is greater and may occur as an early thrombotic microangiopathy (TMA).
Methods: We reported a multicenter study, including 23 patients who presented an early TMA (histological and/or biological) after an ABOi transplantation (< 1 month), compared to 46 matched controls with favourable initial course and a normal biopsy. From this cohort, in blood group O recipients transplanted with a blood group A living donors, we analyzed anti A antibodies with specific Luminex Single Antigen Beads. Anti A-II, anti A-III, anti A-IV IgG and IgM antibodies were measured before KT (after desensitization) and after KT, and compared between the TMA and the control groups.
Results: Twenty-eight controls and 12 patients with TMA were analyzed. There was no correlation between mean fluorescence intensity (MFI) of anti A IgG antibodies and the titer of IgG with hemagglutination (figure 1 a; r = 0.27, p=0.11) and a weak correlation between MFI of anti A IgM antibodies and the titer of IgM (figure 1 b; r = 0.53, p=0.002). MFI of anti A-II, A-III, A-IV, IgG and IgM antibodies before KT were not different before KT between the 2 groups. After kidney transplantation anti A-II IgG and IgM antibodies were higher in the TMA group (p=0.02 for both IgG and IgM). Whereas MFI of anti A-II IgG and IgM (figure 1c and 1d) decreased after transplantation in the control group (median MFI for IgG before KT: 6178 IQR: 2175-13982; median MFI for IgG after KT: 1717 IQR: 587-4471; p< 0.0001; median MFI for IgM before KT: 3116 IQR: 1167-12140; median MFI for IgM after KT: 1725 IQR: 1015-5335; p< 0.0001), there were no difference in the TMA group (median MFI for IgG before KT: 3757 IQR: 1844-9977; median MFI for IgG after KT: 6236 IQR: 1404-16467; p=0.15; median MFI for IgM before KT: 5207 IQR: 3054-15301; median MFI for IgM after KT: 7184 IQR: 1756-16512; p=0.64).
Conclusions: We provide here the first analysis of anti A antibodies with Luminex technology in a real life setting. These first results would help us to better understand the mechanism of TMA in this context, in part explained by the rise of antibodies after KT, not detected with the imperfect test of hemagglutination.

Figure 1.



P526 EARLY CMV REACTIVATION IN RENAL RECIPIENTS IS ASSOCIATED WITH PRE-TRANSPLANT HIGH EXPRESSION OF BCMA TRANSCRIPTS, PLASMABLAST & CLASS-SWITCHED B CELL

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Background: CMV infection is the most common complication in kidney transplant (KT) recipients, occurs in the first 3 months post-TX and is correlated with increased rejection rates and poor graft function. BAFF is also a cytokine implicated in B cells homeostasis and bind to 3 receptors to exerts its function: BAFF-R, TACI and BCMA. CMV induces the BAFF expression that delivers survival and growth signals to B cells and virus-specific plasma cells through BAFF receptors. In this study, we explored transcript levels of BAFF receptors in PBL at pre-KT in CMV-IgG seropositive renal receptors as a way to predict reactivations in early post-KT stages.
Methods: A total of 30 CMV-IgG seropositive KT recipients were included in this prospective study. BAFF-R, TACI and BCMA gene expression levels were determined in RNA of PBL at pre-KT by qPCR. CMV reactivations were also monitored during the first 3 months post-KT through qPCR. KT recipients with more than 500 copies/ml at least in 1 sample were considered +CMV reactivation (CMV+ group,n=12) and rest of them were considered -CMV reactivation (CMV- group, n=18).B cell subtypes were also analysed by flow cytometry and compared with BAFF system gene expression and CMV viral load.
Results: Transcript expression of BCMA was significantly up-regulated in PBL of recipients of CMV+ group compared with those recipients of CMV- group (p=0.046). However, no significant differences were observed in levels of BAFF-R and TACItranscript expression. Next, we evaluated the correlation between transcripts levels and peak viremia in CMV+ group. We observed a significant correlation between BCMA transcript levels and peak viremia (p=0.008). No significant differences were observed in R-BAFF and TACI expression.High expression of the BCMA receptor in patients with early CMV reactivation also correlated with elevated plasmablast and class switched B cell levels (CSBC) and viral load.
Conclusions: Our results show that BCMA transcript levels at pre-KT are up-regulated in KT recipients with early CMV reactivation and these correlate positively with peak viremia and slightly with plasmablast and CSBC levels in PBLs. Our findings suggest that transcript BCMA levels may be useful for predict risk of CMV reactivation post-KT.

P527 CURRENT INSIGHTS INTO THE METABOLOME DURING HYPOTHERMIC KIDNEY PERFUSION

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Background: Kidney metabolism does not halt in the cold. We set out to summarise what is known about kidney metabolism during hypothermic perfusion preservation.
Methods: We systematically reviewed Pubmed, Embase, web of Science and Cochrane library using concepts “kidney”, “metabolism” and “perfusion” to identify papers studying kidney metabolism during hypothermic (<12°C) perfusion.
Results: Of 9794 screened articles, and after snowballing of 1444 additional articles, 54 were included [dog (27), rabbit (2), pig (21), human(7)]. These were published between 1970-2023, partially explaining heterogeneity of the studies with different perfusates (from albumin-based to synthetic), oxygenation levels (up to 750 mmHg) and methods (membrane oxygenation, surface oxygenation, bubble oxygenation, film oxygenation and hyperbaric oxygenation). Different duration of warm ischemia (0h-2h), cold storage (up to >20h) and hypothermic perfusion (up to 6 days) were recorded. Tissue and perfusate metabolites were determined by a variety of methods. In 11 papers, (non)radioactive labelled metabolites were used to study active metabolic pathways (mostly $^{13/14}$C-glucose and ^{14}C-labelled fatty acids (FA)). Kidneys are metabolically active during hypothermic perfusion, regardless of the perfusion setting. This metabolism is a complex interplay of different processes, whereby glucose, amino acid (AA) and FA metabolism act upon each other, citric acid cycle activity and overall energy metabolism. Kidney condition (control vs. ischemic), perfusate, perfusion length, and oxygen level influence this metabolism. Oxygenation seems to increase the adenine nucleotide metabolism and regeneration of highly energised metabolites (17 studies). Carbohydrates, AA or FA in the perfusate have an impact on these complex relationships and provoke changes in the metabolic pattern of kidney tissue and perfusate.
Conclusions: Kidney metabolism during hypothermic perfusion is complex and incompletely understood.

P528 TLJ 3.0 CONSENSUS ON HISTOPATHOLOGICAL ANALYSIS OF PRE-IMPLANTATION DONOR KIDNEY BIOPSY: REDEFINING THE ROLE IN THE PROCESS OF GRAFT ASSESSMENT

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Background: The European Society for Organ Transplantation (ESOT) TLJ 3.0. consensus conference brought together leading experts in the field of transplantation (pathologists, surgeons, nephrologists) to develop evidence-based guidance on the standardization and clinical utility of preimplantation kidney biopsy in the assessment of grafts from Extended criteria donors (ECD).
Methods: Seven emerging themes of interest have been selected by the Steering Committee (4 histopathologists, 4 nephrologists and 2 transplant surgeons) and underwent in-depth analysis after formulation of PICO (patient/population, intervention, comparison, outcomes) questions. After a literature search by the Center of Evidence in Transplantation (CET), the relevant statements for each key question were produced, rated according to the quality of evidence using the GRADE approach. The statements were subsequently presented in-person at an in-person meeting in Prague, discussed and voted upon by ESOT panelists.
Results: After two rounds of discussion and voting, all 7 statements reached an agreement of 100% on the following issues: needle core/wedge/punch technique representativity, frozen/paraffin embedded section reliability, experienced/non-experienced on-call renal pathologist reproducibility and accuracy of the histological report, glomerulosclerosis/other parameters (interstitial fibrosis, tubular atrophy, wall/lumen ratio, arteriolar hyalinosis) reproducibility, digital pathology/light microscopy in the measurement of histological variables,special stainings (Periodic-Acid Schiff, Silver, Picro Sirius Red, Trichrome) /Haematoxylin & Eosin alone comparison in the measurement of histological variables, glomerulosclerosis percentage/interstitial fibrosis, tubular atrophy, arteriolar hyalinosis and cv score reliability to predict transplant outcome.
Conclusions: This methodology has allowed us to reach a full consensus on important technical and interpretational topics regarding pre-implantation biopsy in the process of ECD graft assessment.

P529 PERCEPTIONS, EMOTIONS AND SOCIAL REPRESENTATIONS RELATED TO ORGAN DONATION IN HEALTHCARE WORKERS: A QUALITATIVE RESEARCH STUDY AFTER THE COVID-19

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Background: The study aims at analyzing the perceptions, emotions and representations related to organ donation in healthcare workers of Critical Areas, with a special focus on the procurement difficulties related to the COVID-19. This scenario entailed a change for most medical procedures, that needed to be reviewed and adapted to the new situation. The COVID-19, in fact, had a strong impact on procurement activity and on the attitude of healthcare workers towards organ donation.
Methods: The study sample involves 100 healthcare professionals (doctors and nurses) from Intensive Care and Emergency Departments of 9 hospitals, distributed in 3 Italian regions (Lombardy, Lazio and Sicily).
Individual anonymous open-ended interviews have been conducted, exploring the experience of organ donation during the pandemic on three facets: Emotions, Organization and Future prospectives). Interview texts were analyzed using a content analysis carried out by two independent judges.
Results: Data analysis showed specific emotions of healthcare workers related to COVID-19 experience (mainly fear and helplessness) and the use of primitive defense mechanisms, such as denial and repression, to face the emotional experience. On the other hand, organ donation brought restorative emotions (such as hope and satisfaction) which seem to represent a protective resource for the workers. For the organizational facets, COVID-19 had an impact especially on the logistic related to organ donation and on the relationships between healthcare workers and the families of potential donors. Considering the future prospectives, the need for *adhoc* in-the-field training emerged as well as the need to enhance social awareness toward organ donation, since an ambivalent attitude in the general population has been perceived.
Conclusions: Organ donation activities has represented a protective factor for the healthcare workers during the pandemic, since they fostered a feeling of continuity in daily work experience. However, some critical issues appeared, as the difficulty to communicate to the families due to pandemic restrictions. This work gives various hints to improve the experience of health workers in organ donation during critical times, suggesting the implementation of specific training focused on emotion management strategies.

P531 VALIDITY OF CT DEFINED BODY COMPOSITION AS A PROGNOSTIC FACTOR FOR LONG TERM FUNCTIONAL OUTCOME IN KIDNEY TRANSPLANTATION RECIPIENTS

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Background: Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength which increases the risk of adverse postoperative outcomes. Its prevalence is markedly higher in kidney transplant candidates than in the general population.
Methods: We studied the impact of computed tomography (CT) defined preoperative sarcopenia on postoperative physical functional outcomes (grip strength, 4 meter walking test, timed up and go, sit to stand) at 6 months follow up. A total of 107 patients transplanted between 2015 and 2019 were included in this single center study.
Results: Mean age was 60.3 (±13.1) and 68.2% of patients were male. Ten patients (9.4%) were identified as sarcopenic. Sarcopenic patients were younger (20.9 (±2.7) vs. 27.4 (±3.9)), more likely to be female (60% vs. 28.9%), and had an increased dialysis vintage (19.2 (±16.3) vs. 14.0 (±20.0)) in comparison to their non-sarcopenic counterparts. In univariate analysis they had a significantly lower body mass index (BMI), skeletal muscle area (SMA) and skeletal muscle index (SMI) (P=<0.001). In multivariate regression analysis SMI was significantly associated with grip strength and timed up and go performance.
Conclusions: In conclusion, we identified a significant association between low SMI (sarcopenia) and poorer physical functioning with respect to hand grip strength and timed up and go tests at six months post kidney transplantation. These results could be used to preoperatively identify patients with an increased risk of poor postoperative physical functional outcome, allowing for preoperative interventions to mitigate these risks.

P532 "YOUR DEATH, MY LIFE" - A FOCUS GROUP STUDY REGARDING THE ATTITUDES OF THE GREEK POPULATION TOWARDS ORGAN DONATION AFTER CIRCULATORY DEATH

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Background: There has been growing interest in donation after circulatory death (DCD) in recent years with DCD accounting for about 20% of all deceased donations worldwide. In a European survey, 18 countries reported running DCD programs and 17 countries declared no DCD activity, due to a variety of reasons from legislative to organizational obstacles, yet with half of them interested in developing DCD. Greece appeared reluctant towards DCD. The current study aims to identify and understand the attitudes of the Greek population towards DCD in order to inform future policy.
Methods: We conducted a focus group study with members of the general population across regions, age, socioeconomic and educational background about their attitudes and perceptions regarding organ donation and transplantation, and brain death vs circulatory death. Data were analysed using thematic analysis.
Results: Participants took a positive stand towards organ donation in general as part of an altruistic view of human existence. We identified factors who would favour consent to donation of a family member, as the irreversibility of the donors´ condition, a sense of wasting valuable organic material if not agreeing to donation and feelings of doing something important. Lack of adequate knowledge about the definitions of death and the donation procedure, mistrust towards the health system and hope of bringing back to life the donor, function counterproductive towards the decision to donate. Participants made no difference between DCD and DBD in terms of supporting organ donation, but expressed that the type of death and its perception of permanence and non-irreversibility would influence their decision. Brain death was perceived as more "certain" and there were some doubts regarding the finality of circulatory death. Still all agreed that DCD should be an option. Participants raised concerns as to whether the family is the right party to decide and emphasized the importance of the individual decision for or against donation during lifetime.
Conclusions: DCD would be a viable option complementary to DBD. Its specific characteristics should be taken into account in all stages of the donation and transplantation process and DCD shall be implemented within a broader context that would favour organ donation and includes multidisciplinary efforts.

P534 RACE-FREE VERSUS RACE-DEPENDENT ESTIMATED GLOMERULAR FILTRATION RATE AMONG KIDNEY-TRANSPLANTED PATIENTS ONE YEAR AFTER TRANSPLANTATION

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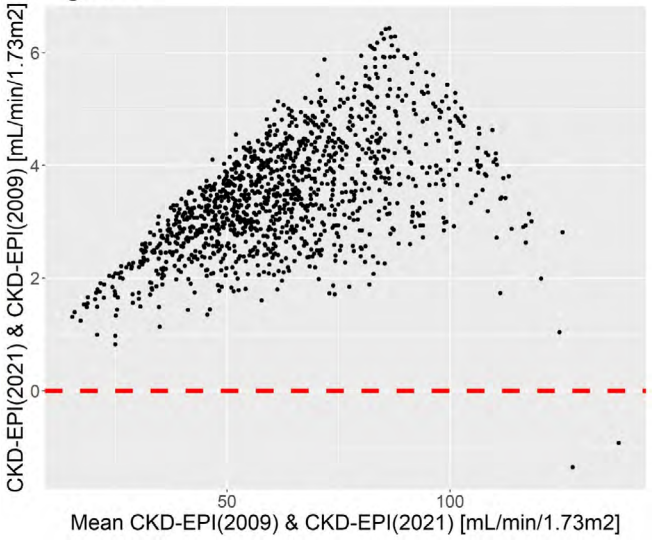
Background: Glomerular filtration rate (GFR) is a measure of kidney function for use in patient diagnostics and research. In our hospital, estimated GFR (eGFR) is regularly done with the CKD-EPI formula (2009) which calculates eGFR by using serum creatinine and incorporate age, sex and race. However, race is not a known factor for the personnel at the central laboratory, so every patient is counted as non-black. We know from earlier studies that eGFR often differ from measured GFR by ±30 % (1) and it is of interest to find the most reliable estimation of GFR. A new GFR formula which is not dependent on race has recently been developed (2021). In this study, we look at the best way of estimating GFR in renal transplant recipients by comparing the two formulas, using GFR measured by iohexol clearance as reference.
Methods: We collected data 1 year after kidney transplantation in 1274 transplant recipients. GFR was estimated with CKD-EPI 2009 (with race) and CKD-EPI 2021 (race-free), respectively, and measured GFR (reference) was assessed by iohexol-clearance. The two eGFR formulas were compared and presented as a Bland Altman plot. P30 values of the two eGFR formulas were calculated with measured GFR (iohexol clearance) as the gold standard to assess accuracy. A chi square test was performed to evaluate the significant difference between the two tests with regards to difference in P30 values.
Results: As shown by a Bland Altman plot, the difference between the two GFR estimates increases with higher eGFR levels and peaks at eGFR 70. The peak is related to a larger spread in data readings indicating discrepancy between the two eGFR estimates. CKD-EPI race-free (2021) estimation gives on average a higher GFR value. The total of eGFR values with *less* than 30 % difference (P30) from measured GFR, was 77.4% with the CKD-EPI (2009) calculations and 69.9% with the CKD-EPI race-free (2021) calculations. The CKD-EPI (2009) estimate gives a significant higher P30 compared to the CKD-EPI race-free (2021) equation (p<0.0001).
Conclusions: In our population, the CKD-EPI (2009) equation is a more appropriate tool to estimate GFR compared to the new CKD-EPI (2021) race-free formula. The results are comparable with recent studies on kidney transplanted patients. Reference: L.A Inker et al N Engl J Med 2021; 385:1737-1749 DOI: 10.1056/NEJMoa2102953

Figure 1



P535 RECIPIENT WARM ISCHEMIA TIME AND ITS IMPACT ON GRAFT FUNCTION AND HISTOLOGY AT 3 MONTHS

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Background: Previous studies showed that longer WIT is associated with an increased risk of delayed graft function and poorer graft survival. Some studies even suggest an association between anastomosis time and patient survival. In an original French transplantation cohort study including predominantly extended criteria donors (ECD), we aimed to evaluate the effect of WIT on graft function and histology at 3 months.
Methods: All patients admitted for a kidney transplantat at a single center (Tenon Hospital, Paris) between July 2017 and December 2019 were included. We evaluated clinical, biological, radiological and histological data prospectively up to 3 months post-transplant.
Results: 175 cadaveric kidney transplants were performed during the study period. We only included the 147 patients in whom the anastomosis time was known. 58% had an ECD based on UNOS criteria. Median recipient age was 56 years (interquartile range 44-61). Median donor age was 61 years (49-71). Median recipient BMI was 24.0 kg/m^2 (21.8-27.3). Median cold ischemia time was 14.3 hours (11.9-17.9). Median WIT was 58 minutes (43-7143 (29.2%) patients had delayed graft function (DFG) or primary non-function (PNF). Median 3-month estimated glomerular filtration rate – calculated using the CKD-EPI equation – was 44.1 ml/min/1.73 m^2 (30.0-46.4).
WIT was associated with DGF/PNF in both univariate and multivariate analyses. WIT was 71 minutes in the DGF/PNF group (n = 43) and 59 minutes in the no DFG/PNF group (n = 104) (p=0.029). In the ECD subgroup, no association between WIT and DGF/PNF nor 3-month eGFR was found. With regards to histology, no association was found between interstitial fibrosis at 3 months post-transplant and a longer anastomosis time in the general cohort (p = 0.805).
Conclusions: Recipient WIT was longer in our study, compared to historic cohorts. In our population, most patients received ECD kidneys, a longer WIT associated with DGF and PNF. We found no association between recipient WIT and histology or eGFR at 3 months after transplantation in the general and ECD donor cohorts.

P536 IMMEDIATE VERSUS DELAYED ABDOMINAL WALL CLOSURE AFTER PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION USING A GORE-TEX® PATCH: A SINGLE CENTER EXPERIENCE

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Background: Living donor liver transplantation (LLT) is a demanding procedure that often requires a transient expansion of the abdominal wall. Delayed abdominal closure (DC) is indicated in cases with post reperfusion swelling, an improper graft/recipient weight ratio (GRWR) and a frail portal inflow.
Methods: The use of a Gore-Tex® patch for a transient abdominal wall expansion was assessed in this retrospective study. Primary end-points were the occurrence of microbial contamination and abdominal wall hernias. Secondary endpoints include survival rates as well as early postoperative complications. We enrolled 66 LLTs performed in infants between 2002 and 2020 at the Medical University of Innsbruck.
Results: DC was performed in 34 patients (51.5%), immediate closure (IC) in the remaining 32 (48.5%). Children requiring DC were significantly younger (DC: 0 [0 – 0] vs. IC: 1 [0 – 7.5] p < 0.001), smaller (DC: 6.2 [5.26 – 7.60] vs. IC: 11,4 [7.04 – 22.22]; p < 0.001), and had a higher GRWR (DC: 4.4 [3.33 – 5.03] vs. IC: 2,35 [1.42 – 3.18] p < 0.001). Significantly more microbial contamination was observed in the DC group compared to the IC group (DC: 4.4 [3.33 – 5.03] vs. IC: 2.35 [1.42 – 3.18] p < 0.001). No abdominal wall hernias were recorded in our cohort. Infants in the DC group required a median of 3 (2 – 4) operations until definite abdominal closure. Regardless, duration of hospital stay was with a median of 51 vs. 44 days comparable between the DC and IC group (p = 0.077). Similar frequencies of vascular, biliary and bleeding complications were observed. The technique of abdominal wall closure did not influence patient (PS) and graft survival (GS) (1-year PS: [IC: 96.9% vs. DC: 97.1%]; 1-year GS: [IC: 87.5% vs. DC: 93.9%]).
Conclusions: Primary abdominal closure can be achieved in approximately half of the cases. Smaller infants and a higher GRWR are risk factors for DC. While a higher rate of microbial contamination was seen, this did not translate into a longer hospital stay and resulted in similar survival and postoperative complication rates without added risk for hernia development.

P537 ASYMPTOMATIC GRAFT INFECTION

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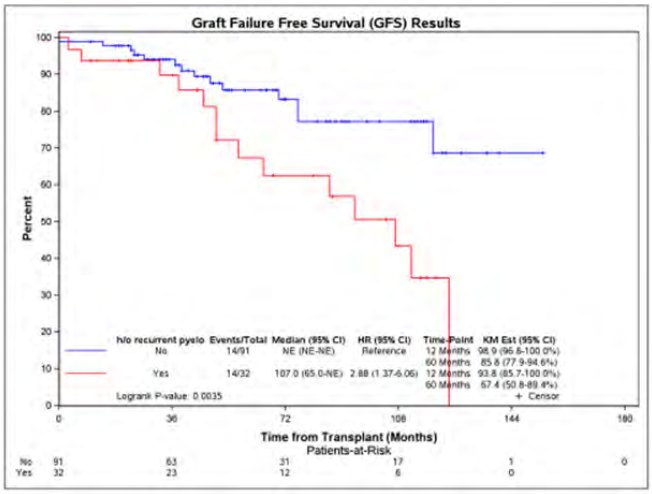
Background: Urinary Tract Infections represent the most common infection post-transplant and can have variable presentations. We describe a cohort of renal transplant recipients who had evidence of graft infection on allograft biopsy and were asymptomatic. Graft infection was defined as neutrophil cast or neutrophilic tubulitis, interstitial infiltrates with predominant neutrophils and no evidence of rejection or glomerulonephritis.
Methods: 123 kidney transplant recipients were included in the cohort. Of these, 95 were protocol biopsies, and 28 had a biopsy for elevated creatinine. We compared the above to the whole cohort to understand the risk factors for asymptomatic graft infection. We then compared it to a 1:3 matched cohort to study the impact of asymptomatic graft on graft survival.
Results: The mean age for the cohort was 55 years, 52% were females, and 78% received deceased donor transplants. The risk factors for asymptomatic graft infection on multivariate regression were recipient female sex (1.89), DM (2.48), and deceased donation (1.69). Most of the asymptomatic graft infection was identified at a 4-month biopsy (30%). 52% had positive urine cultures, 40% had negative, and 9% did not have urine cultures at the time of the biopsy. Escherichia coli was the most common bacteria on urine culture. In the culture-negative group, 14% had a positive culture in the 3 months prior to the biopsy, 39% had Urinary tract Infections in the next 6 months of the biopsy diagnosis, and 27% had positive urological history. The subjects with asymptomatic graft infection had inferior graft survival compared to the overall cohort. When compared to matched cohort, a trend toward increased graft loss was seen after 3 years. On subgroup analysis, there was an inferior graft survival in the group with recurrent pyelonephritis 2.88 (1.37-6.06), and those with renal dysfunction at the time of biopsy,2.59 (1.14-5.9). There was no difference in graft survival in the culture-positive vs. the culture-negative groups 1.09 (0.42-2.83). This could be because the majority received antibiotic treatment irrespective of the culture status.
Conclusions: We describe a cohort of subjects with Asymptomatic pyelonephritis and its association with poor graft survival, particularly in those with recurrent pyelonephritis and AKI.

Asymptomatic Graft infection group comparing recurrent vs. non-recurrent graft infection



P538 LETERMOVIR AS A RESCUE THERAPY IN KIDNEY TRANSPLANT RECIPIENTS WITH VALGANCICLOVIR/GANCICLOVIR REFRACTORY/RESISTANT CMV DISEASE

Ellen von Hoerschelmann[1], Johannes Münch[1], Linde Gao*[1], Christian Lücht[1], Marcel Naik[1], Danilo Schmidt[1], Ulrike Weber[1], Mira Choi[1], Fabian Halleck[1], Klemens Budde[1]

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Background: CMV infections remain a challenging complication after kidney transplant and its management is further complicated by occurring resistance against the first line treatment with Valganciclovir(VGCV)/Ganciclovir(GCV). The purpose of this study was to analyze CMV treatment using letermovir in case of VGCV/GCV resistance in kidney transplant recipients.
Methods: In a single center retrospective study kidney transplant recipients (KTR) receiving letermovir as a rescue therapy in VGCV/GCV refractory/resistant CMV disease were analyzed regarding CMV history, immunosuppression, and outcome.
Results: Out of 201 KTR treated for CMV-DNAemia or CMV-disease between 2017 and 2022, 8 patients received letermovir as CMV treatment following treatment failure with VGCV/GCV. All patients received CMV-prophylaxis with VGCV according to center protocol, 7/8 had a high risk (D+/R-) CMV constellation. In 7/8 cases CMV-DNAemia (n=1) or CMV-disease (n=7) occurred under VGCV prophylaxis. 1/8 developed CMV-DNAemia without ongoing prophylaxis. Treatment with oral VGCV (n=8) and iv GCV (n=4) was intensified according to manufacturer recommendation. In all patients letermovir was started under rising virus loads. One patient received letermovir as a rescue therapy in VGCV/GCV refractory CMV-disease. In 7/8 patients a resistance in the UL97 gene associated with decreased response to VGCV/GCV was detected. Median VGCV/GCV treatment duration until detection of resistance was 11 weeks with a wide range (2-43 weeks). In 6/8 patients CMV virus load decreased <2000 cop/ml after24±12 weeks (range 6-41 weeks) of treatment with letermovir. However, 2/8 developed a letermovir resistance under the course of a two-months treatment period. Both patients with the letermovir resistance showed a restored VGCV/GCV sensitivity in the further course and could be treated effectively with VGCV accompanied by additional treatment with CMV hyperimmunoglobulin.
Conclusions: Letermovir, which is currently evaluated for CMV prophylaxis in kidney transplantation, showed promising results for treatment of patients with VGCV/GCV resistance despite a low threshold to develop letermovir resistance. Additional studies are needed to further define its role in the treatment of patients with CMV resistance.

P539 ORTHOTOPIC ROBOT-ASSISTED KIDNEY TRANSPLANTATION: A NOVEL TECHNIQUE AND CASE SERIES

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Background: Orthotopic kidney transplant is a good alternative for patients with an end-stage renal disease non-suitable for a heterotopic kidney transplant (KT). Recently, robot-assisted kidney transplant (RAKT) has been shown to achieve excellent patient and graft outcomes, while reducing surgical morbidity. From the experience in RAKT, we developed this technique in orthotopic transplantation. The aim of this study is to describe the technique of Orthotopic robotic assisted kidney (ORAKT) and present the case series.
Methods: From 127 RAKT performed in Hospital Universitari de Bellvitge, 10 ORAKT from October 2018 to January 2023. Recipient, donor, surgical and postoperative data are analyzed. *Surgical Technique:* A 6Fr double J stent is placed in the left ureter. A 10 cm laparotomy is performed on the left iliac fossa and ports are placed (Figure 1). Da Vinci Robot® is docked following renal surgery protocol and 30º camera is used. Left nephrectomy: renal vein (RV) is prepared, a robotic clamp is placed and the vein is cut as long as possible. The splenic artery (SA) or renal artery (RA) and their divisions are identified, dissected and clamp is placed. The ureter is dissected. Artery flow can be check using doppler ultrasound (US), blood flush or fluorescence. The graft is prepared as RAKT protocol. When kidney is introduced insufflation is maintained at 12 mmHg. RV and RA are anastomosed in end-to-end continuous fashion using a 6/0 GoreTex® CV6. At reperfusion, with insufflation maintained at 8 mmHg, doppler US is checked. A latero-lateral urinary anastomosis to native urinary tract is done with 4/0 Monocryl. 24-hour US is done, and ureteral stent is removed at 4 weeks.
Results: Median donor and recipient age were 66 (IQR 17) and 66 years old (IQR 8), 7 of them in dialysis (Median 33 months, IQR 58). 9 arterial anastomosis were performed to SA and 1 to the RA. Surgical and postoperative data are shown in table 1.
Conclusions: ORAKT is a feasible minimally invasive alternative for selected patients non-suitable for heterotopic KT in centers with RAKT experience. The potential advantages of the robotic approach are the reduction of lumbotomy morbidity, the precise vessels dissection and vascular anastomosis. Urinary tract complication is commonly present.

Figure 1

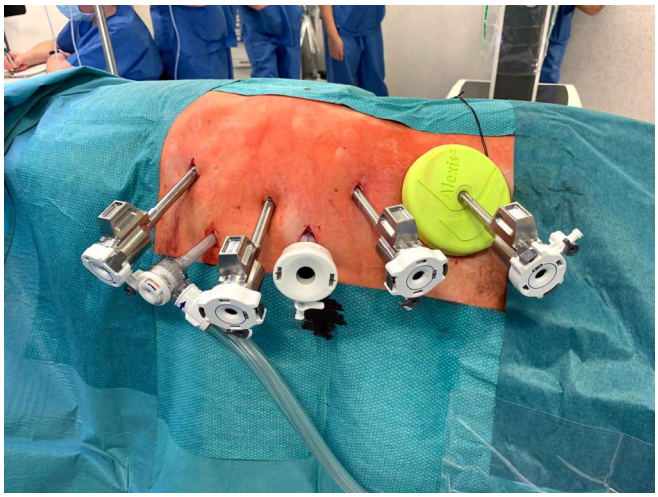

Table 1

Case (Donor)	Operative Time (min)	Vascular Anastomosis (min)	Re-warm time (min)	Postoperative complication <30d (Clavien-Dindo)	DGF (HD 1 week)	Stay (days)	eGFR 1 m (mL/min	eGFR 6m (mL/min)	>30 days complication
1 (CD)	389	47	59	Prostatitis (II)	-	41	38	56	Ureteral stenosis (Surgical resolution)
2 (CD)	300	41	44	Urinary Fistula (IIIa)	Yes	40	16	31	Ureteral stenosis / Rejection/ HD
3 (LD)	272	46	50	-	-	7	41	39	-
4 (CD)	248	61	75	-	-	8	45	39	-
5 (CD)	333	42	54	Urinary Retention (I)	-	7	42	42	-
6 (CD)	312	41	54	Arterial Thrombosis (IIIb)					-
7 (CD)	180	41	46	Urinary Fistula (IIIa)	-	28	35		-
8 (CD)	295	37	19	-	Yes	17	29		-
9 (LD)	276	33	44	-	-	29	46		-
10 (LD)	782	25	31	Urinary Retention (I)		14			-

CD: cadaveric Donor; LD: Living Donor

P540 PROGNOSTIC VALUE OF A POSITIVE CROSSMATCH BEFORE DESENSITIZATION IN A COHORT OF HIGHLY-SENSITIZED PATIENTS

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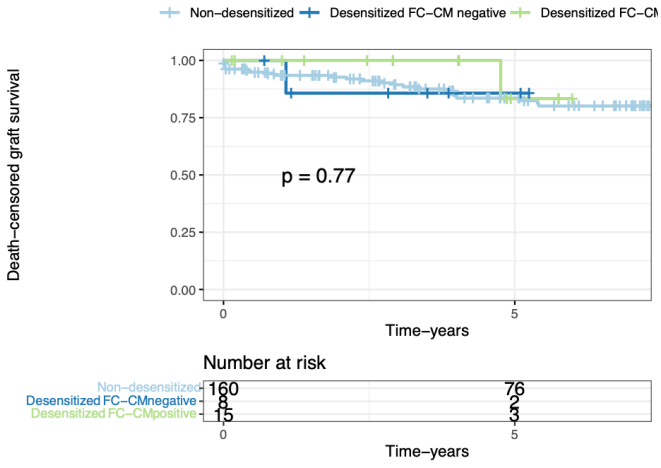
Background: Human Leukocyte antigen (HLA) sensitization in patients is a barrier for Kidney Transplantation (KT) access, and highly-sensitized patients remain on the waiting list longer than other patients which results in a higher morbidity and mortality. Desensitization may be an option to increase their access to KT. All patients in this context have a negative Complement-Dependent Cytotoxicity crossmatch (CDC-CM) the day of KT. However, the stratification of the long-term risk of graft loss according to flow cytometry crossmatch (FC-CM) and to CDC-CM during the desensitization period remains unknown.
Methods: In this retrospective study, all highly-sensitized patients (Panel Reactive Antigen (PRA) ≥ 85) in our center were included. CDC-CM and FC-CM were performed on samples before and during the desensitization period and clinical follow-up data were retrieved. Pre-KT desensitization strategy consisted in two Rituximab infusions (375mg/m^2) and a variable number of apheresis associated with a classical immunosuppression-based regimen (tacrolimus, mycophenolate and steroids).
Results: A total of 183 highly-sensitized recipients received a KT between 2014 and 2022. Of these, 23 were desensitized prior to KT and among them 18 had a positive FC-CM before KT and 5 had no positive FC-CM on all assessed serums. Mean follow-up was 5.2±4 and 3±2 years for non-desensitized and desensitized patients respectively. Mean time on the waiting list was 5.8±4 versus 7.5±4 years respectively. Death-censored graft survival and patient's raw survival, using cox-survival analysis, were not statistically different between the desensitized kidney transplanted patients and the highly-sensitized patients without desensitization (p=0.77 and p=0.57 respectively). In sub-group analyses, the positivity of FC and/or CDC-CM did not add an additional risk of graft loss or patient mortality.
Conclusions: Desensitization allows highly-sensitized patients to access KT with an HLA-incompatible graft (with a positive CDC or FC-CM on the serum collected prior to desensitization), with the same graft survival as similarly sensitized patients transplanted with an HLA-compatible graft without desensitization.

Figure: Death-censored graft survival in highly sensitized kidney transplant recipients.



P542 EDUCATIONAL INTERVENTION AS AN APPROACH TO SUPPORT COUNTRIES IN EUROPEAN REGION TOWARDS ACHIEVING SELF-SUFFICIENCY IN TRANSPLANTATION

Seow Huey Choy[1], Chloe Balleste*[1;2], Carmen Blanco[1], Aleksandra Karandashova[1], Ricard Valero[1;2], Martí Manyalich[1]

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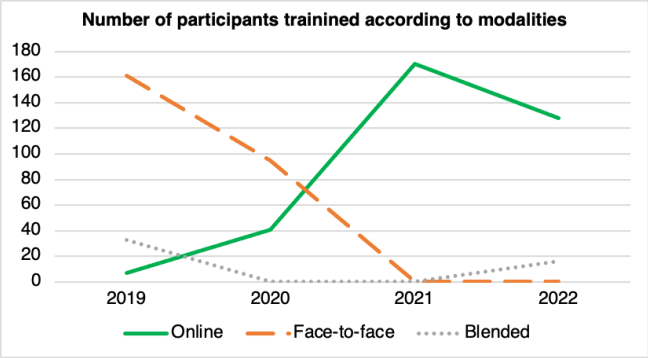
Background: Training of healthcare professional is an essential component in improving quality, safety and capacity of donation and transplantation. The disruptions brought by the COVID-9 pandemic did not deter the educational interventions. A wide range of training experience on donation and transplantation in the European region was presented in this study.
Methods: A variety of programs focusing on enhancing healthcare professionals' skills and knowledge in donation and transplantation were implemented. The programs were diversified and available at different levels to adapt to the different needs and advancements of the donation and transplant communities. There are courses that covered the key donation processes such as identification, evaluation, and management of donors. A more specific trainings or workshops on family approach, donation after cardiac death, tissue banking and regenerative medicine were also encompassed. Three modalities of training namely face-to-face, online, or blended were used. When face-to-face could not be conducted, innovative strategies were developed and these included virtual classroom and internship, interactive gaming, immersive experience with virtual reality tool, and simulation in clinical setting.
Results: A total of 651 participants from 46 countries in the European region were involved in courses that were held between 2019 and 2022. The number participants remained relatively constant with an average of 164 trained per year. In 2019 and 2020, 80% (n= 161) and 70% (n= 95) of the participants were trained face-to-face respectively. In 2021, the participants were 100% trained online. The trend continued in 2022, with 89% of them trained in the online modality.
Conclusions: The training experience donation and transplantation among health professionals in pre- and post- covid time was shown. The training modality switched from face-to-face to online modality from 2020 onwards. The training opportunity and quality could not be compromised even in the unprecedented event, and these could be achieved through innovative adaptations.



P544 VISIONEM AN AI PLATFORM FOR ORGAN ASSESSMENT

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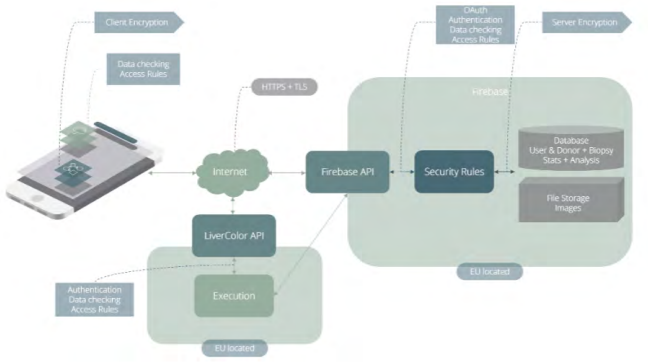
Background: The decision to use or discard an organ is based on the surgeon´s assessment from visual (color and texture) analysis, which is fast but subjective and highly error-prone, tightly rely on the surgeon´s experience. Liver esteatosis is one of the major reasons to discard livers for transplantation since it increases the risk of early allograf dysfunction and primary non-function. Currently, liver biopsy is the gold standard to evaluate hepatic steatosis, but it is invasive, costly and not always available during liver procurement. Thus, there is a need for a simple, rapid and accurate method for detecting steatosis in the donor.
Methods: To this end, we started creating an innovative co-designed method that uses image analysis and machine learning to support the medical decision process for graft liver assessment from a simple picture, referred to as LiverColor. Visionem is the AI platform where LiverColor is integrated. Visionem consists of 4 main interrelated components: 1) Mobile Application during surgical procedure; 2) the database and repository of images and clinical data; 3) the image processing and data analysis tools based on machine learning; 4) the web portal application. Various predictive models were trained and validated in an in-house dataset. Usability-related aspects of the system were also assessed both in simulated and real clinical settings. Other organs as Kidney (KidneyColor) and Pancreas (PancretIA) with different endpoints are also being trained in this platform.
Results: Surgeons appreciated the functionalities provided by the platform not only the algorithm assessment but also the dashboarding to summarise and display procurement-related data. For liver assessment, a total of 115 livers, (228 photographs and 4,560 patches) were included. The best results were obtained using the random forest classifier, achieving an AUROC=0,78, with 83,3% of accuracy, being higher than the one obtained by visual inspection by the surgeon.
Conclusions: Image analysis coupled with machine learning can help to safely identify valid livers during procurement.



P545 ENHANCED VIABILITY AND FUNCTION DURING PROLONGED CARDIAC GRAFT PRESERVATION USING THE VP.S ENCORE® OXYGENATED MACHINE PERFUSION DEVICE

Kristina Andrijauskaite*[1], Rafael Veraza[1], Riley Lopez[1], Exal Cisneros[1], Isabella Cano[1], Zachary Maxwell[1], Milos Marinkovic[2], Israel Jessop[1], Michelle Watt[1], Leonid Bunegin[1]

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Background: Machine perfusion has become an important paradigm in the field of organ preservation; however, most machine perfusion devices are complex and expensive. We have developed a portable, simple to use, cardiac preservation device called the VP.S ENCORE® which was granted the FDA breakthrough designation status and is currently under development pending FDA approval. In this study, we show the efficacy of our device using preclinical data of testing porcine, ovine, and human hearts.
Methods: After recovery, isolated porcine (n = 30), ovine (n = 14) and human hearts rejected for transplantation (n = 8) were placed in the VP.S ENCORE® and perfused at 4-25°C for different time points including 4h, 6h, 8h, and 24 hours or were kept at static cold storage (SCS). During perfusion, hourly flow, pressure, temperature, and blood gas measurements were recorded. Following either preservation method, hearts were placed in a Langendorff model for reperfusion and evaluated for cardiac function. Biopsy samples were taken for histological & gene expression analyses, and two ovine hearts underwent orthotopic heart transplantation at the Texas Heart Institute.
Results: Most perfusion experiments were conducted at hypothermia (4-8°C); while some were run at subnormothermia (25°C) by adding haemoglobin-based oxygen carrier. Venous and arterial lactate concentrations were less than 2.5mmol/L across most experiments, with no or minimal edema. Perfused porcine hearts at 4 h had significantly increased contractility ($p<0.05$) as demonstrated by +dP/dT(mmHg), while perfused sheep hearts had an increased contractility ($p<0.01$) at 8 hours when compared to SCS. Perfused human hearts indicated left ventricular contractility within the range of a healthy human heart +dP/dT (mmHg/s >1000) for 4, 6, and 8 hours of perfusion. Transplant data demonstrated lower vasopressor index (0.08) and less time needed on bypass (119 min) for the VP.S ENCORE® preserved hearts versus SCS hearts (0.17,147min). Finally, gene expression data revealed downregulation of most inflammatory and cell death markers in perfused hearts.
Conclusions: Our preclinical data demonstrate that the simple to use VP.S ENCORE® cardiac preservation device can serve as an alternative to the SCS and could potentially become a new paradigm to prolong organ preservation.

P546 SEARCHING NEW DONATION SCENARIOS: POTENCIAL RECEPTORS "ON THE OTHER SIDE OF THE MIRROR"

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Background: Advances in the field of extracorporeal circulation have improved the prognosis and survival of patients in situations of respiratory failure or cardiogenic shock. However, due to disease progression or not considering the inclusion on the waiting list, the purpose of extracorporeal support treatment may be considered futile. These patients who were waiting for an organ can become new donation scenarios, placing a potential receptor just "on the other side of the mirror". The descriptively study analyzed the potential receptor of a thoracic organ with extracorporeal assistance who become donors in controlled asystole.
Methods: Retrospective observational study of those donors who met the aforementioned criteria from January-2016 to September-2021 in a tertiary care hospital. Demographic, clinical, organ traceability, and donation effectiveness variables were collected.
Results: 9 real donors were collected. 77.8% were men with a median age of 56 years. 55% had some cardiovascular risk factor. The mean ICU stay was 12.1 days. 7 patients carried veno-arterial ECMO due to: postinfarction cardiogenic shock (4), pulmonary thromboembolism (1), primary heart transplant failure (1), non-ischemic dilated cardiomyopathy (1). 2 patients with veno-venous ECMO due to pulmonary fibrosis pending transplantation. 19 organs were obtained (7 livers and 12 kidneys), which represents a ratio of 2.1 organs per donor and an effectiveness of 88.9%.
Conclusions: The shortage of donors forces us to broaden the search for new scenarios of donation. Although this type of "mirror" donor represents a significant change in treatment and emotional stress for their families, it is a source to consider once their care team considers the adequacy of life-sustaining treatment.

P547 PERSISTENT HYPERPARATHYROIDISM AFTER PREEMPTIVE KIDNEY TRANSPLANTATION

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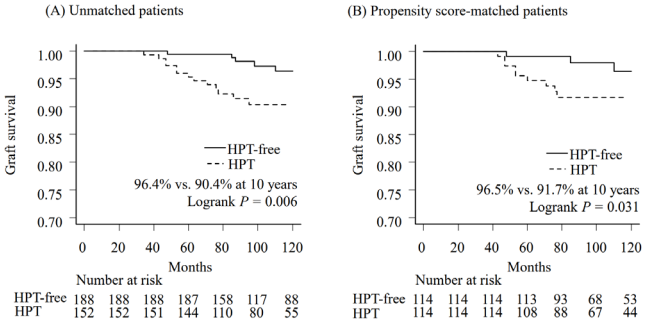
Background: Long dialysis vintage is one of the typical predictors of persistent hyperparathyroidism (HPT) after kidney transplantation. Recently, preemptive kidney transplantation (PKT) has increased. However, the incidence, predictors, and clinical implication of HPT after PKT are unknown. This retrospective cohort study attempted to clarify these questions.
Methods: Patients who underwent PKT between 2000 and 2016 were included in the study. Those who lost their graft within one year posttransplant were excluded. Hyperparathyroidism was defined as when intact parathyroid hormone (PTH) levels exceeded 80 pg/mL, or hypercalcemia unexplained by causes other than HPT. The patients were divided into two groups based on the presence of HPT one year after PKT. The primary outcome was the predictors of HPT after PKT, and secondary outcome was graft survival.
Results: Among the 340 consecutive PKT, 188 did not have HPT (HPT-free group), and 152 had HPT (HPT group). The multivariate logistic regression analysis revealed that pretransplant PTH level ($P < 0.001$; odds ratio [OR], 5.480; 95% confidence interval [CI]: 2.070– 14.50), and preoperative donor estimated glomerular filtration rate ($P = 0.033$; OR, 0.978; 95% CI: 0.957–0.998) were the independent predictors for HPT after PKT. Death-censored graft survival was significantly lower in the HPT group than in the HPT-free group (90.4% vs 96.4% at 10 years, $P = 0.009$).
Conclusions: Pretransplant PTH levels and donor kidney function were the independent predictors for HPT after PKT. Additionally, HPT was associated with worse graft outcomes even after PKT.

Multivariate Logistic regression for HPT after PKT			
Factors	OR	95% CI	P-value
Recipient age (yeas)	1.010	0.994–1.030	0.212
Male recipient	0.855	0.507–1.440	0.557
Diabetes mellitus	0.769	0.412–1.440	0.410
Serum calcium before PKT (mg/dL)	1.090	0.751–1.580	0.655
Serum phosphorus before PKT (mg/dL)	0.941	0.770–1.150	0.554
Log intact PTH before PKT (pg/mL)	5.480	2.070–14.50	<0.001*
Parathyroid gland size (mm)	1.030	0.965–1.090	0.415
Donor age (years)	1.010	0.986–1.040	0.374
Male donor	0.720	0.427–1.210	0.217
Preoperative donor eGFR (mL/min/1.73m²)	0.978	0.957– 0.998	0.033*
*P-value < 0.05			



P548 A RANDOMISED CONTROLLED TRIAL TO COMPARE STANDARD AND TORQUE TENO VIRUS GUIDED IMMUNOSUPPRESSION AFTER KIDNEY TRANSPLANTATION - TTVGUIDEIT PROTOCOL

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Background: Immunosuppression after kidney transplantation is mainly guided by tacrolimus (TAC) trough levels, which are not able to predict graft rejection and infection sufficiently. The plasma load of the non-pathogenic and highly prevalent Torque Teno Virus (TTV) is associated with the immunosuppression of its host. Non-interventional studies suggest TTV load to identify patients at risk for graft rejection and infection. The primary objective of the current trial is to demonstrate safety, tolerability and preliminary efficacy of TTV-guided immunosuppression.
Methods: A two-arm, randomised, controlled, interventional, non-inferiority, patient and assessor-blinded, and investigator driven, phase II trial was designed: A total of 260 adult stable immunological low risk recipients of a kidney graft with TAC based immunosuppression and TTV infection after month 3 post-transplant will be recruited at 13 centres in 6 European countries. At month 4 post-transplant subjects will be randomised at a 1:1 ratio to receive either a TAC dosing guided by TTV load or according to local centre standard for 9 months. In the active cohort the TAC dosing depends on whether TTV load is targeted in an optimal range from 4.6 log10 to 6.2 log10 copies/mL. If TTV is not within this range, the TAC trough level target has to be adapted by one step (2 +/-1 ng/mL) up or down. The primary composite end point includes occurrence of infections, biopsy proven graft rejection, graft loss or death. Main secondary end points include estimated glomerular filtration rate, graft rejection detected by protocol biopsy at month 12 post-transplantation including molecular microscope, de novo donor specific antibodies, health-related quality of life and medication adherence. Date of first recruitment was August 2022 and planned end is April 2025.
Results: Conclusions: The assessment of an individual kidney transplant recipient immune function might enable clinicians to personalise immunosuppression, thereby reducing infection and rejection. The TTVguideIT trial might act as a proof of principle for TTV-guided immunosuppression.

P549 VACCINATION RESPONSES TO PNEUMOCOCCUS, TETANUS AND INFLUENZA AFTER KIDNEY TRANSPLANTATION USING TACROLIMUS WITH AND WITHOUT MYCOPHENOLATE MOFETIL

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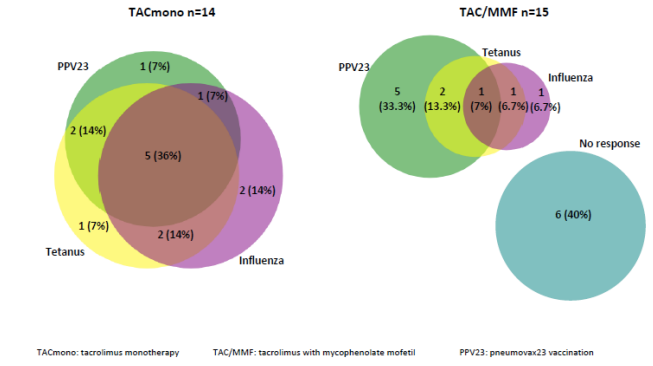
Background: Immune suppressive medication is a risk factor for severe infections and insufficient vaccination responses. The impact of mycophenolate mofetil (MMF) on top of tacrolimus (TAC) on vaccination responses is not well characterized in a randomized cohort of kidney transplant recipients.
Methods: A randomized controlled trial was performed in immunologically low risk kidney transplant recipients (EudraCT nr.: 2014-001372-66). Patients were randomized to standard TAC/MMF or to TAC monotherapy (TACmono) from 9 months onwards after transplantation, without steroids. One year after transplantation patients were vaccinated against pneumococcus (PPV23), tetanus (tetanustoxoid) and, if in season, influenza. Blood was sampled before and 21 days after vaccination. Adequate vaccination responses were defined as: for PPV23 ≥9 serotypes with antibodies ≥1.00 mg/mL; for tetanus antibodies ≥1.0 IU/mL and ≥ 1.5-fold increase if baseline was ≤1.0 IU/mL or ≥2.5-fold increase if baseline was > 1.0 IU/mL; for influenza post-vaccination titers ≥40 IU/mL or 4-fold increase for all 3 strains.
Results: 71 patients received PPV23 and tetanus vaccinations (TAC/MMF n=37,TACmono n=34). Of those, 29 were also vaccinated against seasonal influenza (TAC/MMF n=15, TACmono n=14). Patients were 60 (54-66) years of age and 72% male, with median eGFR of 54 (44-67) ml/min. 42% of the patients had diabetes. TAC trough levels were 6.1 (5.4-7.0) µg/L in both groups and MMF dose was 1000 mg daily (500-2000) in TAC/MMF. Adequate vaccination responses were measured for PPV23 in 43% vs 74%, for tetanus in 35% vs 82% and for seasonal influenza in 20% vs 71% of TAC/MMF vs TACmono patients, respectively p= 0.03, p <0.001 and p= 0.009. Only 7% of TAC/MMF responded adequately to all 3 vaccinations compared to 36% of TACmono, p= 0.08. Furthermore, only 60% of TAC/MMF patients responded adequately to at least one of the three vaccinations, compared to 100% of TACmono, p= 0.02.
Conclusions: MMF on top of tacrolimus severely hampered serological responses to pneumococcus, tetanus and influenza vaccinations.

Table 1. Baseline characteristics of kidney transplant recipients randomized for either TACmono or TAC/MMF, vaccinated for pneumococcus and tetanus 12 months post-transplantation

	TAC-mono (n = 34)	TAC/MMF (n = 37)
Age, median (range in years)	59 (37-71)	59 (29-80)
Sex, n male (%)	25 (74%)	26 (70%)
BMI, median (range in kg/m^2)	28 (21-36)	27 (20-35)
Transplant type, n living donor transplant (%)	23 (68%)	21 (57%)
CKD-EPI eGFR, median (range in ml/min/1,73 m^2)	60 (32-105)	53 (29-84)
Proteinuria protein/creatinine ratio, median (range in mg/mmol)	18.6 (6.0-94.9)	13.9 (5.1-33.3)
TAC trough level, median in ug/l (IQR)	6.4 (1.8)	6.2 (1.3)
MMF trough level, median in mg/l (IQR)	-	2.4 (2.1)
Daily dose MMF, median in g (IQR)	-	1.0 (0.5)

TACmono: tacrolimus monotherapy n: number BMI: body mass index eGFR: estimated glomerular filtration rate TAC: Tacrolimus MMF: Mycophenolate mofetil IQR: Interquartile range

Figure 1. Serological vaccination responses in kidney transplant recipients using tacrolimus with or without mycophenolate mofetil. The number and percentage of patients with an adequate serological response for pneumococcus, tetanus and seasonal influenza are shown in this venn diagram. This figure depicts the 29 out of 71 patients that received all 3 vaccinations.



P550 INCREASING ACCESS TO LIVING DONOR TRANSPLANTS BY OVERCOMING BARRIERS TO RECIPIENTS IDENTIFYING A LIVING DONOR

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Background: Many patients in need of a kidney transplant do not consider a living donor (LD). We studied the effect of having a dedicated "LD-navigator" meet with potential recipients during the evaluation to educate and provide resources for identifying a LD.
Methods: We designed an intervention to increase the number of LD kidney transplants. Pre-evaluation phone calls improved recipient knowledge of LD transplantation. Recipients were encouraged to bring potential donors or a support person to the initial evaluation. The LD navigator met with each patient and assessed their comfort with living donation. The LD navigator educated the patient and support person on living donation and dispelled myths using data. Next she focused on which methods or tools were comfortable and easy to use for that patient or their advocate: How does the patient want to tell their story? With who do they want to share it? Examples offered: e-mail, social media, or a bulletin from organizations. If the patient expressed reluctance to speak out in their own behalf, we inquired about comfort with someone else telling their story? This is aimed at identifying advocates or a donor champion. The coordinator reviews the microsite option with the patient and offers them an invitation. Patients leave the appointment with a written action plan and follow up dates.
Results: Pre-intervention (11 mo), among 114 kidney transplant evaluations, only 12 (10.5%) of patients identified a potential LD. 4 received deceased donor transplants and 0 received a LD transplant in the following 12 months. Post-intervention (12 mo), 152 patients were evaluated. 53 (34.8%) identified a potential living donor. 10 received a deceased donor transplant and 8 received a LD transplant within 12 months. This number is expected to increase given its proximity to the data capture period.
Conclusions: There is benefit in utilizing a dedicated person to assess, educate, and guide patients through the LD process. Many recipients unsure of how or uncomfortable in approaching others about LD. Providing guidance and support to recipients helps increase their ability to find a living donor and shortening waiting time.

	# Living Donors Called Program (#, % recipient evals)	# Living donor transplants completed
Pre-intervention	12 (10.5 %)	0
Intervention Period	53 (34.8%)	8

P551 PRE-TREATMENT OF DONOR TISSUE IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION: A SYSTEMATIC REVIEW

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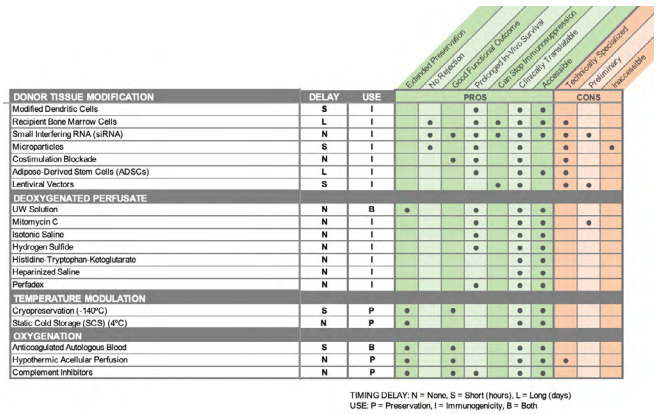
Background: Vascularized composite allotransplantation (VCA) is the top of the reconstructive ladder for injuries or deformities of the central face or distal upper extremity. However, its success is largely compromised by high rates of graft rejection and ischemia-reperfusion injury (IRI). 'Pre-treatments' refer to interventions applied to the donor tissue, after procurement and prior to transplantation, that aim to reduce the immunogenicity of the graft, or decrease the extent of IRI. We reviewed, categorized and delineated the most promising pre-treatments published to date.
Methods: A literature search of PubMed, Cochrane, and Embase databases was conducted, yielding 25 studies in the final analysis. Of these studies, 19 distinct pre-treatments were described. Pre-treatments were grouped into four categories: Temperature Modulation, Donor Tissue Modification, Deoxygenated Perfusate, and Oxygenation.
Results: Temperature modulation and oxygenation methods were primarily investigated to extend the timeframe in which allografts are viable ex-vivo and decrease IRI, while donor tissue modification and deoxygenated perfusate were primarily concerned with reducing rejection burden post-transplantation. Cryopreservation and oxygenation with autologous blood have been shown to markedly increase functional outcome and decrease IRI over standard storage on ice. Introduction of recipient bone marrow cells into donor tissues yielded a successful hematopoietic chimera that survived rejection-free 2.7x longer than a traditional VCA.
Conclusions: While pre-treatments aimed at extending ischemic graft survival/reducing IRI have seen moderate clinical translation, pre-treatments aimed at reducing donor immunogenicity remain largely experimental, with limited clinical adoption. The results of this study demonstrate the promise of these latter techniques and future research, in particular, multi-center clinical trials of donor tissue modification methods are warranted.

Figure 1. Timing of use (Delay), Goal of intervention (Use) as well as Pros and Cons for Pre-Treatment modalities in VCA.



P552 ASSOCIATION BETWEEN INTRAOPERATIVE FLUID MANAGEMENT AND POSTOPERATIVE OUTCOMES IN LIVING KIDNEY DONORS

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Background: Intraoperative fluid management during living donor nephrectomy may have a significant effect on postoperative outcomes. Although aggressive fluid management (34.3 ml/kg/hour) was reported to increase the postoperative complications, the so-called standard fluid management (14.8 ml/kg/hour) might be aggressive. So, we aimed to compare the postoperative outcomes of living kidney donors according to the intraoperative fluid management of our hospital.
Methods: Medical records of living kidney donors of our hospital were reviewed. Donors were divided into three groups according to the intraoperative fluid management. Primary outcome was the postoperative maximal rise of creatinine during hospital stay [(maximal postoperative creatinine - preoperative creatinine) / preoperative creatinine]. Secondary outcomes were incidence of prolonged hospitalization (defined as length of hospital stay ≥14 days), pulmonary complication, renal dysfunction, wound infection/dehiscence, incisional hernia, reoperation, postoperative furosemide use, and rehospitalization for acute kidney injury.
Results: Total 507 living kidney donors were included in final analysis. Donors were divided into tertiles according to the intraoperative crystalloid infusion rate. Mean ± standard deviation of intraoperative crystalloid administration was 3.40 ± 0.47, 4.59 ± 0.31, and 6.29 ± 1.05 ml/kg/hour for group 1, 2, and 3, respectively. Maximal rise of creatinine was inversely correlated with the intraoperative fluid management (Pearson correlation, R=-0.23, p<0.001). Moreover, maximal rise of creatinine in group 1 was significantly higher than group 2 (0.65±0.20 vs. 0.57±0.16, p<0.001) and group 3 (0.65±0.20 vs. 0.56±0.18, p<0.001), although there was no significant difference between group 2 and 3 (p=1). Incidence of prolonged hospitalization was highest in group 1 (6.5%) and lowest in group 3 (1.2%) (p=0.036). Other postoperative outcomes did not differ between groups.
Conclusions: Too less intraoperative fluid management was associated with poor postoperative outcomes. More study about the ideal intraoperative fluid management during living donor nephrectomy is required.

P553 RNA-SEQUENCING REVEALS A CONSERVED MECHANISM OF ACUTE REJECTION IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION ACROSS PATIENTS AND ANATOMICAL LOCATION

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Background: Despite substantial advances that make vascularized composite allotransplantation (VCA) viable for patients with devastating soft tissue injuries, acute rejection remains a major morbidity. Molecular mechanisms of VCA rejection have not been fully elucidated, including potential variation across different patients and recipient anatomical sites, e.g. face and hand.
Methods: NanoString RNA sequencing (RNAseq) was performed on 18 FFPE skin biopsies (12 face, 6 hand) from 3 VCA recipients; 6 were categorized as nonrejection (NR); 12 as acute rejection (AR) by clinical status (**Figure 1A**, made with BioRender). Single cell RNA sequencing (scRNAseq) was performed on 10 biopsy specimens (5 face, 5 hand) from a VCA recipient; 2 were NR and 8 as AR. Data analysis and visualization was performed (NanoTube, Seurat, and ggplot2 packages in R), in addition to Metascape for pathway analysis.
Results: We first investigated interpatient variation in VCA rejection, revealing 74 differentially expressed genes (DEGs) between AR face biopsies from patient #1 (n=3) and all NR face biopsies (n=6) (**Figure 1B**). Fold changes of these DEGs displayed strong positive correlations across all 3 patients (all $r \geq 0.67$, all $p < 0.05$). We then investigated transcriptional variation in VCA rejection based on recipient anatomical site. Comparing all AR face biopsies (n=6) versus all NR face biopsies (n=6) revealed 140 DEGs (**Figure 1C**). Similarly, fold changes of these DEGs displayed strong positive correlations with hand specimens (all $r \geq 0.6$, all $p < 0.05$). These 140 DEGs were significantly enriched for immune response, leukocyte activation, and chemokine pathways (all $p < 0.05$). The top 20 most enriched DEGs from AR face biopsies localized to CD8 T cell and NK cell clusters on scRNAseq. This strongly suggests that the immunopathogenesis of VCA rejection involves stimulation of CD8 T cells by allograft antigen, leading to cytotoxicity.
Conclusions: We demonstrate that the molecular mechanism of acute VCA rejection appears to be conserved across different patients and recipient anatomical sites. Antigen-activated T cells and NK cells mediate AR through production of cytokines and recruitment to graft tissue. Longitudinal sampling for RNA-seq will identify key genes driving the mechanism of VCA rejection and inform targeted therapies.

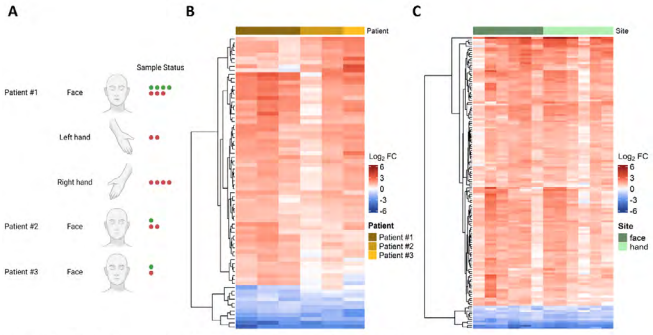

Figure 1. NanoString RNA-sequencing of VCA biopsies with corresponding DE analysis.

P554 STREAMLINING DONATION TRANSPLANTATION COMMUNICATION VIA HIPAA-COMPLIANT APP

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Background: Communication across the donation transplantation ecosystem is fractured and ineffectual, often necessitating the use of unsecured methods such as texting to accomplish time-sensitive tasks. A transplant software company developed a secure, HIPAA-compliant, and fully integrated app to facilitate timely communications across diverse interdependent donation organizations, including Organ Procurement Organizations (OPOs), transplant hospitals, tissue banks, laboratories, transportation providers, and more.
Methods: The app provides a secure method of chat communications across multiple organizations involved in a donor case, enabling coordination of OR times, transportation, and other time-sensitive issues. Uniquely and critically, the app enables secure sharing of key and real-time donor and case information directly from the host donation organization's EMR software within chat rooms. Host donation organizations can securely invite third-party organizations and users such as recovery and transplant partners to join their specific app domain and chat rooms. The app integrates GPS-location tracking and EMR data to allow for real-time visualization of staff locations in the field alongside current active referrals, enabling efficient dispatch of staff to referring organizations based on proximity. Additionally, the app desktop companion enables streamlined communications between call centers and mobile staff on site at hospitals.
Results: Since launch over 45,000 chat messages have been sent across the platform and numerous donation organizations have formally adopted the app. Across multiple organizations there are over 2,400 app users.
Conclusions: The app has the potential to centralize and streamline communications across the complex donation-transplant ecosystem. With key integration to the EMR software, the app has the capability to modernize workflows throughout the donation management process across numerous organizations.

P555 STREAMLINING TRANSPLANTATION VIA A COMPREHENSIVE AND SECURE DIGITAL TRANSPLANT MANAGEMENT PLATFORM

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Background: In the current fragmented transplantation ecosystem, costly inefficiencies exist as systems operate in silos without seamless sharing of key data. Outdated paper and manual processes lead to errors, compliance issues, time-intensive procedures, and patient safety concerns. The implementation of an integrated, real-time clinical workflow platform can alleviate workflow burdens.
Methods: A donation and transplant software company developed a comprehensive, modern, digital interoperative platform to manage the transplantation workflow, working in conjunction with a transplant hospital to design the system specifically curated to the needs of transplant centers. The platform is a modern web-based system which provides advanced patient tracking, data visualization, and communication tools and has the potential to securely interface with external systems such as Organ Procurement Organization's (OPO) software systems.
Results: The comprehensive secure donation platform streamlines the clinical workflow by providing: 1) access to the latest chart information across multiple staff; 2) real-time and retrospective data quality tools to flag potential errors; 3) reporting and compliance tools; and more.
Conclusions: Adoption of a comprehensive clinical workflow platform curated to the processes of transplant centers has the potential to streamline the transplantation workflow and enable increased compliance, patient safety, and transplants.

P557 TECHNICAL FEASIBILITY OF WHOLE-EYE VASCULAR COMPOSITE ALLOTRANSPLANTATION: A SYSTEMATIC REVIEW

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Background: There are over 43 million individuals in the world who are blind. As retinal ganglion cells are incapable of regeneration, treatment modalities for this condition are limited. Since first incepted in 1885, whole-eye transplantation (WET) has been proposed as the ultimate cure for blindness. As the field evolves, different aspects of the surgery have been individually explored, including allograft viability, retinal survival, and optic nerve regeneration. Due to the paucity in the WET literature, we aim to systematically review proposed WET surgical techniques to assess surgical feasibility. Additionally, we hope to identify barriers to future clinical application and potential ethical concerns that could be raised with surgery.
Methods: We conducted a systematic review of PubMed, Embase, Cochrane Library, and Scopus from inception to June 10, 2022, to identify articles pertaining to WET. Data collection included model organisms studied, surgical techniques utilized, and postoperative functional outcomes.
Results: Our results yielded 33 articles, including 14 mammalian and 19 cold-blooded models. In studies performing microvascular anastomosis in mammals, 96% of allografts survived after surgery. With nervous coaptation, 82.9% of retinas had positive electroretinogram signals after surgery, indicating functional retinal cells after transplantation. Results on optic nerve function were inconclusive. Ocular-motor functionality was rarely addressed.
Conclusion: Regarding allograft survival, WET appears feasible with no complications to the recipient recorded in previous literature. Functional restoration is potentially achievable with a demonstrated positive retinal survival in live models. Nevertheless, the potential of optic nerve regeneration remains undetermined.

Table 1. Mammalian Model Organisms - Surgical Techniques

First author (year of publication)	Model organism	Allograft structures	Number of eyes studied	Transplant location	Nerves coopted	Donor vessels	Recipient vessels
Bradford (1885)	human (living) / rabbit	Eye, CN II	1	eye orbit	CN II	N/R	N/R
May (1886)	rabbit	Eye, CN II	24	eye orbit	CN II	N/R	N/R
Koppanyi (1925)	mouse	Eye	25	eye orbit	N/A	N/R	N/R
Burns (1971)	human (living)	Eye, CN II, lateral rectus muscle	1	eye orbit	N/A	anterior ciliary artery	anterior ciliary artery
Freed (1980)	mouse	Eye	12	leg	N/A	N/R	N/R
Sher (1980)	rat/dog	Eye	25	cortical brain	N/A	ophthalmic artery (dog)	femoral artery (rat)
Sher (1981)	sheep	Eye, CN II, recti and oblique muscles	20	eye orbit	CN II, III	1) ciliary artery 2) internal ophthalmic arteries	1) ciliary artery 2) internal ophthalmic arteries
Shi (2009)	pig	Eye, CN II	20	neck	N/A	ophthalmic artery	carotid artery
Davidson (2016)	human (cadaver)	Eye, recti and oblique muscles, CN II, III, IV, VI	8	eye orbit	CN II, III, IV, VI	ophthalmic artery	superficial temporal or internal maxillary artery
Siemionow (2018)	human (cadaver)	Eye, recti and oblique muscles, bony orbit, skin ,CN II, CN III	5	N/A	CN II, III	1) facial artery and superficial temporal artery 2) ophthalmic artery	N/R
Zor (2019)	mouse	Eye, recti and oblique muscles, CN II, earlobe	5	neck	CN II (donor) greater auricular nerve (recipient)	common carotid artery	common carotid artery
Bravo (2020)	pig (cadaver)	1)Eye, bony orbit, earlobe 2) Eye, bony orbit 3) Eyes, bilateral bony orbit, frontal bone, ears	8	N/A	N/A	external carotid artery	external carotid artery (theoretical)
Badaro (2022)	rabbit	Eye, CN II	6	eye orbit	CN II	N/A	N/A
Komatsu (2022)	mouse	Eye, bony orbit, eyelid, auricle, CN II	7	eye orbit	CN II	carotid artery	carotid artery

N/A, not applicable; N/R: not recorded

P558 SAFETY AND UTILITY OF ADJUVANT AND CONCOMITANT PANNICULECTOMY IN RENAL TRANSPLANT CANDIDATES

Matteo Laspro[1], Thor Stead[1], Hilliard Brydges[1], Brooke Barrow[1], Ogechukwu Onuh[1], Bruce Gelb*[1], Ernest Chiu[1]

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Background: As the obesity crisis in the United States continues, different renal transplantation centres have loosened their BMI criteria necessary for surgery. With more individuals of larger body-habitus comorbid with End-Stage Renal Disease (ESRD) qualifying for renal transplantation, surgical modalities existing in other fields have migrated to serve this patient population. Panniculectomy has been successfully carried in ESRD patients prior to transplantation as an attempts to improve surgical field access and post-transplant outcomes.
Methods: In order to assess surgical outcomes of panniculectomy in the context of renal transplantation and ESRD, the authors performed a systematic review following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 Anticipating lack of primary studies, we also retrospectively collected data on patients with ESRD undergoing panniculectomy form the National Surgical Quality Improvement Program (NSQIP) to evaluate outcomes of body contouring in this patient population.
Results: From the systematic review, a total of 783 ESRD patients underwent panniculectomy among the studies identified. Of these, 91 patients underwent panniculectomy simultaneously to RT while 692 had their pannus resected prior to kidney transplant. The most common complication was hematoma followed by wound dehiscence. From the NSQIP analysis, 24,868 patients met the inclusion criteria for analysis. In the setting of renal transplant, patients with diabetes, hypertension requiring medication, and requiring dialysis were more likely to suffer postoperative complications (OR 1.31, 1.15, and 2.2, respectively). However, upon sub-analysis of specific types of complications, the only retained association was between diabetes and wound complication
Conclusion: Panniculectomy in ESRD patients appears to be safe and may improve transplant candidacy. Pannus resection is associated with good post-transplantation outcomes with good long-term graft survival. Panniculectomy prior to transplant appears to be safe without increased comorbidity in the ESRD population

Table 1. Multivariate analyses: Predicting complications in panniculectomy patients with ESRD

		Odds Ratio (OR)	95% Confidence Interval	p-value
Any Complication	Age*	1.017	[1.013, 1.02]	<0.0001
	BMI*	1.051	[1.048, 1.055]	<0.0001
	Female Sex*	0.84	[0.76, 0.92]	0.0003
	Diabetes*	1.31	[1.18, 1.45]	<0.0001
	Hypertension*	1.15	[1.06, 1.26]	0.0016
	ESRD/Dialysis*	2.2	[1.47, 3.3]	<0.0001
PE/DVT	Age*	1.022	[1.012, 1.033]	<0.0001
	BMI*	1.026	[1.015, 1.037]	<0.0001
	Female Sex	1.08	[0.77, 1.5]	0.6501
	Diabetes	1.19	[0.86, 1.65]	0.3042
	Hypertension	1.02	[0.77, 1.37]	0.8699
	ESRD/Dialysis	0.63	[0.09, 4.57]	0.65
Thrombotic Complication	Age*	1.031	[1.021, 1.041]	<0.0001
	BMI*	1.023	[1.013, 1.033]	<0.0001
	Female Sex	0.87	[0.66, 1.14]	0.3156
	Diabetes	1.26	[0.95, 1.67]	0.1153
	Hypertension	1.17	[0.9, 1.52]	0.2338
	ESRD/Dialysis	1.94	[0.7, 5.34]	0.2003
Wound Complication	Age	1.004	[0.999, 1.008]	0.101
	BMI*	1.052	[1.047, 1.056]	<0.0001
	Female Sex	1.04	[0.91, 1.18]	0.6023
	Diabetes*	1.26	[1.11, 1.44]	0.0005
	Hypertension	1.07	[0.95, 1.21]	0.2411
	ESRD/Dialysis	1.32	[0.74, 2.35]	0.3521

***Statistically Significant at α = 0.05**

P559 THE ROLE OF T-LYMPHOCYTES IN ACUTE REJECTION FOLLOWING VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

Nikhil Dave[1], Hilliard Brydges[1], Ogechukwu Onuh[1], Bachar Chaya[1], David Tran[1], Massimo Mangiola[1], Bruce Gelb*[1], Catherine Lu[1], Daniel Ceradini[1], Eduardo Rodriguez[1]

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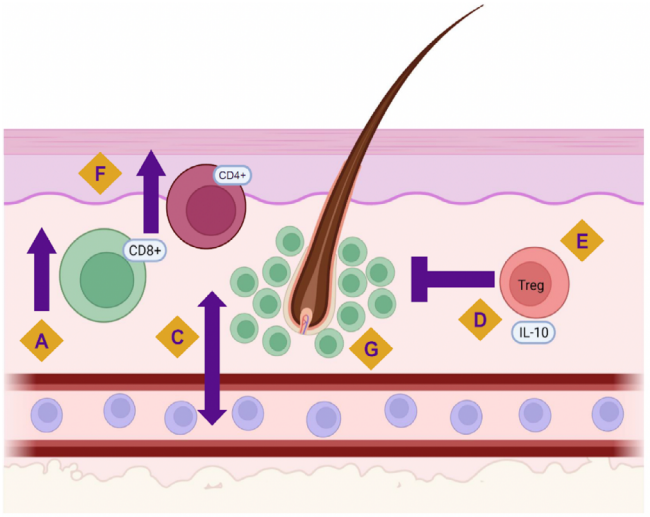
Background: The mechanisms behind acute rejection (AR) following vascularized composite allotransplantation (VCA) have yet to be clearly elucidated. The role of T-lymphocytes (T-cells) in AR has implications for patient care. This systematic review endeavors to uncover how T-cells contribute to AR in VCA.
Methods: Adhering to PRISMA guidelines, Pubmed, Embase, and Cochrane databases were reviewed. After screening, data regarding study design as well as commonalities and discordances of these studies were extracted, and consensus themes were derived.
Results: Twenty-one studies were included in the final analysis, Figure 1 highlights consensus themes among them. Overall, findings closely parallel the solid organ transplantation (SOT) literature, with notable exceptions. Similarly to SOT, a high graft infiltrate of CD8+ T-cells as well as pro-inflammatory cytokines (IL-2, TNF-α and, IFN-γ) were identified during AR. Distinct T-cell populations were found in blood and tissue compartments. Over time, the CD4+:CD8+ ratio in the graft increased, as did FoxP3 expression followed by increased T-regs and Il-10 (leading to downregulation of AR). Discordantly, within the allograft t-cells clustered surrounding pilosebaceous units during AR.
Conclusions: Elucidating the biomolecular mechanisms of AR in VCA is a requisite step for safely and effectively managing this ubiquitous, devastating complication. Like SOT, we found that T-cells play a crucial role in both instigating and halting AR in VCA, a balance that must be carefully weighed when designating management approaches. Further, unique aspects of AR in VCA, including interactions with hair follicles, warrant further exploration.

Figure 1. Consensus findings regarding the role of T lymphocytes in acute rejection following vascularized composite allotransplantation.



Label	Consensus Finding	Studies Citing Finding
A	High CD8+ graft infiltrate	11
B	Increased [IL-2], [TNF-α], [IFN-γ]	6
C	Compartment Specific T-cell Populations (tissue vs. blood)	4
D	T_{regs} downregulate acute rejection via IL-10	3
E	Increased expression of FoxP3 in allograft	3
F	CD4+ : CD8+ ratio increases over time	2
G	Donor and recipient T-cells cluster around vessels and pilosebaceous sites	2

P560 CHARACTERIZING B-LYMPHOCYTE MEDIATED REJECTION IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

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Background: Classically, rejection following vascularized composite allotransplantation (VCA) has been considered as a largely T-lymphocyte (T-cell) mediated process. However, the relative role of B-lymphocytes (B-cells) including and beyond their capacity for antibody production and antigen presentation remains to be determined. Recent clinical findings demonstrating improved immunologic outcomes in VCA patients treated with B-cell depleting induction therapy portends the true role of these cells may yet remain understated. To clarify this, a systematic review of clinical and experimental data regarding the role and mechanisms of B-cells in acute VCA rejection was conducted.
Methods: A systematic review of PubMed, Embase, and Cochrane databases was done adhering to PRISMA guidelines. Studies reporting primary data regarding the role and mechanisms of B-cells in VCA rejection were included. Study design along with concordances and discordances between included studies were extracted. Data were organized thematically and contextualized with findings from the solid organ transplant (SOT) literature.
Results: Nine total studies were included in the final analysis. Table 1 illustrates points of consensus between studies. Interestingly, the presence of B-cells within the allograft is a point of contention, with both evidence, demonstrating B-cell infiltration into the allograft and B-cell absence. The deposition of antibodies within allograft was also uncovered to have supporting evidence between studies. Anti-AT1R and anti-ETAR antibodies were correlated with rejection. Evidence also supports no difference in the presence of non-HLA or anti-donor antibodies between VCA and SOT or controls.
Conclusions: Uncovering the role of B-cells in acute rejection has implications for guiding the treatment of this destructive complication in patients. We found that current literature illustrates differing pictures regarding the presence of B-cells, their activity, and antibody-mediated responses.

Table 1. Consensus findings regarding B lymphocyte function in acute rejection following vascularized composite allotransplantation

Concordance and Discordance between Studies			
B-cell Presence in Allograft			
Points of Concensus between Studies	*Study*		*Evidence*
B-cells are present in the allograft.	Kaminska	2017 Observational	# of Bcells same between HTx and controls.
	Baran	2015 Observational	B cells infiltrate allograft (not native).
No B-cells present in allograft.	Hautz	2012 Observational	No B-cells at all time points.
	Hautz	2010 Observational	Bcells absent.
Presence of Antibody and Correlation with Rejection			
Points of Concensus between Studies	*Study*		*Evidence*
Anti-AT1R and Anti-ETAR antibodies correlated with rejection.	Sikorska	2022 Observational	Patient with Positive Result of AT1R-Ab and also ETAR-Ab had highest # of rejections.
	Banasik	2014 Observational	Anti-AT1R and Anti-ETAR elevated in VCA who experience rejection.
Deposition of anti-body in allograft.	Wu	2011 Experimental	IgG deposition present in hyperacutely rejected KTx, but not accelerated rejected VCTA
	Unadkat	2009 Experimental	Staining for tissue antibody deposition revealed patterns similar to complement deposition.
No difference in non-HLA or anti-donor antibodies between VCA and SOT or controls.	Sikorska	2022 Observational	There were no difference in the concentrations of non-HLA antibodies between patients after HTx (with episodes of acute and chronic rejection) and stable patients after KTx (without any features of rejection).
	Unadkat	2009 Experimental	No significant difference in the presence of antidonor antibodies between the 3 groups late after transplantation.

P561 MINIMALLY AND NON-INVASIVE REJECTION MONITORING MODALITIES IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

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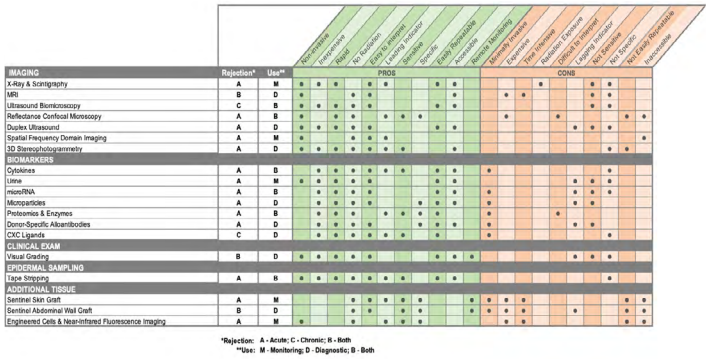
Objective: Rejection following Vascularized Composite Allotransplantation (VCA) is nearly ubiquitous with 85% of patients experiencing at least one episode. Current monitoring modalities aim to catch rejection before it occurs, but are highly invasive and compromise outcomes. We reviewed the most promising non- and minimally invasive techniques (NIMMs) for diagnosing and monitoring rejection in VCA.
Methods: A literature search of PubMed, Cochrane and Embase databases was conducted, yielding 28 studies that were included in the final analysis. Of these studies, 19 distinct NIMMs are described. NIMMs were grouped into five categories: Imaging, Biomarkers, Epidermal Sampling, Clinical Grading Scales, and Introduction of Additional Tissue.
Results: Imaging based NIMMs are among the most well studied. They are excellent at detecting vasculopathy, which is quite sensitive but not specific for rejection. There are several biomarkers such as MMP3 and cell-free DNA that have been shown to rise consistently before rejection episodes, which makes them extremely attractive for routine patient monitoring. Epidermal sampling is completely non-invasive and allows for accurate measurement of cytokine & enzyme levels implicated in rejection. Clinical grading scales are useful for grading rejection, but cannot preemptively identify it. Lastly, introducing additional tissue has been shown to preemptively identify rejection but must be weighed against the cost of additional trauma to the patient.
Conclusion: NIMMs have great potential to dramatically improve rejection rates in VCA, however standardization among VCA centers is needed to integrate them into the standard of care.



P563 DEVELOPMENT OF DECEASED ORGAN DONATION IN A MULTICULTURAL COUNTRY_ UAE ORGAN DONATION AND TRANSPLANT SYSTEM

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Background: 88.5% of the United Arab Emirates-UAE population is foreign with more than 200 nationalities. The country's unique multi-ethnic, multi-religious and multi-cultural characteristics present both a challenge and an opportunity to build a deceased organ donation for transplantation system that could not only impact the UAE but also the country of origin of its habitants. Organ transplantation from brain death donors (DBD) in the UAE began in 2017 when the UAE Ministry of Health and Prevention (MOHAP) approved the regulation on the brain death declaration. Identify the actions that have led to the development of the donation system in the UAE.
Methods: Three levels of deceased donation structure where established, the National Transplant Committee at MOHAP, the Emirates Organ and Tissue Centre (Acting as the Organ Procurement Organization) at the Department of Health of Abu Dhabi, and the hospital-based organ donation units within the major hospitals. Stakeholders' engagement, healthcare workers education on best practice in organ donation, and the application of the DBD quality key performance indicators were the foundations for the UAE donation and transplant system implementation. Education and meetings were facilitated in collaboration with a team of international subject matter experts.
Results: The UAE DBD grows from 0.91 dpmp in 2020 to 5.4 dpmp in 2022. 41% increase in UAE dpmp rates was observed in 2022 compare to 2021. The 130 DBDs achieved up to to date have benefit 457 transplant recipients. The UAE organ donation and transplantation program has been helping patients from 48 different nationalities.
Conclusions: Although the leading practices in organ donation are known worldwide, the challenge remains in their adjustment and adoption according to the healthcare system, the cultural, political, and geographical local reality. The UAE's collaborative approach to establishing of both OPOs and hospital-based organ donation units has proven to be a key element in developing deceased organ donation in the UAE.

P565 OUTCOMES OF KIDNEY TRANSPLANTATIONS FROM DECEASED DONORS WITH ANURIC/OLIGURIC ACUTE KIDNEY INJURY

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Background: In an era of organ shortage, kidney transplantations (KT) from deceased donors with acute kidney injury(AKI) has been increasing with favorable outcomes in the literature. Nevertheless, the discard rate of donor kidneys with AKI remains high due to fear of a persistent impairment of kidney function. Amount of urine output is an important donor factor to predict outcomes after KT. However, outcomes of KT from anuric or oliguric deceased donors have been rarely reported. Herein, this single center study purposed to evaluate the clinical outcomes from anuric/oliguric donors.
Methods: We retrospectively analyzed the medical records of 136 recipients who underwent KT from in-house deceased donors between 2010 and 2020 at Korea University Anam Hospital. A total of 68 recipients and 16 recipients underwent KT from donors without AKI and with anuric/oliguric AKI, respectively.
Results: Last hourly urine output of donors without AKI was 181.0 ± 123.8 ml and of donors with anuria/oliguric AKI was 6.1 ± 6.1ml (P < 0.001). Donors' initial and last Cr was higher in anuria/oliguria group (2.1 ± 0.5 vs. 1.7 ± 0.9; P = 0.021, 1.1 ± 0.5 vs. 3.4 ± 1.9; P < 0.001). The incidence of delayed graft function (DGF) was significantly higher in anuria/oliguria group than in non-AKI group (5 (31.2%) vs 2(2.9%); P = 0.002). There was no significant difference in the incidence of biopsy-confirmed rejection. Serum Cr and estimated glomerular filtration rate of postoperative 1 month were statistical differences between two groups. However, there was no significant difference in graft functions after 6 months.
Conclusion: KT from donors with anuric/oliguric AKI showed comparable outcomes to KT from non-AKI donors despite a higher incidence of DGF. Thus, donors with AKI need to be considered more actively to expand donor pool, even in case of anuria or oliguria.

Table 1. Graft outcomes

	Non-AKI (n = 68)	Anuric/Oliguric AKI (n = 16)	P-value
DGF, n (%)	2 (2.9)	5 (31.2)	0.002
Biopsy-proven acute rejection, n (%)	24 (35.3)	7 (43.8)	0.732
Serum Creatinine (mg/dl), mean ± SD			
1 month after KT	1.4 ± 0.6	2.4 ± 1.6	0.021
6 months	1.6 ± 0.6	2.0 ± 1.5	0.290
1 year	1.4 ± 0.8	1.6 ± 1.0	0.714
2 years	1.6 ± 1.4	1.3 ± 0.2	0.123
eGRF (ml/min), mean ± SD			
1 month after KT	48.2 ± 18.9	31.2 ± 22.2	0.022
6 months	44.9 ± 17.4	40.1 ± 17.2	0.324
1 year	49.0 ± 19.3	50.5 ± 14.1	0.748
2 years	50.7 ± 19.6	55.1 ± 17.7	0.489

P566 THE PREDICTIVE VALUE OF AORTOILIAC CALCIFICATION OF DECEASED DONORS FOR CHRONICITY SCORE OF BIOPSIES AND GRAFT OUTCOMES IN KIDNEY TRANSPLANTATION

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Background: The quality of the deceased donor (DD)'s kidney is closed related to graft survival after kidney transplantation (KT). Vascular calcification is a highly associated with inferior patients and graft outcomes in KT This study aimed to evaluate the predictability of vascular calcification in DDs as determined by a computer tomography (CT) scan-based calcification scoring system and its correlation with kidney biopsy scoring and graft outcomes.
Methods: A review of the patients' database at Korea University Anam Hospital revealed that a total of 147 brain-death donors underwent organ procurements between 2010 and 2020. Of these patients, 52 donors were included with available pre-transplant CT scan and time-zero biopsy(TZB). The aorto-iliac calcification score was assigned as the sum of calcification scores at the infrarenal aorta and the common iliac arteries. A calcification score ≥3 was regarded as moderate-to-severe (MTS) group and <3 as a non-to-mild (NTM) group. Chronicity score were reviewed based on Banff and Remuzzi scoring systems by a single pathologist. The calcification score, chronicity score of TZB, and baseline characteristics were collected and correlated with graft outcomes.
Results: In 52 patients NTM was 30 (57.7%) and MTS was 22 (42.3%). The mean age of MTS group was higher (49.7 ± 12.8 vs. 58.2 ± 5.2; P=0.002). Diabetes mellitus(DM) were higher in MTS group (3 (10%) vs. 11 (50%); P=0.004). MTS showed a higher KDPI score (59.4 ± 25.1 vs. 79.0 ± 15.2; p=0.001). In TZB grading, there were statistical differences in IF and TA score (14 (46.7%) vs. 18 (81.8%); P=0.022). There were no statistical differences in delayed graft function and biopsy-proven acute rejection (4 (13.3%) vs. 3 (13.6%); P=1.000, 10 (33.3%) vs. 7 (31.8%); P=1.000). Serum creatinine and estimated glomerular filtration rate of postoperative 1 year, 2 years and 3 years were no statistical differences.
Conclusions: Aortoiliac calcification of DDs is associated with donors' aging, DM and KDPI, which has been proven as a predictor of renal function after KT. It is also correlated with IF/TA of allograft baseline biopsies. Short-term graft outcomes according to the degree of calcification were not statistically significant, but considering the associated factors, it is thought to be related long-term outcomes after KT.

P567 SUCCESSFUL LUNG TRANSPLANTATION FROM HEPATITIS C VIREMIC DONORS IN CRITICALLY ILL RECIPIENTS

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Background: Hepatitis C viremic (HCV+) donors were previously an untapped pool. Recently, with the advent of direct acting antivirals (DAA) with a >95% cure rate, the interest in HCV+ donors has increased. However, published studies have been limited to successful outcomes in candidates with lower lung allocation score (LAS). Here, we report our early experience with lung transplantation (LTx) from HCV+ donors in critically ill candidates with high LAS, defined as LAS >50, who are at high risk of waitlist mortality.
Methods: This single institution prospective study reports our experience with HCV+ donors in the period between January 2022 to December 2022. The sustained virologic response (SVR) was measured at 4 weeks and 12 weeks following an eight-week course of DAA treatment. In addition to recipient demographics, we examined postoperative course, rejection episodes, and SVR at 4 and 12 weeks.
Results: During the study period, 4 out of 77 (5%) lung transplants were performed from HCV+ donors. All 4 were double lung transplant (DLTx) in male recipients (Table 1). All four were inpatient prior to transplant with LAS ranging from 50.59 to 94.26, with one patient requiring preoperative veno-arterial extracorporeal membrane oxygenation support as a bridge to transplant. All 4 started DAA treatment within 2-6 days following DLTx. They were successfully discharged from the hospital to home without oxygen. Following completion of the 8-week course of DAA therapy, three have SVR at 4 weeks (1 pending result) and 2 at 12 weeks (2 pending results). There were no rejection episodes.
Conclusions: Our results show a 5% increase in donor pool by successful utilization of hepatitis C viremic donors at our institution during the study period. Furthermore, our preliminary short-term outcomes support the use of HCV+ donors in the critically ill cohort with high LAS. Expanding the donor criteria to include HCV+ donors holds promise to reduce waitlist mortality.

Table 1. Recipient Demographics and Pre- and Post-Operative Course

Patient	Age (yrs)	Gender	LAS at LTx	Pre-LTx Hospital Status	Post-LTx LOS (days)	DAA Duration	DAA Start within 6 days of LTx	HCV RNA Peak (IU/mL)	SVR4	SVR12	Rejection 1 month Post-LTx
1	45	M	94.26	Inpatient	34	8 weeks	YES	-	Yes	Yes	A0B0
2	68	M	64.15	Inpatient	18	8 weeks	YES	50,243	Yes	Yes	A0B0
3	61	M	73.71	Inpatient	14	8 weeks	YES	776,800	Pending	Pending	A0B0
4	59	M	50.59	Inpatient	54	8 weeks	YES	34	Yes	Pending	A0B0

LTx: Lung Transplantation, LAS: Lung Allocation Score, LOS: Length of Stay, DAA: Direct-acting Antiviral, SVR: Sustained Virologic Response (at 4 weeks and 12 weeks following completion of DAA)

P568 PURE RETROPERITONEOSCOPIC LIVING DONOR NEPHRECTOMY- A SINGLE CENTRE EXPERIENCE

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Background: Minimally invasive approach for donor nephrectomy helps in the early recovery of the donors with less pain, less morbidity and early return to work. Pure retroperitoneoscopic technique for donor nephrectomy is less practiced across the transplant centres in the world although it has an added advantage of early hilar identification and avoidance of peritoneal transgression.Here we share our experience with the same technique.
Methods: Retrospective data of forty two voluntary kidney donors who underwent pure retroperitoneoscopic donor nephrectomy between may 2020 to September 2022 were analysed
Results: Thirty two were female while 10 were male donors.Mean age of the donors was 47.21years (SD 9.96). Mean BMI was 23.43(SD 2.19).Mean WIT was 217.26 seconds (SD115.82). Mean operative time was 185.6 minutes (SD 36.24). In 3 cases right retroperitoneoscopic Donor nephrectomy was performed where the renal vein was controlled with endo TA (Auto Suture, US Surgical, Norwalk, CT, USA)stapler. Eleven retrieved kidneys had double renal artery and 3 cases had left retroaortic renal vein.No major or minor complications were observed. Mean hospital stay was 2.9 days(SD 1.04). All the recipients showed a declining trend of serum creatinine which reached normal levels within 72 hours.
Conclusions: Pure Retroperitoneoscopic donor nephrectomy is a safe procedure with negligible complications and early discharge from hospital with good recipient outcome. The technique should be propagated across the transplant centres in the world.

P569 UROLOGIC COMPLICATIONS IN OUR ORGAN TRANSPLANT UNIT AFFECTING RECIPIENTS FROM BRAID DEAD DONORS DURING THE LAST DECADE

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Background: Urologic complications remain the most common problem following renal transplant with a reported incidence in the range of 2.5 and 30%. Major urologic complications involve ureter obstruction, urine leak and vesicoureteral reflux (VUR) and they are associated with high readmission rates and decreased graft survival time. We aimed to study the rates and types of urologic complications in our kidney transplant unit during the last decade.
Methods: We retrospectively identified 225 kidney transplant recipients from brain dead donors from January 2013 to December 2022. All ureteroneocystostomies were performed under the care of the same lead surgeon using the Lich-Gregoir technique. PJ stent was placed intraoperatively and removed routinely 30 days post op. A negative pressure Blake drain was left in situ. Graft ultrasound doppler and 99mTc-EC dynamic renal scan were performed routinely to identify evidence of acute kidney injury or rejection on day 1 and day 7 respectively. We attempted to associate our complications with the following factors: sex, age, viral status, and donor characteristics.
Results: In a total of 225 recipients, we identified 17 (7.6%) with urologic complications. These would involve: 4 anastomotic stenosis (23.5%), 7 ischemic ureter stenosis (41.2%) 2 ureter kinking (12%) and 4 anastomotic leaks (23.5%). 11 complications (64.7%) involved the distal ureter. The majority of the patients presented with deterioration of graft function and urosepsis. In 16 cases (94.1%) percutaneous nephrostomy under U/S guidance was performed and this was followed from JJ stent placement in 7 (43.75%) of them. 9 out of these 17 recipients (52.3%))required surgical treatment. & underwent redo of their anastomosis, 1 required psoas hitch and 1 Boari-flap procedures. 2 of them died of sepsis (11.76%) and 2 of them died later during their follow up from unrelated causes.
Conclusions: Despite the fact that renal transplant is the best therapeutic option for end stage renal disease , urologic complications and ureteroneocystostomy related complications in particular remain the Achilles' heel of the procedure leading to major complications and prolonging hospital stay for renal transplant patients.

P570 BUBBLE AND INTERMITTENT SURFACE OXYGENATION ARE AN EFFECTIVE ALTERNATIVE FOR MEMBRANE-OXYGENATED HMP-KIDNEYS TO MAINTAIN AEROBIC METABOLISM

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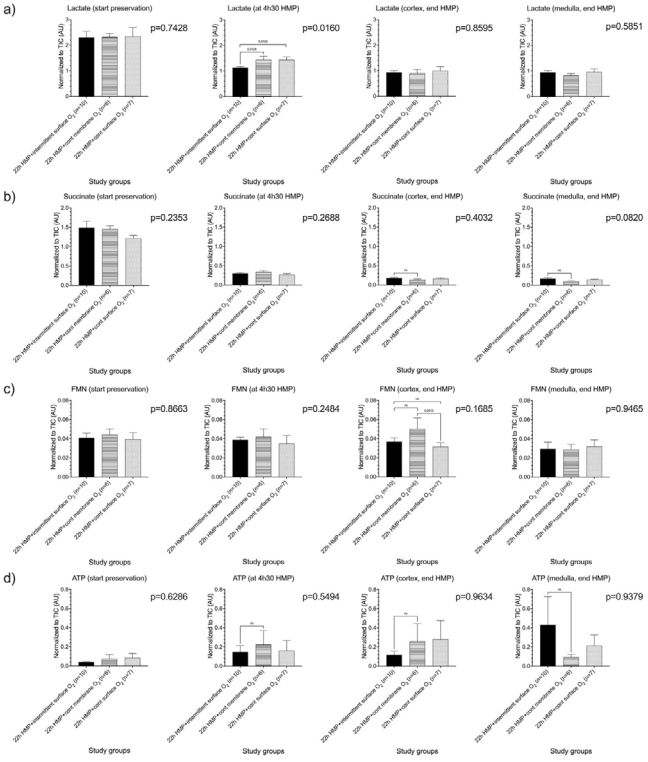
Background: Since 2022, brief bubble and subsequent surface oxygenation are an alternative oxygenation technique for membrane-oxygenated kidneys during hypothermic machine perfusion (HMP) in clinical practice. The aim of this study was to evaluate the metabolic effect at the end of the preservation period of the interruption of surface oxygenation (O_2) for 4 hours (mimicking organ transport) during HMP as compared to continuous surface and membrane oxygenation in a pig kidney ex vivo preservation model.
Methods: A kidney of a ±40 kg pig was exposed to 30 minutes of warm ischemia and preserved according to one of the following study groups: 1) 22h HMP+intermittent surface O_2 (n=12), 2) 22h HMP+continuous membrane O_2 (n=6), and 3) 22h HMP+continuous surface O_2 (n=7). Brief O_2 uploading of the perfusion fluid before kidney perfusion was obtained either by a hollow fiber membrane oxygenator (study group 2) or by direct bubble oxygenation (study group 1 and 3).
Results: O_2 uploading of the perfusion fluid by minimum 15 minutes of direct bubble oxygenation was as efficient as membrane oxygenation to achieve pO_2 levels above 450-500 mmHg (at 4°C) before connecting the kidney to the perfusion device. Metabolic tissue analysis (i.e., lactate, succinate, glutamate, ATP, NADH and Flavin Mononucleotide (FMN)) by mass spectrometry (Figure 1) and ^{1}H-NMR (i.e., glutamate, glucose, lactate, and succinate) and perfusion analysis by ^{1}H-NMR demonstrated a similar mitochondrial protection/preservation in all study groups after 270 minutes and at 22 hours of HMP. Perfusate FMN levels measured by spectrometry were significantly higher at the end of the preservation period in the membrane-oxygenated groups as compared by both surface-oxygenated HMP groups but comparable after 270 minutes of preservation.
Conclusions: Brief bubble and intermittent surface oxygenation of the perfusate during standard HMP at procurement site might be an effective and less expensive preservation strategy to protect mitochondria when compared with membrane-oxygenated kidneys eliminating the need for a membrane oxygenator and oxygen source during transport.

Figure 1.



P571 COMPARATIVE STUDY OF PATHOGENS AFFECTING OUR KIDNEY TRANSPLANT UNIT FOLLOWING CHANGE IN ANTIBIOTIC PROPHYLAXIS PROTOCOL DURING THE PERIOD 2010-2022

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Background: Transplanted patients are more susceptible to infections. Thus, it is important that we study the pathogens responsible and prevent the course of the disease. Following a review of the most common pathogens in our Organ Transplant Unit we adjusted our antibiotic prophylaxis protocols in 2018. Our aim is to discuss the primary results of this action.
Methods: Kidney transplant recipients who presented with at least one episode of urine infection or bacteremia during the first 30 post-transplant days between 2010 and 2022 were included in this study. The patients were divided into two large groups, based on the antibiotic prophylaxis protocol used. Group A includes kidney transplant recipients from 2010 to 2017, whereas Group B includes recipients from 2018 to 2022. Group A was given cefuroxime for 7 days and ciprofloxacin for 30 days, while Group B was given one dose of vancomycin pre op and meropenem pre op and till post-transplant day 3. We analyzed the pathogens cultured during episodes of urine infection and/or bacteremia for the first 30 post-transplant days. We also analyzed the hospital stay and the effects on graft function for the same period.
Results: Group A with 163 patients had a total of 181 episodes of urine infection and 28 episodes of bacteremia. Most common pathogens in the urine had been E. faecium (36%), E. coli (25%), E. faecalis (20%), Kl. pneumoniae (11%) and Ps. aeruginosa (7%). Blood infections had been caused by E. coli (28%), Kl. pneumoniae (25%), E. faecalis (17%), Ps. aeruginosa (14%), A. baumannii (7%) and Staph. epidermidis (7%). Group B with 84 patients had a total of 173 episodes of urine infection and 43 episodes of bacteremia. Most common pathogens in the urine were: E. coli (25%), Kl.pneumoniae (19%), Pr. mirabilis (8%), E. faecalis (1%), Ps. aeruginosa (1%). Blood infection pathogens: E. faecalis (11%), Kl. pneumoniae (11%), E. coli (11%), Staph. epidermidis (4%) and A. baumannii (4%).
Conclusions: Change in the antibiotic prophylaxis protocol in our unit resulted in a change of the most common pathogens seemingly diminishing enterococcus related and VRE infections. The flora change was associated with less in hospital stay and no major difference in graft function for the first post op period.

P572 THROMBOTIC MICROANGIOPATHY AND EARLY HUMORAL REJECTION AFTER ABO INCOMPATIBLE KIDNEY TRANSPLANTATION: A FRENCH MULTI-CENTER CASE-CONTROL STUDY

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Background: Although long-term graft survival is comparable to that of ABO-compatible renal transplantation, the risk of humoral rejection following ABO incompatible (ABOi) transplantation is greater and can occur as an early thrombotic microangiopathy (TMA) after kidney transplantation.
Methods: A multicenter study, including all patients who presented a TMA (histological and/or biological) after an ABOi transplantation (< 1 month), compared to matched controls who had a favourable initial course with a normal biopsy.
Results: Between 2013 and 2022, 375 ABOi kidney transplants were performed and 23 patients (6.1%) developed TMA (median: 1 day; IQR: 0-3). Eleven patients (47.8%) were on dialysis. Twenty-one patients (91.3%) had biological TMA. Among 21 early graft biopsies, histological evidence of active MAT was found in 17 cases (80.9%). All patients received treatment: 20 at least one session of plasmapheresis; 19 at least one injection of Eculizumab. Seven early graft losses (30.4%) occurred (median: 7 days; IQR: 3-16). In the control group (n=39), graft survival at 1 year was significantly higher (100% vs 69%, p < 0.0001). IgG and IgM isoagglutinin levels (peak and last pre-graft assay) were significantly higher in the TMA group (peak: p=0.01 for IgG and p=0.0006 for IgM; last assay before KT: p< 0.0001 for IgG and p=0.0003 for IgM). A level ≥ 1/8 for IgG and ≥ 1/4 or IgM before transplantation was predictive of the occurrence of TMA with a sensitivity and specificity of 71.4% and 71.8% for IgG (AUC= 0.782; p=0.0003), and 80% and 67.7% for IgM (AUC=0.796; p= 0.001). No other predictive factors were found.
Conclusions: TMA after ABOi transplantation is a rare phenomenon but associated with a poor prognosis. Isoagglutinin titer performed by hemagglutination is an imperfect marker of the occurrence of such a phenomenon.

P573 CLINICAL RELEVANCE OF THE LIVING KIDNEY DONOR PROFILE INDEX IN ASIAN KIDNEY TRANSPLANT RECIPIENTS

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Background: The Living Kidney Donor Profile Index (LKDPI) was developed in the United States to predict graft outcomes based on donor characteristics. However, there are significant differences in donor demographics, access to transplantation, proportion of ABO incompatibility, and posttransplant mortality in Asian countries compared with the United States.
Methods: We evaluated the clinical relevance of the LKDPI score in an Asian kidney transplant cohort by analyzing 1,860 patients who underwent kidney transplantation between 2000 and 2019. Patients were divided into three groups according to their LKDPI score: <0, 1–19.9, and ≥20.
Results: During a median follow-up of 119 months, 232 recipients (12.5%) experienced death-censored graft loss, and 98 recipients (5.3%) died. High LKDPI scores were significantly associated with increased risk of death-censored graft loss independent of recipient characteristics (LKDPI 1–19.9: HR 1.389, 95% CI 1.036–1.863; LKDPI ≥20: HR 2.121, 95% CI 1.50–2.998) as well as increased risk of biopsy-proven acute rejection and impaired graft renal function. By contrast, overall patient survival rates were comparable among the LKDPI groups.
Conclusions: High LKDPI scores were associated with an increased risk of death-censored graft loss, biopsy-proven acute rejection, and impaired graft renal function among the Asian kidney transplant cohorts.

P574 SOTROVIMAB AS PRE-EXPOSITION PROPHYLAXIS IN KIDNEY TRANSPLANT RECIPIENTS: NEUTRALIZATION OF OMICRON BA.1 AND BA.2 VARIANTS

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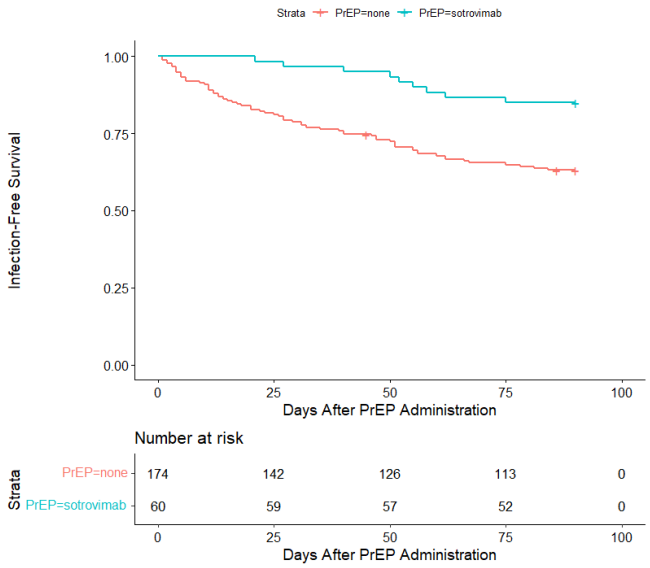
Background: Pre-exposition prophylaxis (PrEP) with monoclonal antibodies (mab) is used to prevent coronavirus disease 2019 (COVID-19) in high-risk individuals. However, a significant reduction of the in-vitro neutralization capacity against the Omicron BA.1 variant (B1.1.529) was observed for most mabs. Sotrovimab (Xevudy, VIR Biotechnology GlaxoSmithKline) retained substantial in-vitro neutralization capacity against BA.1, and a half-life of 48.8 days made it a candidate for off-label use as PrEP in high-risk individuals.
Methods: We enrolled 60 kidney transplant recipients (KTR) receiving PrEP through a compassionate use indication for sotrovimab between January 4 and February 28, 2022 into a prospective cohort study. Patients received 500mg of sotrovimab intravenously and were followed at our outpatient clinic. The rate of breakthrough infections was compared to a cohort of vaccine non-responder not receiving PrEP (i.e. < 264 BAU/mL). Serum was collected at four and eight weeks after antibody infusion. Variant-specific live virus neutralization tests (NTs) were performed with BA.1 and BA.2 variants.
Results: Over a 90-day follow-up period, 15% of patients receiving sotrovimab tested positive for SARS-CoV-2 compared to 37% of patients in the control group (Figure 1, log-rank test: p=0.001). All individuals neutralized BA.1 at four weeks follow up (FU) and all but one individual retained neutralization capacity against BA.1 at eight weeks. In contrast, neutralizing capacity against BA.2 in serum was only present in 60% at four weeks and further decreased to 15% at eight weeks FU.
Conclusions: PrEP with sotrovimab significantly reduced the rate of SARS-CoV-2 infection during the BA.1 wave in Austria. Activity against BA.1 was retained for eight weeks while activity against the BA.2 variant was already limited at four weeks after infusion. Our data show that sotrovimab can be used as PrEP for up to eight weeks depending on in-vitro activity against the dominant SARS-CoV-2 subvariant.

Figure 1: Kaplan-Meier curve of SARS-CoV-2 infection-free survival in KTR who received PrEP with sotrovimab and KTR who did not have protective SARS-CoV-2 humoral immunity and did not receive any form of PrEP



P577 SPLIT RENAL FUNCTION, RENAL VASCULAR VARIATIONS AND DONOR PREFERENCES: CHALLENGE AND CROSSROADS TOWARDS RIGHT KIDNEY CHOICE

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Background: Renal vascular variations, split renal function (SRF) and potential donor's preferences interplay on the donation decisions in living donor kidney transplantation (LDKT). This study aimed to assess the challenges in decisions for choosing the proper kidney for donation.
Methods: Retrospective study was performed through a review of the medical history charts and national electronic database of LDKT from 2013 – 2022, in one transplantation center. Those with significant missing data, were excluded from the final analysis. Demographic characteristics, CT angiographic findings and Tc-99m DTPA renal scan for SRF and donor preferences were analysed. The bilateral presence and number of accessory renal arteries, their hilar or polar position in respect of the renal artery, early artery branching, variations of the veins number and left vein course were assessed. Significantly different SRF was defined as ≥10%.
Results: Out of 137 consecutive LDKT, 124 donors were included in the study. The mean age of donors was 59.00 ±11 years, 40 (32%) were male and 14 (11%) were unrelated. There were no variations in 88(64%) renal arteries on the right and 69(56%) on the left. The most common variation on both sides was an accessory hilar artery in both sides in 15%. An accessory inferior renal polar artery was observed in 15% and superior in 13% of patients. Three renal arteries or three veins on one side were observed in one patient. Variation of renal arteries on both sides was 13(10%). Early artery branching was found in 25% (8%-right and 18%-left side). Two renal veins were observed in 8(6%). The Nutcracker phenomenon was found in 6(4.8%). From the donated kidneys in 60% it was the left one and 10% were with vascular variation. In 33 (27%) of donor kidneys we found at least one vascular variation. In 41 (33%) of donors SRF was significantly different and 8 (18%) of those donated the better kidney because of donors preference.
Conclusions: Variations in renal vascular anatomy and different SRF are very often in kidney donors. Donors preferences additionally interfere the transplantation process. The quality of the decision process relies on good institutional policy and adequate pretransplant donor evaluation.

P578 NOVEL PROGNOSTIC MARKERS FOR LIVER CIRRHOSIS IN PATIENTS ON THE ROMANIAN WAITING LIST FOR LIVER TRANSPLANT

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Background: Chronic liver disease is a global public health problem, cirrhosis being on the top of the causes of mortality in Romania. Models that predict individual risk of disease complications are becoming more common in hepatology. The aim of our study was to assess already known and novel prognostic markers for patients with liver cirrhosis awaiting liver transplant (LT).
Methods: We analysed the following prognostic factors: Model of End-stage Liver Disease (MELD), MELD Na, MELD 3.0, albumin-bilirubin score (ALBI), occurrence of acute-on-chronic liver failure (ACLF) from grade 1 to 3, occurrence of liver cirrhosis complications, infections, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio, platelet-to-lymphocyte ratio in 108 patients included on the waiting list (WL) for LT in the last 5 years. Univariate and multivariate Cox proportional hazards model was used to identify prognostic markers.
Results: There were 64.81% males, with a median age of 55 ± 11.35 years. The most frequent aetiology of the liver disease was B + delta hepatitis viral infection in 36.11%, followed by alcoholic aetiology in 35.18% of cases. 30.55% of patients had associated hepatocellular carcinoma. The median waiting time for all patients was 270 ± 659.5 days. During the follow-up on the WL, 26.85% of patients had various infectious complications and 25% developed ACLF grade 1 to 3. LT was performed in 71.29% of cases, and 22.22% patients died during follow-up. Univariate analysis demonstrated that the following factors were associated with mortality on the WL: occurrence of ACLF episodes during follow-up (p<0.0001), refractory ascites (p=0.032), acute kidney injury (p=0.0013), hepatic encephalopathy (p=0.0257), infectious complications (p=0.0007), a higher MELD score (p=0.0137), MELD Na (p=0.0018) and MELD 3.0 score (p=0.0028) and a higher NLR (p=0.033). Multivariate Cox regression analysis identified the following independent prognostic factors: presence of ACLF during follow-up (p=0.021) and a higher NLR score (p=0.036).
Conclusions: Acute-on-chronic liver failure and neutrophil-to-lymphocyte ratio are significant prognostic markers on the WL for LT that should be included in the graft allocation system.

P580 RECOMBINANT SARS-COV-2-ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS WITHOUT NEUTRALIZING ANTIBODIES FOLLOWING FULL VACCINATION (RESCUE-TX)

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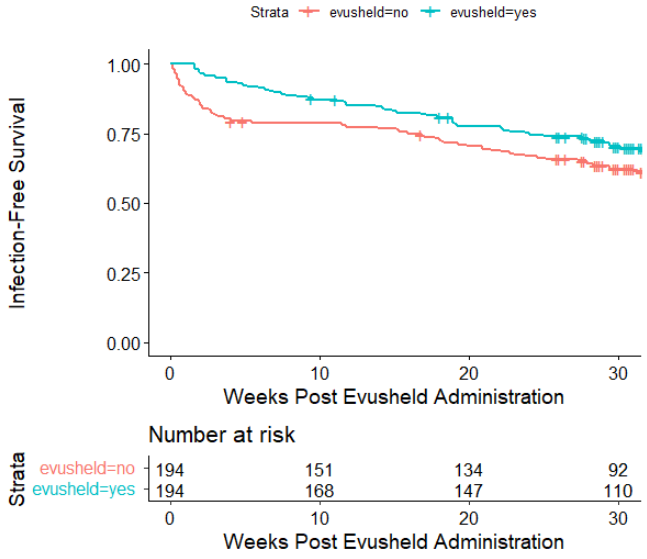
Background: Pre-exposition prophylaxis (PrEP) with monoclonal antibodies (mab) is used to prevent coronavirus disease 2019 (COVID-19) in high-risk individuals. Currently, cilgavimab/tixagevimab (Evusheld) remains the only mab combination approved for PrEP.
Methods: We started the RESCUE-TX trial in kidney transplant recipients (KTR) not responding to at least two doses of SARS-CoV-2 vaccine. A total of n=194 patients received 300 mg of cilgavimab/tixagevimab (i.m.) between March 4 and May 3, 2022. Patients are followed at our outpatient department at 2, 4, 8, 12, 24 and 48 weeks after dosing. Serum is stored for drug level quantification (PPD diagnostics; primary endpoint) and SARS-CoV-2 neutralization testing (secondary endpoint). Additional secondary outcomes include the rate of breakthrough infections compared to a cohort of vaccine non-responder not receiving PrEP (i.e. < 264 BAU/mL). Vaccine non-responders were best possibly matched for time since transplantation.
Results: Until end of September, 2022 (~31-week observation period), 58 patients receiving cilgavimab/tixagevimab tested positive for SARS-CoV-2 compared to 74 in the control group (infection rate 30% vs 38% for cilgavimab/tixagevimab and controls, respectively; log-rank test: p=0.04). The geometric mean of peek serum levels of cilgavimab and tixagevimab observed at 2 weeks after PrEP was 16 µg/mL and 17 µg/mL, respectively. Concentrations of both mabs declined in the following weeks and reached 9 µg/mL at 12 weeks after PrEP. SARS-CoV-2 Omicron BA.2 and BA.5 neutralization tests (NT) in sera from a subgroup of 30 patients confirmed strong activity against BA.2 for 12 weeks after PrEP but was low at week 24. BA.5 neutralization activity in patient sera was severely reduced at all timepoints and at week 24 only 20% of patients showed protective NT titers.
Conclusions: PrEP with cilgavimab/tixagevimab significantly reduced the rate of SARS-CoV-2 infection during the BA.2 wave in Austria. In line, neutralization activity against BA.2 was strong in most KTRs for up to 12 weeks but significantly reduced against BA.5 across all time points.

Figure 1: SARS-CoV-2 infection free survival in vaccine non-responders with and without PrEP with Evusheld.



P582 MORTALITY OF THE CIRRHOTIC PATIENTS ON THE LIVER TRANSPLANT WAITING LIST DURING THE COVID-19 PANDEMIC

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Background: Cirrhotic patients on the liver transplant waiting list may be at increased risk of severe acute respiratory syndrome and death from COVID19. Likewise, there is also a risk when transplanting a patient during the pandemic. The aim of this study was to determine the incidence of COVID-19 infection in patients on the liver transplant waiting list during the pandemic in a small-volume liver transplantation center in Romania, and to compare the mortality from COVID-19 in patients on the waiting list versus transplant patients, and the effect of vaccination on mortality.
Methods: In this study were included all the cirrhotic patients from the liver transplant waiting list. For the analysis of the impact of vaccination, it was considered vaccinated if the patient received at least 2 doses.
Results: During the study period we analyzed 125 recipients on the liver transplant waiting list. Fifty-seven patients were confirmed with COVID-19. The mortality rate was 24.5% (14 patients). There were also 29 patients with liver transplant followed-up during this period. Twenty-two (75.8%) patients developed COVID-19 infection, most of them mild and moderated forms. None of these patients died during follow-up. The vaccination rate was 39.2% in the liver transplantation waiting list and 93.1% in patients with liver transplant. In the multivariate analysis, the probability of death in liver transplant waiting list patients and COVID-19 infection was associated with age over 55 years (OR=1.63, 95% CI 1.301-1.822, p=0.025), admission to intensive care (OR=2.81, 95% CI 2.101-4.227, p=0.015), and mechanical ventilation requirement (OR=16.7, 95% CI 9.322-36.303, p=0.002). Vaccination was a protective factor against mortality (OR=0.06, 95% CI 0.031-0.058, p<0.001).
Conclusions: A high mortality of COVID-19 was observed in recipients on the waiting list for liver transplant compared to liver transplant patients, and COVID-19 vaccination was efficient in preventing severe forms of COVID-19 infection.

P583 PRETRANSPLANT EVALUATION OF LIVING KIDNEY DONORS AND RECIPIENTS: FROM THEPERSPECTIVE OF THE TRANSPLANT COORDINATORS

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Background: Low organ donation rates in Greece inevitably result in high waiting time for a kidney transplantation from a deceased donor. For Greek patients undergoing dialysis, a potential living donor is often the only hope. The aim of this study is to present the pairs of potential living donors and recipients evaluated at our center during a three-year period, 2020-2022, and recorded by transplant coordinators.
Methods: We retrospectively evaluated all potential pairs of living donors and recipients referred to our transplant center during 2020-2022. This is an ongoing study, as the pairs presented during the last semester of 2022 will hopefully be transplanted in due course.
Results: 300 potential pairs of living donors and recipients were recorded. Mean age of the potential recipients was 45 years (range: 11-75). 99 potential recipients (29.6%) were referred for preemptive transplantation, whereas the remaining 211 (70.4%) were already on dialysis. The proportion of preemptive potential recipients showed significant increase in the last two years. 33 potential recipients (11%) were pediatric. The mean age of the potential living donors was 58.14 years (range: 21-85). The distribution of potential donors regarding relation to the recipient was as follows: parents 49%, spouses 29%, other relatives 17%, non-related/emotional 5%. One hundred forty pairs (46.7%) have already been transplanted. Thirty-six pairs (12%) are expected to proceed within the next months. Sixty pairs (20%) were lost to follow up. The remaining 64 pairs (21.3%) were rejected due to medical conditions diagnosed during evaluation, mainly associated with donors' comorbidities or immunological incompatibility. Mean time to the completion of pretransplant evaluation was 7.5 months (range 1-22).
Conclusions: Pretransplant evaluation of potential living donors and recipients is a laborious and time-consuming process. Transplant coordinators in close cooperation and collaboration with nephrologists and transplant surgeons are working hard to increase living kidney donation rates and the preliminary results of this multidisciplinary approach are encouraging giving the opportunity of kidney transplantation in significant proportion of dialysis patients.

P586 COMPARISON OF THE IMPACT OF NORMOTHERMIC AND HYPOTHERMIC PRESERVATION METHODS ON KIDNEY LIPIDOMIC PROFILE USING SPME CHEMICAL BIOPSY

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Background: Normothermic ex vivo kidney perfusion (NEVKP) is designed to replicate physiological conditions to potentially reduce cold ischemia injury and improve graft outcomes. However, this application is still in the experimental stage. A comparison of the impact of hypothermic and normothermic organ preservation techniques on graft quality was performed by lipidomic profiling using solid-phase microextraction (SPME) chemical biopsy as minimally invasive sampling approach.
Methods: Direct kidney sampling was conducted using SPME probes coated with a mixed-mode extraction phase in a porcine autotransplantation model of the renal donor after cardiac death, comparing three preservation methods: static cold storage (SCS), NEVKP, and hypothermic machine perfusion (HMP). The lipidomic analysis was done using ultra-high-performance liquid chromatography coupled with a Q-Exactive Focus Orbitrap mass spectrometer.
Results: Chemometric analysis showed significant differences between SCS, HMP, and NEVKP preservation methods. The renal tissue lipidome in the NEVLP group was separated from the SCS and HMP groups. Further in-depth analyses were performed to identify compounds that statistically differentiate the hypothermic and normothermic preservation methods. Significantly ($p<0.05$, VIP>1) higher levels of CARs, PCs, ether-linked PCs, ether-linked PEs, PIs, TGs, most LPC and LPE, and longer-chain PEs were observed in the hypothermic preservation group. In parallel, higher levels of Cer, PSs, and shorter-chain PEs were observed in the normothermic preservation group.
Conclusions: SPME chemical biopsy enables low-invasive and repeated sampling of the same tissue, allowing monitoring alterations in the graft throughout the entire transplantation procedure. The results showed a more significant impact on the kidney lipidomic profile related to preservation temperature rather than its mechanical character. Higher levels of lipids observed in the hypothermic preservation group may be related to ischemia-reperfusion injury, mitochondrial dysfunction, pro-inflammatory effect, and oxidative stress. Obtained results suggest the NEVKP method's beneficial effect on graft function. Acknowledgment: The study was supported by grant Opus 2017/27/B/NZ5/01013 from National Science Centre

P587 MEDIA COVERAGE OF PATIENTS WAITING FOR A TRANSPLANT INFLUENCES HEALTHCARE WORKERS IN AN UNPREDICTABLE WAY, BUT NOT THE SOCIETY

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Background: Traditionally, Chile has put efforts in sensitizing the population towards organ donation (OD) as a strategy to decrease familial refusal to donation, and thus, increasing OD rates. Almost every year there is a mediatic case: A person who needs a transplant who, because of familial efforts or media interest, is covered in news. The final intent of these coverages is to find an organ for them. But do these mediatic cases reach their objective?
Methods: We analyzed all mediatic cases in Chile between 2015-2019 extracting news from e-newspapers. We used a deductive-inductive approach to find codes in news and created a database with them. We addressed agreement among the 3 experts who coded the news using Gwet's AC1. We grouped observations by month and compared them to the national organ procurement database. We used descriptive statistics and fit linear and dynamic time series regressions (DTSR) up to the 4th lag for number of effective organ donors (ED), familial refusal (FR), and possible donors (PD) as dependent variables, and news codes' frequency as independent.
Results: We included 21 cases, 250 news (12 ± 6.7 news/case; range 3-29), and 30 independent variables (6/30 obtained <60% agreement and were excluded). 64% of news referred to a person needing a transplant, but 47% to the patient receiving it. 16% promoted a media campaign for obtaining an organ, 11% actively called to donate, 7% encouraged talking with family about OD, and 2% mentioned how to become an organ donor. The monthly number of news were not correlated with ED (0.13, p=0.3), FR (0.21, p=0.1), nor PD (0.03, p=0.8). There were no significative DTSR that fit ED nor FR. The DTSR that fit PD ($R2=0.69$, $p<0,002$) had as larger contributors mentioning the law (+) at lags 3 and 4, and brain death (-) at lag 4.
Conclusions: Albeit mediatic cases' intention, news fail to communicate the basics to achieve the goal. Neither the number of news nor any other variable were correlated with or explained ED or FR, for any lagged period. News seem to explain just the number of PD, suggesting they sensitize, positively or negatively, healthcare workers (HCW) for detecting and caring for PDs. Covering mediatic cases is not useful for increasing OD, and yet, it could be negative. Efforts should be put in improving education for HCW and improving procurement processes.

P588 LUMINEX SINGLE ANTIGEN ASSAY ON 1:10 DILUTED SERUM PREDICTS THE DROP IN ANTI-HLA ANTIBODIES BEFORE DESENSITIZATION OR TREATMENT OF HUMORAL REJECTION

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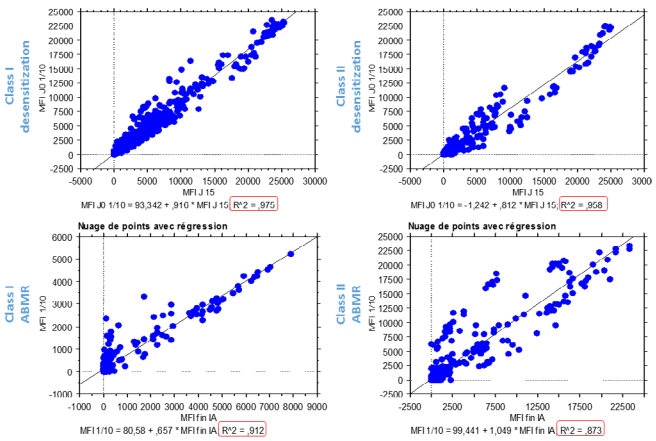
Background: Even if anti HLA antibodies testing by Luminex single antigen assay has allowed a better appreciation of the pre-transplant immunological risk, the interpretation of the results is sometimes difficult with in particular a phenomenon of saturation of the beads. The study of serum diluted to 1/10th could allow a better appreciation of the evolution of antibodies after plasmapheresis.
Methods: We studied with a Luminex Single antigen test (One Lambda Labscreen*) the pure and 1/10th diluted serum of 11 patients awaiting a renal transplantation before HLA desensitization, and the pure serum after 10 sessions of immunoadsoprtion (IA), that is to say the evolution of 1067 Luminex beads in class 1 and 855 in class 2. We performed the same evaluation before and after humoral rejection treatment in 19 patients, i.e. the evolution of 485 Luminex beads in class 1 and 1574 in class 2.
Results: (figure 1) Regarding pre-transplant desensitization, there was a strong correlation between the antibody intensity on the 1:10 diluted serum before and after 10 sessions of IA in class 1 ($r=0.99$, 95% CI: 0.98-0.99; $p<0.0001$) and class 2 ($r=0.98$, 95% CI: 0.97-0.98; $p<0.0001$). The dilution test correctly predicted the decrease in antibodies with an MFI of more than 3000 on the pre-serum and less than 3000 on the post-serum after 10 sessions of AI in 92.3% in class 1 (167 out of 181 beads; Se: 92.3%, Sp: 95.6%) and in 80.6% in class 2 (87 out of 108 beads; Se: 80.6%; Sp: 97.7%). The same was true for patients with humoral rejection after renal transplantation for whom there was a strong correlation between the MFI of the antibodies on the 1:10 diluted serum and that on the pure serum post treatment in class 1 and class 2.
Conclusions: The 1:10 dilution of serum appears to be a useful tool for predicting the decline in HLA antibodies after desensitization. This test could also predict the evolution of DSA before treatment of humoral rejection in order to adapt therapies rapidly.

Figure 1. Correlation between the antibodies intensity on the 1:10 diluted serum before and the pure serum after 10 sessions of IA, and after treatment of ABMR.



P589 REENGINEERING, THE TOOL THAT CAN REVOLUTIONIZE ORGAN PROCUREMENT IN CHILE

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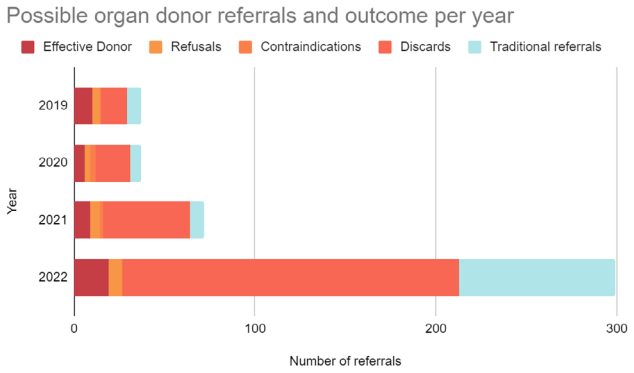
Background: Chile has historically had a low and stagnated organ donation rate (ODR) of 8 donors pmp on average, despite the efforts to improve it. This phenomenon is mainly due to the lack of detection and referral of possible organ donors (PD) at the ERs and ICUs. In fact, between 2013-17, 87% of PD were lost. What would happen if there was an intervention capable of improving and easing the PD's referral? Could the number of patients entering procurement follow-up increase, and with it, effective donors?
Methods: We developed Kefuri, a smartphone app, which allows ER and ICU healthcare professionals to refer PDs easily and quickly to the Procurement Unit (PU). We implemented it gradually in 6 hospitals in: 5/19;12/20;12/21;3/22; 4/22; 8/22), 3 from the capital, and 3 from other cities, using change management strategies. We used descriptive statistics for analysis.
Results: During the study period (5/19 - 12/22), 337 PD referrals were made with Kefuri, 80% of total referrals, and 70% of follow-ups (including PU active search). Including 2018, PD referrals have increased at a rate of 1.16% per month, and Kefuri is responsible for 68% of that increase ($p<0.001$); while PU searches have remained constant (growth ~0, $p=0.4$). Annual attributable PD referral rate difference (AAPDRRD) during Kefuri period has increased significantly ($p=0.013$), and AAPDRRD ratio was 74% on average (±21%, range 45-100). During 2022, when all hospitals were active, total PD referral rate (94 pmp) was 35% larger than the average of previous years (59 pmp) ($p<0.001$). Effective ODR increased 11% compared to previous years (though not significantly, $p=0.78$), where 79% were referred using Kefuri.
Conclusions: Kefuri has shown to significantly increase the number and rate of PD referrals in the centers where it has been implemented, albeit 3 out of 6 have not yet completed 1 year of use. We acknowledge there are gaps that must be addressed for further improving results, and implementation science tools would be a good fit for that. We recognize that ODR did not increase, maybe because next organ procurement process stages must be intervened too. We believe that Kefuri has the potential not only to increase PDs in the whole country, but also to have new functionalities to automate and standardize the rest of the process and also to be incorporated in other countries.



P591 ORGAN DONATION A CROSS-SECTIONAL SURVEY AMONG MEDICAL STUDENTS IN ROMANIA

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Background: Health professionals can positively influence the rate of organ donation by educating families and modifying the public perception of organ donation. The aim of this study was to assess fourth-year medical students' attitudes and knowledge of organ donation
Methods: Medical students, from a North-Eastern Romanian University of Medicine and Pharmacy, were prospectively surveyed in their fourth year by an anonymous online 17-item questionnaire.
Results: Between 2018 and 2021 total of 963 students completed the questionnaire, 79.7% females, and 90.7% aged between 18-29 years old. Most of the responders (89%) were Orthodox, and 69.9% were urban area residents. Their attitude to transplantation was strongly positive (86%). Those who disagreed with the concept of organ donation had religious beliefs (33.5%), and the fear of not receiving the best medical care (19.4%), had no reliable medical informations (17.4%), and they were influenced by negative mass-media campaigns (8.2%). The students would accept a human donor organ (90.6%), although only 61.9% of them will accept to be a donor. Only 33.5% discussed with their families the possibility of being a donor, and a very small proportion (7.2%) discussed this topic with the primary care physician. The respondents had a good knowledge of the criteria for brain death. Only 0.41% (4 responders) had themselves an organ transplant, and 2.69% (26 responders) had relatives with an organ transplant
Conclusions: Medical student attitude to organ donation was found to be satisfactory, although needs to be improved. An educational program that will provide training concerning organ donation for healthcare providers is therefore needed.

P592 PANCREATIC ISLET CONDITIONING FOR TRANSPLANTATION BY RNA INTERFERENCE

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Background: The tissue factor (TF) is a powerful stimulator of thrombogenesis after transplantation (Tx) of pancreatic islets (PI) to portal vein. As a safe method not interfering the nuclear DNA, we tested RNA interference for reduction of TF presence on PI before Tx.
Methods: Male Brown Norway rats (250-270g) served both as (PI) donors and recipients. PI were isolated using collagenase digestion according to standard protocol. After overnight cultivation PI were transfected with anti-TF siRNA (s130189, ThermoFisher Scientific, USA) using lipofection (Lipofectamine RNAiMAX, 50nM; n=6) or electroporation (Neon, 2 pulses, 950 V, 20 ms, 200 nM; n=6). One day later, PI were Tx to portal vein of streptozotocin diabetic animals in marginal dose (2 PI/g) for metabolic evaluation or to healthy controls (1000 PI) for imaging experiment.
Results: Both methods of transfection led to a comparable decrease in TF mRNA expression - electroporation reduced the TF mRNA by 76/55%, lipofection by 75/70% after 24/48 hours, respectively. There was detected comparable effect on TF protein levels in vitro. But there was detected 60% / 99% reduction of liver perfusion impairment by electroporation and lipofection, respectively. Tx PI normalized glycemia of all recipients treated with lipofected PI but none with electroporated PI.
Conclusions: AntiTF-siRNA transfected by electroporation efficiently reduced the amount of TF for 24 and 48 hours but did not improve the function of transplanted PI. AntiTF-siRNA transfected by lipofection efficiently reduced amount of TF for 24 hours and significantly improved the function of transplanted PIs. Electroporation likely caused the Off-target effect in PI graft. Acknowledgment: Funded by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Pr. EXCELES, No. LX22NPO5104) - The Next Generation EU. This work was supported also by MH CR (DRO IKEM IN 00023001).

P593 PREGNANCY INDUCED SENSITISATION AND HLA-ANTIBODY INCOMPATIBLE KIDNEY TRANSPLANTATION (HLA-AIT): NOT ALL IS BAD NEWS FOR LONG TERM GRAFT SURVIVAL

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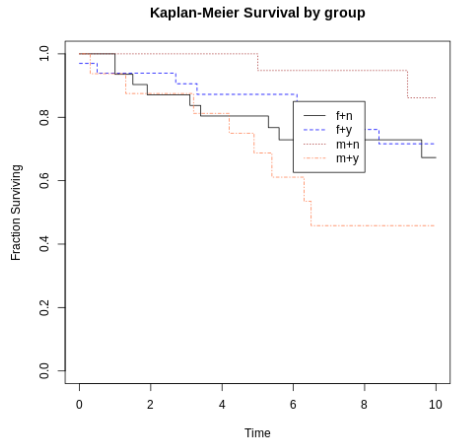
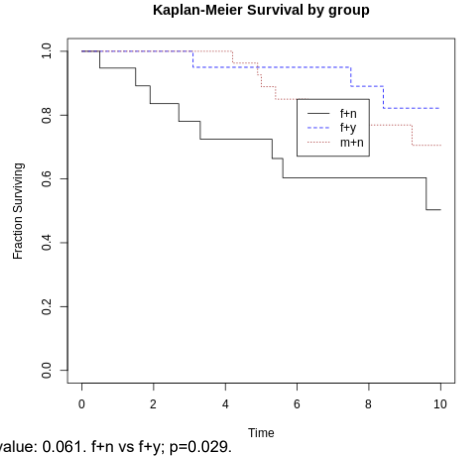
Background: Sensitisation against HLA from pregnancy disadvantages female patients by reducing access to a compatible transplant and by the high risk considered when transplanting against a repeat, foetal HLA mismatch. We investigated the graft survival (GS) following HLA-AiT, particularly in female recipients.
Methods: 134 patients were transplanted against donor-HLA-specific antibodies (DSA). 43 cases were excluded due to insufficient follow-up data. We were able to obtain reliable assignment of cause of primary sensitisation in 73 patients. Post-transplant DSA dynamics were classified by unsupervised machine learning into five distinct DSA response groups (Table 1).
Results: Pregnancy sensitised females had the highest rate of ER (18/24), significantly more than the combined transplant and transfusion sensitised cases (21/49; p=0.014). We saw no difference in ER between males and females overall, but males with ER had significantly poor 10-year GS compared with females (Fig 1a). Superior GS was seen in the pregnancy sensitised females (Fig1b), with significantly better GS than the non-pregnancy sensitised females (p=0.029), with males in between. Overall, the post-transplant DSA responses are significantly different between the sexes with females having higher proportions of modulating responses (Table 1), particularly one with pregnancy sensitisation.
Conclusions: Our analysis challenges the notion that pregnancy is a risk factor for GS in HLA-AiT. Careful selection of cases with pregnancy induced sensitisation can reduce inequity to access to transplantation in female patients.

Fig 1a. Sex and impact of ER on 10 year graft survival. f=female, m=male; y=ER, n=no ER.



Overall; p=0.028985. m+y vs m+n p-value: 0.003. m+y vs f+y; p=0.049.

Fig1b. Source of sensitisation and 10 year graft survival. f=female; y=pregnancy sensitised, n=non-pregnancy sensitised



Overall; p-value: 0.061. f+n vs f+y; p=0.029.

Table 1 Early post-transplant donor-specific antibody responses

	Number of cases in each response group					Significance
	no response	fast modulation	slow modulation	rise to sustained	sustained	
Sex						p=0.008
Female recipients	12	12	21	5	7	
Male recipients	7	2	6	10	9	
Female only						ns
Pregnancy sensitised	4	8	5	1	1	
Non-pregnancy sensitised	3	3	5	2	2	

P594 ADULT KIDNEY TRANSPLANT RECIPIENTS AT RISK OF CMV INFECTION AND DISEASE: AN OBSERVATIONAL STUDY

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Background: Infections with Cytomegalovirus (CMV) are associated with significant morbidity and mortality in solid organ transplant recipients and a major cause of decreased graft and patient survival in kidney transplant recipients. An important risk factor for post-transplant CMV infection and disease is the CMV serostatus of the donor and recipient. Currently used antiviral drugs are associated with significant adverse effects and are limited in their clinical efficacy by the increasing resistance situation. Aim of the present study was to assess the incidence of CMV disease within 52 weeks post-transplant within the context of current clinical practice for CMV prophylaxis in kidney transplant patients.
Methods: We performed a retrospective, multicenter cohort study in five German kidney transplant centers in which the clinical practice of valganciclovir prophylaxis in CMV-seronegative kidney transplant recipients who received an organ from a CMV-positive donor was documented. Follow-up was 52 weeks after transplantation.
Results: 240 patients who received a kidney transplant from 2011 – 2021 were included. Most common indication for transplantation was high blood pressure (20,8%), polycystic kidney disease (10,3%) and IgA nephropathy (10%). During the study period, prophylactic valganciclovir was given at an average dose of 333,67 mg/d according to kidney function. The incidence of CMV infection in recipients was 31,5%, the incidence of CMV disease was 8,8%. When disease occurred, the average CMV DNA was 14.835,28 copies/ml. The most common CMV disease was enterocolitis (2,9%), pneumonia (1,6%), colitis (0,8%) and hepatitis (0,8%). Side effects occurred in 20 cases during prophylaxis with valganciclovir. Hemodialysis was continued in 14 patients after transplantation. At week 28 and 52 only 1 patient continued with hemodialysis.
Conclusions: CMV infections pose a significant risk for post-transplant patients. CMV prophylaxis as well as close monitoring to detect possible side effects are beneficial. Resistance testing should be implemented in daily practice if prophylaxis in the right dosage is without efficacy. Further research is needed to improve our understanding of CMV disease in this patient population and to develop more effective strategies for its prevention and treatment.

P595 ASSOCIATION OF BODY COMPOSITION WITH PRESENCE OF SUBCLINICAL TARGET ORGAN DAMAGE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: A significant number of studies have demonstrated the association between target organ damage and cardiovascular events, poor renal and overall survival in kidney transplant recipients (KTRs). Obesity is an established cardiovascular risk factor in this population. The purpose of this study is to investigate a possible association of body composition with the presence of subclinical target organ damage in KTRs.
Methods: The study included 150 KTRs who underwent measurement of pulse wave velocity (PWV) with Sphygmocor device, urinary protein/creatinine ratio (UPCR) and carotid intima-media thickness by ultrasound. Body mass index (BMI) was calculated, body composition was analyzed by multi-frequency bioelectrical impedance and waist circumference was measured to determine the distribution of body fat.
Results: Mean age of the study group was 51(15± 12.5) years and two thirds of patients were male (66%). From the total cohort, 39.2% of patients had normal body weight, while 43.2% were overweight and 15.5% were obese. According to waist circumference, 49.3% of patients had central type obesity, while 47.3% had increased percentage of body fat. Increased waist circumference (>102cm for men and >88cm for women) was significantly associated with the presence of proteinuria (r=-1.181, p=0.036) and increased PWV (r=-1.453, p=0. 024), after adjusting for, age, sex, time from transplantation, dialysis vintage and estimated glomerular filtration rate (eGFR). Percentage of body fat and BMI were not associated with the parameters studied.
Conclusions: A significant proportion of the study population were overweight or obese and had increased waist circumference. The presence of central obesity is associated with the presence of proteinuria and increased arterial stiffness. Our findings suggest that increased body fat and central obesity in KTRs are of great importance, as they are modifiable risk factors that may interfere with arterial damage.

P598 REDUCED FRAILTY AND IMPROVED FUNCTIONAL CAPACITY IN EXERCISING LIVER TRANSPLANT CANDIDATES

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Background: Liver transplantation remains the golden standard in end-stage liver disease treatment. The Model for End-stage Liver Disease (MELD) is mainly used for patient prioritization since it can successfully predict short-term mortality. However, this comes with limitations despite its great value, as it cannot incorporate all comorbidities of hepatopathy, such as sarcopenia and physical frailty. It is evident that such variables influence patient survival. Subsequently, physical frailty and functional capacity gather growing interest in liver transplantation, as they appear to strongly relate with mortality in transplant candidates and recipients, as well as having a role in improving their survival rates.
Methods: The patients listed in the liver transplant waiting list of the "Hippokration" General Hospital of Thessaloniki were recruited for this study. Patients that were bedridden, had recent cardiovascular incidents, or required inpatient treatment for more than 5 days in the last 6 months were excluded from the study. Twenty patients agreed to participate. The following variables were evaluated: activity level via the International Physical Activity Questionnaire (IPAQ), functional capacity via the Six-Minute Walking Test (6MWT) and Cardiopulmonary Exercise Testing (CPET), and physical frailty via the Liver Frailty Index (LFI).
Results: IPAQ responses allowed for a division of patients based on the presence of adequate weekly activity levels. According to this, an active group (A, 10 patients) and a sedentary group (S, 10 patients) was formed. After a comparison of means, the following results were identified: MELD (A: 12.05 ± 5.63 vs. S: 13.99 ± 3.60, P > 0.05), VO2peak (A: 29.78 ± 6.07 ml/kg/min vs. S: 18.11 ± 3.39 ml/kg/min, P < 0.001), AT (A: 16.71 ± 2.17 ml/kg/min vs. S: 13.96 ± 1.45 ml/kg/min, P < 0.01), 6MWT (A: 458.2 ± 57.5 m vs. S: 324.7 ± 55.8 m, P < 0.001), LFI (3.75 ± 0.31 vs. 4.42 ± 0.32, P < 0.001).
Conclusions: A better musculoskeletal and functional capacity, as well as retention of a level of robustness, is achieved by exercise in liver transplant candidates, despite the progression of liver disease and the sarcopenia associated with it. This effect also appears to be independent of the liver disease severity. This offers a pre-transplantation treatment target to improve survival and prognosis.

P600 EXPERIENCE OF LIVER TRANSPLANTATION IN NATIONAL SCIENTIFIC CENTER FOR SURGERY NAMED AFTER A.N. SYZGANOV

Maxat Doskhanov[1], Bolatbek Baimakhanov*[1], Erbol Serikuly[1], Aidar Skakbayev[1], Shokan Kaniyev[1], Manas Seisembayev[1], Baglan Askeyev[1], Abzal Ismatov[1], Serik Tileuov[1], Aziza Khadjiyeva[1], Zhambyl Ospan[1], Shakhmurat Teipov[1], Daniyar Mukazhanov[1], Mazdak Asan[1]

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Background: Liver transplantation (LT) is a radical treatment method for recipients with end-stage liver disease. The first LT in Kazakhstan was performed in December 2011 year. Our hospital has more than 10 years of experience in LT by December 2022. This study shows the results after LT in a leading clinic of Kazakhstan.
Methods: From December 2011 to December 2022, 233 LT were performed at the National Scientific Centre of Surgery named after A.N. Syzganov. 24 (10.3%) LT were performed from deceased donor and 169 (72.5%) from a living donor. Paediatric LT from a living donor was performed in 40 cases (17.1%). The next graft types were used: right lobe - 155, left lobe - 23, posterolateral sector-1, Dual-graft-1, left lateral sector - 29, whole liver - 24. Indications for LT were cirrhosis in the outcome: Hepatitis C - 27, Hepatitis B - 18, Hepatitis B with delta agent- 102, primary biliary cirrhosis - 30, primary sclerosing cholangitis – 5, cryptogenic cirrhosis – 8, alimentary-toxic hepatitis – 3, Budd-Chiari – 1, Myofibroblastic tumor – 1, Steatohepatitis – 2, Wilson-Konovalov – 1, Biliary atresia - 23, secondary biliary cirrhosis - 2, autoimmune hepatitis - 10. Clinical results were retrospectively analyzed.
Results: The overall 5 and 10 year survival rate after LT were 75% and 72.4% correspondingly. Biliary complications after LT were observed in 32 (13.7%), vascular complications in 10 (4.2%), bleeding in 25 (10.7%), rejection crisis in 12 (5.1%) cases.
Conclusions: LT in Kazakhstan and in our hospital is actively developing. The main problem at present is the need to develop organ transplantation from deceased donors.

P601 REVISED CRITERIA FOR DIASTOLIC DYSFUNCTION OF CIRRHOTIC CARDIOMYOPATHY AND MAJOR ADVERSE CARDIAC EVENTS AFTER LIVER TRANSPLANT

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Background: Cirrhotic cardiomyopathy (CCM) was associated with the development of Major adverse cardiac events (MACE) after liver transplant. Particularly, the diastolic dysfunction is a prominent feature of CCM. Recently, the diagnostic criteria for diastolic dysfunction of CCM has been revised. However, the association with postoperative MACE and revised diastolic dysfunction was not comprehensively evaluated.
Methods: This retrospective study included adult recipient of living donor liver transplant at a tertiary referral center, Samsung Medical Center, between May 2010 to December 2020. Patients without sufficient echocardiographic data for characterization of diastolic dysfunction by revised criteria for CCM and patient with preoperative renal replacement therapy were excluded. Diastolic dysfunction was defined as at least two of the following criteria: septal e' < 7 cm/s, tricuspid regurgitant maximum velocity > 2.8 m/s, left atrial volume index > 34 ml/m2, or ratio of early diastolic transmitral flow to early diastolic mitral annular tissue velocity ≥ 15. The main outcomes were MACE. Multivariable logistic regression was performed to evaluate the association of CCM and MACE within 30-day after liver transplant.
Results: Of the 674 recipients included for the analysis, 117 (18.3%) patients had diastolic dysfunction of CCM and 44 (6.5%) developed MACE within 30-day. Multivariable analysis demonstrated that preoperative diastolic dysfunction is significantly associated with increased risk of post-transplant MACE after adjusting known risk factors (odds ratio [OR]= 4.43 [2.27–8.62], P<.001).
Conclusions: Preoperative diastolic dysfunction defined by the revised criteria for CCM was associated with higher incidence of post-transplant MACE.

P602 NEW NON-INVASIVE MARKERS OF PORTAL HYPERFLOW AND ITS ROLE IN CIRRHOSIS AND POST-LIVER TRANSPLANT OUTCOME

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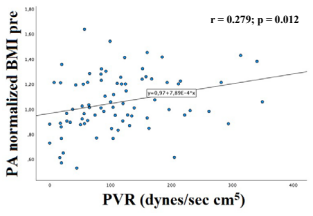
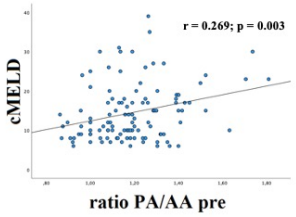
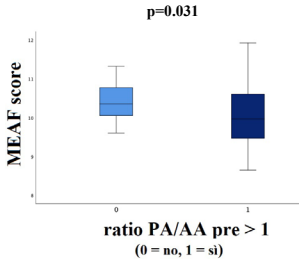
Background: in cirrhotic patients, portal hyperaflow (PH), secondary to portal hypertension, induces systemic morpho-hemodynamic changes proportional to disease severity. These changes persist in the peri-liver transplant (LT) period with an impact on post-LT outcome. The degree of PH is usually derived from morphological stigmata (e.g. porto-systemic shunts), but systemic hemodynamic alterations of PH are not considered. The aims of this study are: i) to investigate noninvasive markers of systemic PH hemodynamic changes, ii) their relationship with cirrhosis severity, and iii) their impact on post-TL outcome.
Methods: Retrospective study on LT performed for chronic liver disease from 01/2017 to 12/2019. Clinical and hemodynamic data were registered. After pre- and post-LT CTs evaluation, literature based morphologic parameters describing thoraco-abdominal vascular remodeling were considered (e.g. ratio between pulmonary artery and aorta diameter - PA/AA - and PA diameter normalized for body mass index - nPA). Data are presented as mean±SD.
Results: 133 patients were included in the study. Pulmonary hypertension secondary to PH was diagnosed in 18% of cases with a PA/AA of 1.16±0.14. Pre-LT PA/AA and nPA were positively correlated with hemodynamic parameters that describe PH (wedge pressure, p=0.012; pulmonary vascular resistance, p=0.033) and worst cirrhosis severity (MELD,p=0.003; CHILD,p=0.040; skeletal-muscle-index,p=0.048). At pre-LT CT, an increase in these parameters of hemodynamic impairment secondary to PH was associated with greater postoperative complications (Comprehensive Complication Index at hospitalization, p=0.046; rate of infections, p=0.032; acute renal failure, p=0.032; graft loss, p=0.027) and worst predictors of allograft function (EASE p=0.004; MEAF p=0.031). PH morphological parameters improved post-LT in 47% of cases. When they did not improve, the persistent PH was related to graft loss (p=0.027).
Conclusions: In this study, we identified possible noninvasive markers of PH that are related to the severity of cirrhosis and could predict worst post-LT graft function. Systemic involvement of PH should be considered, together with portal vein and morphological parameters, in the pathogenesis of PH-related graft dysfunction and small-for-flow syndrome.







P604 SARS-COV-2 SUBGENOMIC RNA IN KIDNEY TRANSPLANT RECIPIENTS. UTILITY IN PROGNOSIS OF PATIENTS WHO HAVE RECEIVED REMDESIVIR

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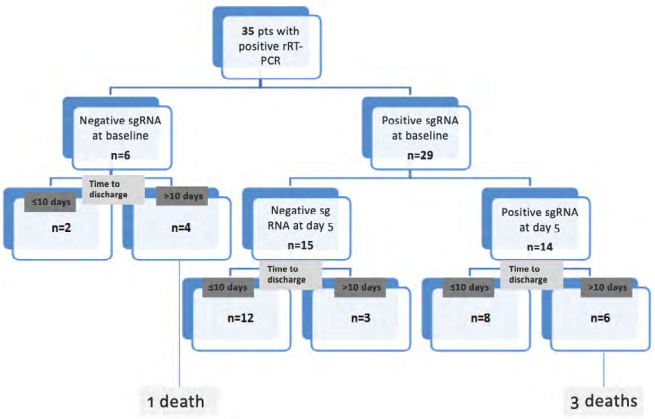
Background: COVID-19 clinical evolution in kidney transplant recipients (KTRs) is less linear and foreseeable than in general population due to immunosuppression, as well as the response to antiviral treatment. We aim to evaluate the virological response to Remdesivir in KTRs by means of longitudinal evaluation of subgenomic RNA (sgRNA) and qRT-PCR test.
Methods: Thirty-five KTRs who received Remdesivir for COVID-19 from November 2021 to February 2022 were included. The analysis of both sgRNA and qRT-PCR was performed at baseline and after treatment.
Results: Thirty-five KTRs were included in the study. Mean age was 64±15 and 57% were males. Median time since transplantation was 80[IQR 3-321]. Triple therapy with tacrolimus, mycophenolate and steroids was employed in 69% of patients, while 17% were under prednisone, tacrolimus and everolimus. In 76% of cases, a 3-dose mRNA vaccination schedule was administered. A single dose of 200mg of Remdesivir were administered followed by 2 or 4 more daily dose of 100mg. A total of 3 KTRs (8%) received 3 doses and 32 KTRs(91%) received 5 doses. Remdesivir was administered with a median time of 5[3–8.5]days after symptoms' onset. Three(8%) KTRs presented asymptomatic disease, 25(71%) moderate disease and 7(20%) severe disease. At baseline, 83% KTRs had positive sgRNA. Of the total of 29 KTRs who were positive, 15 KTRs(51.7%) were negative after remdesivir treatment, while 14 (48.3%) were still positive. The qRT-PCR test was positive in all patients at baseline and after Remdesivir treatment. Among patients who maintained positive sgRNA after treatment, there were 3 deaths(21.4%), while no deaths were observed in patients whose sgRNA was negative after Remdesivir(Figure 1). In regression logistic analysis the only factor associated with a positive sgRNA after treatment was diabetes(4.5 [1.1-19], P=0.04).
Conclusions: Qualitative sgRNA may be a valuable tool to monitor the virological response to Remdesivir in KTRs and predicts prognosis.



P605 LIVER AUTO-TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS TO DEFINE INDICATIONS AND DETERMINE SURVIVAL

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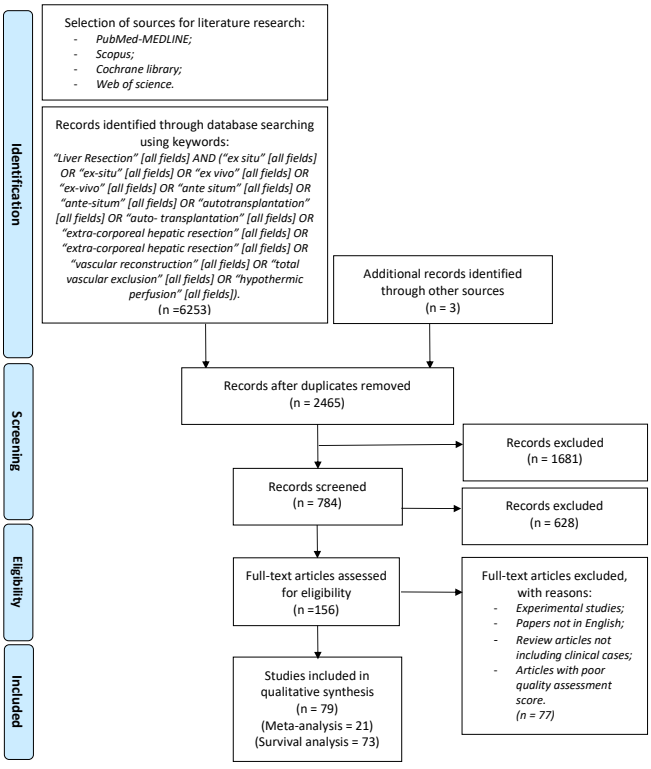
Background: Liver auto-transplantation (auto-LT), which includes ex vivo and ante situm surgery, is a surgical option for the treatment of liver tumors with vascular infiltration or retrohepatic extension not eligible for conventional surgery, although its indication is not yet clearly established. Interestingly, ex situ surgery has relevant overlaps with conventional liver transplantation, both from the technical point of view and perioperative management. We present a systematic review and meta-analysis collecting all the reported cases of auto-LT. Clinical indications for surgical treatment, survival analysis and short-term prognostic factors are reported.
Methods: A literature search was performed on PubMed-MEDLINE, Scopus, Cochrane Library and Web of Science, including all the case reports and series published in English, with no time limit. Experimental studies were excluded. Bibliographic sources were identified using specific keywords.
Results: The analysis revealed 177 cases of ex vivo and 62 of ante situm. The 90-day survival was 86,5%, with better survival for ante situm compared to ex situ (94,7% vs 82,4%, *p=0.027*). Survival varies according to different tumors: cholangiocarcinoma (CCA) had the worst prognosis, followed by colorectal metastasis, and hepatocarcinoma (*p=0.039*). The most relevant prognostic factors in cox's analysis were the year of publication, patient's age, surgical technique and diagnosis of CCA. The occurrence of complications and in particular postoperative liver failure had a significant impact on auto-LT (*p=0.021*).
Conclusions: Auto-LT is a challenging technique, burdened with a high rate of morbidity and mortality. Post-operative liver failure is of major concern, and it is one of the main causes of peri-operative mortality together with sepsis. An adequate selection of candidates with careful evaluation of underlying liver conditions, anticipated liver remnant, and patient comorbidities seems to be the key issues to improve results, in particular for ex vivo resections. The type of tumor is a significant prognostic factor, as well as the patient age. Auto-LT seems to be an efficient strategy in well-selected cases, and the best perspective for patients not eligible for conventional surgery, who otherwise would have a low life expectancy and a poor prognosis.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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P606 NUCLEIC ACID TESTING TO FACILIATE KIDNEY TRANSPLANTATION FROM INCREASED-INFECTIOUS RISK DECEASED DONORS: CLINICAL OUTCOMES AND VIRAL TRANSMISSION RISK

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Background: Accepting organs from donors at higher risk of blood borne viruses (BBV; Hepatitis B, C and HIV) is one way to expand the pool of organs for transplantation; but may confer a raised risk of viral transmission. Nucleic acid testing (NAT) can mitigate this risk as it shortens the period in which donors may be infected with BBV but serologically negative.
Methods: We gathered data retrospectively from all patients receiving kidneys from donors with an increased risk of BBV infection since 2019.
Results: 12 patients received kidneys from donors who had undergone NAT. Mean age of donors was 42 years; of recipients was 53 years. Reasons for NAT included past Hepatitis C virus infection (n=4), history of IV drug use (n=6), perceived high risk exposure (e.g., sexual assault, n=2) and known HIV (n=1, this organ went to an HIV positive recipient, with NAT to exclude concomitant Hepatitis B/C infection). Recipients were often highly sensitised (median peak calculated Reaction Frequency=24%, range 0-100%) and had been waiting a long time (median waiting time=890 days, range=405-2225). Donor cause of death included overdose (n=3), intracranial haemorrhage (n=3), hypoxic brain injury (n=3) and other (n=3). Median cold ischaemic time was 12:05 hours (range=6:30–20:00). Post-transplant patient survival was 100%. 2 patients (16.7%) returned to dialysis. Of these, 1 had refractory acute T-cell mediated rejection and the other was HIV positive and had recurrent urinary infection, leading to graft loss. Of the 7 patients with functioning grafts at 1 year follow up, median eGFR was 50 ml/min (IQR=7) and median creatinine was 141 µmol/L (IQR=32.5). 1 patient developed donor derived Hepatitis E virus infection (HEV); donor HEV was identified post-donation. 7 recipients were tested for HIV after 6 months post-transplant and all were negative. 5 recipients were tested for Hepatitis B & 6 for Hepatitis C post-transplant, and all were negative.
Conclusions: Patient survival was excellent, and patients with functioning grafts at 1 year had excellent kidney function. We observed 1 case of donor transmitted HEV infection, with no evidence of donor derived BBV in patients with adequate follow up. For appropriately counselled patients, use of kidneys from increased infectious risk donors who have undergone NAT appears to be safe and effective.

P607 COMPARING OUTCOMES OF FIRST AND SECOND DECEASED DONOR KIDNEY TRANSPLANTATION: A RETROSPECTIVE STUDY

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Background: The demand for re-transplantation among kidney transplant patients has increased due to the growing number of transplants performed and increased life expectancy. However, the second deceased donor kidney transplantation(DDKT) poses a higher immunologic risk and there is a debate surrounding its comparison in terms of graft survival and patient survival with the first DDKT. This retrospective study compared the outcomes of second DDKT with those of first DDKT, with the aim of determining specific risk factors for graft and patient survival.
Methods: Data was collected for 636 patients (age ≥ 18) who underwent DDKT at a single center between February 1995 and May 2020. The demographic information of recipients and donors, immunologic factors, and outcomes of the second DDKT patients were compared to those of first DDKT patients using propensity score matching.
Results: In this study, 636 patients were analyzed, with 561 receiving their first DDKT and 75 undergoing their second DDKT. A matched cohort of 102 patients from the first DDKT group and 58 from the second DDKT group was created through a nearest neighbor propensity score matching process. The 5- and 10-year graft survival rates were found to be similar between both groups, with the first DDKT group having a 5-year graft survival rate of 98.3% compared to 93.5% for the second DDKT group (p=0.23) and a 10-year rate of 90.7% compared to 76.2% (p=0.18). Similarly, the 5- and 10-year patient survival probabilities were comparable between both groups, with the first DDKT group having a 5-year survival rate of 96.9% compared to 95.2% for the second DDKT group (p=0.67) and a 10-year rate of 96.9% compared to 83.5% (p=0.12). Univariable analysis showed that the presence of donor specific antibody (DSA) is associated with an increased risk of graft failure(hazard ratio [HR], 3.51; p=0.01). Multivariable analysis showed that a previous transplantation history was not a significant risk factor for either graft loss (HR, 1.01; P=0.98) or patient death (HR, 1.12; P=0.82).
Conclusions: Our study showed that second DDKT can be a viable option for patients with previous transplant not functioning optimally, provided that careful patient selection and proper management are followed.

P608 ASSOCIATION BETWEEN BODY COMPOSITION AND ANKLE-BRACHIAL INDEX IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The risk of peripheral arterial disease (PAD) in kidney transplant recipients (KTRs) is lower compared with patients with end stage renal disease, however it remains high compared to the general population and it is linked to poor renal and overall survival. Obesity is an established risk factor for cardiovascular disease in this population. The aim of this study was to investigate the possible association between ankle branchial index (ABI), as a diagnostic index for PAD and body composition and obesity in KTRs.
Methods: This cross-sectional study included 150 KTRs, who underwent measurement of ABI, which was calculated by dividing the systolic pressure measured in each lower limb by the systolic blood pressure of the arm with the higher pressure, using an automated oscillometric device. ABI <0.9 was indicative of PAD while ABI>1.4 was indicative of presence of noncompressible lower extremity arteries. Body mass index (BMI) was calculated, body composition was analyzed by multi-frequency bioelectrical impedance and waist circumference was measured to determine the distribution of body fat.
Results: Mean age of the study group was 51(15+12.5) years and the majority were men (66%). Overweight was observed in 43.2% of patients and obesity in 15.5% of patients. Central type obesity according to waist circumference was evident in 49.3% of patients, while 47.3% had increased percentage of body fat. Only 6 patients (4%) had ABI <0.9 and 14 (9%) had ABI>1.4. Multivariate analysis revealed no significant association between body composition, BMI and waist circumference and ABI.
Conclusions: According to our findings, 13% of patients had abnormal values of ABI. Anthropometric characteristics, body composition and distribution of body fat did not reveal any significant association with ABI. More studies are warranted to further elucidate the association between anthropometric characteristics and body composition with PAD in KTRs.

P609 THE EARLY ALLOGRAFT FAILURE SIMPLIFIED ESTIMATION SCORE OUTPERFORMS CLASSIC OLTHOFF EAD IN PREDICTING 90-DAY GRAFT LOSS IN DCD LIVER TRANSPLANTATION

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Background: The use of DCD liver grafts has significantly increased. Early allograft failure (EAF) following liver transplantation (LT) unequivocally predicts adverse graft and patient outcomes. The original Olthoff Early Allograft Dysfunction (EAD) definition is still most widely used. However, it appears to be unsuitable for donation after circulatory death (DCD) LT, because this score is mainly dictated by postoperative levels of transaminases and EAD was validated in cohorts with at most 10% DCD recipients. In DCD, transaminases are significantly higher, without necessarily affecting outcome. This study validates the existing risk scores for EAF to predict 90-day graft survival in DCD-only LT.
Methods: Between 2001 and 2021, the data of all DCD liver transplant recipients in the Erasmus MC were retrospectively analyzed. Patients who were re-transplanted or died before post-operative day 3 and machine-perfused grafts were excluded. The Olthoff EAD, UK-DCD risk, L-Graft$_7$, MaDiRe, MEAF and EASE score were determined. The ability to predict 90-days graft survival was assessed.
Results: 203 patients received a DCD liver graft. Out of the calculated scores, the EASE score outperforms the classic Olthoff EAD in predicting 90-days graft survival with an AUC of 0.81 vs AUC of 0.61, p=0.0013. According to the EASE-score patients could be stratified in 3 distinct categories showing good separation in 90-days graft survival of 96%, 83%, 53%, which also translated to good separation at 1 year. However, the EASE score was not accurate at predicting 3-year graft survival with an AUC of 0.64.
Conclusions: This study shows that the EASE-score is superior in a pure DCD cohort to estimate the EAF risk and to predict 90-days graft survival. The EASE-score outperforms the classic Olthoff score and would be preferable as surrogate marker in future studies addressing DCD liver transplantation.

P610 OUTCOME OF PATIENTS WITH C3 GLOMERULONEPHRITIS AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Background: C3 glomerulonephritis (C3GN) results from dysregulation in the alternative complement pathway and is characterized by C3 depositions with no or minimal Ig depositions in the immunofluorescence. Studies regarding the outcome of patients with C3 glomerulonephritis after kidney transplantation are limited.
Methods: We retrospectively studied patients with C3GN who underwent living donor kidney transplantation between 2016 and 2022. Demographic data, C3GN recurrence after kidney transplantation, as well as the treatment used and the graft failure rates were recorded. In all cases the diagnosis was confirmed by renal biopsy and genetic testing for disorders of the complement pathway.
Results: A total of 7 patients (57% men) with C3GN underwent living donor kidney transplantation from 2016 to 2022. The mean age was 36 years. All patients received a triple immunosuppressive regimen. Genetic mutations were found in 3 of 7 patients, while alternative complement pathway activation was established in all 7 patients (increased C3bBbp and C5b-9 and in one C3NeF). C3GN recurrence was confirmed in 5 patients (71.4%). The mean time to recurrence after kidney transplantation was 18.4 months (1-31) and the diagnosis was established by renal biopsy with dominant C3 staining (3-4+). At the time of recurrence, the majority of patients had proteinuria, microscopic hematuria and low C3 levels. Three of the recurrent cases were treated with eculizumab. Graft failure occurred in 40% of the patients with recurrent C3GN. The median time to graft failure was 55 months (47-62) post-transplantation. After a median follow-up time of 52 months, the mean creatinine level of patients with a functioning graft was 1.7 mg/dl.
Conclusions: In a case series of graft recipients with G3GN, disease recurrence was frequent with a high rate of allograft loss.

P611 EPRO DIARY LIVER: A NEW WAY TO PROMOTE PATIENT COMPLIANCE AND MORE

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Background: Adolescent liver transplant recipients represent a challenging "care management" during their transition towards adulthood. Indeed, compliance is a critical issue in this population. Low executive functions and quality of life markers were found to be similar between liver transplant recipients and other chronic diseases.
Methods: In our liver transplant center we follow a large cohort of both paediatric and adult liver transplant recipient (1024 adults, 677 adolescents). 167 patients have been already enrolled in a transitional outpatient clinic once they turn 17. In the transitional outpatient, all adolescents are evaluated jointly by a dedicated psychologist and the pediatric and adult hepatologists. To improve the compliance and the relationship between adolescent patients and the physicians, a web-based APP for smart devices has been developed. It allows patients to set up reminders for drug schedules, lab and instrumental tests and medical appointments. The system is built to alert patients in case of approaching deadlines and significant test alterations. A section dedicated to Patient Reported Outcomes (PROs) and psychological testing was also developed. All data entered in the app can be exported by the patient and the medical team. The main features of the study population are as reported: female 75 (44,9%), male 92 (55,1%), R-OLT 29 (17,4%), average time since LT 16,8 years, median time 18 years; main indication to LT is biliary atresia (49,6%). The enrollment of the transitioning patients is currently ongoing.
Conclusions: ePRO Diary Liver was approved by our ethical committee. This app can provide modern support to young patients undergoing liver transplants who are transitioning from pediatric to adulthood. It allows both adolescent patients and their caregivers to manage their relationship with the health managing team with the opportunity of monitoring the clinical situation in real time. In the coming months we shall be able to show the first reports of the project.

P612 MEDICATION ADHERENCE IN KIDNEY TRANSPLANT PATIENTS: A COMPARISON BETWEEN SHORT-TERM (3 YEARS) AND PATIENTS WITH A FAILING TRANSPLANT

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Background: Non-adherence to immunosuppression is known to be a major risk factor for poor patient and graft outcomes. Rates of immunosuppression non-adherence are high within kidney transplant recipients (KTR), with estimates of between 36% and 55%. This study explored whether adherence varies between patients less than a year post-transplant, over three years post-transplant and patients with a failing graft attending Transplant Support Clinic.
Methods: This cross-sectional study conducted between 26/09/2022 - 09/01/2023 investigates adherence in three discrete cohorts of kidney transplant recipients attending Kidney Clinic; (i) patients less than a year post-transplant, (ii) long-term recipients over three years post-transplant (LTR) and (iii) patients with a failing graft attending Transplant Support Clinic (TSC). Patients completed electronic questionnaires on an iPad. Adherence was measured using the Medicines Adherence Report Scale (MARS). Patients were classified as non-adherent if they scored < 30. Results are presented in Table 1.
Results: N=92 KTR in total completed the questionnaires. Of these, there were N=20 less than one year post-transplant, N=47 LTR and N=25 TSC patients. The rate of non-adherence across all three cohorts was 56.5%. A chi-square test revealed there was no significant difference in rates of non-adherence between cohorts (p = 0.065).
Conclusions: Our comparative analysis did not identify a significant difference in adherence between patient cohorts. However, rates of non-adherence particularly within LTR and TSC recipients were high. Further interrogation of factors associated with non-adherence in each cohort is necessary. This is a preliminary analysis and ongoing data collection will allow for more thorough investigation in the coming months.

Table 1. *A comparison of MARS scores between groups*

	Less than 1 year post-transplant (n = 20)	More than 3 years post-transplant (n = 47)	Recipients with a failing graft (n = 25)
MARS (%)			
Adherent (score of 30)	65.0%	34.0%	44%
Non-adherent (score of <30)	35.0%	66%	56%

P613 ASSOCIATION BETWEEN PHENOTYPES OF BLOOD PRESSURE CONTROL AND BODY COMPOSITION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Hypertension is considered the most prevalent risk factor for cardiovascular disease in kidney transplant recipients (KTRs). Several studies have demonstrated that these patients achieve poor blood pressure (BP) control. Obesity is a known risk factor for cardiovascular events in this population. The aim of our study was to investigate the possible associations between different phenotypes of BP control and body composition in KTRs.
Methods: Our study included 150 KTRs, who underwent office BP measurements and 24-hr ambulatory BP measurements (ABPM) with Mobil-O-Graph device. Arterial hypertension was defined as: (1) office BP ≥140/90 mmHg or use of antihypertensive agents, (2) ambulatory BP ≥130/80 mmHg or use of antihypertensive agents. Phenotypes of BP control were defined as follows: (1) concordant control with both methods, (2) concordant lack of control with both methods, (3) white-coat hypertension, (4) masked hypertension, as defined by the European Society of Cardiology/European Society of Hypertension(ESC/ESH) guidelines. Body mass index (BMI) was calculated, body composition was analyzed by multi-frequency bioelectrical impedance and waist circumference was measured to determine the distribution of body fat.
Results: All patients were hypertensive. Regarding BP control, uncontrolled hypertension with either method was observed in 61.1% of patients (concordant lack of control: 17.4%, white-coat hypertension: 4.9%, masked hypertension: 38.9%). Among patients with uncontrolled hypertension, 37.5 % had normal body weight, overweight was observed in 40.9% and 18.2% were obese, while classification according to BMI in patients with concordant control with both methods was not significantly different. Waist circumference was significantly higher in patients with uncontrolled hypertension (Mean Difference=0,217±2,676, p=0.019). Both masked hypertension and uncontrolled hypertension with either method were associated with % of body fat (p=0.049).
Conclusions: The use of ABPM reveals a high prevalence of masked hypertension in KTRs. Overweight and obesity is highly prevalent among patients with uncontrolled hypertension with either method. Improving BP control in such patients is of great importance in order to reduce cardiovascular morbidity and mortality.

P615 BK VIREMIA IN KIDNEY TRANSPLANT RECIPIENTS UNDERGOING REGULAR SCREENING

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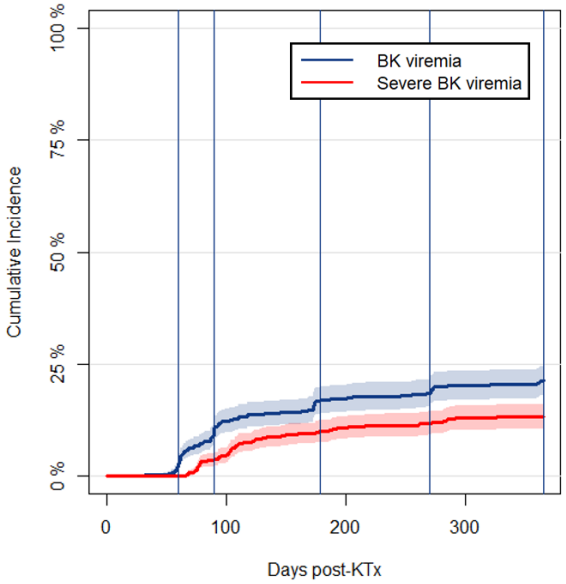
Background: BK polyomavirus (BKV) infection is common in kidney transplant (KTx) recipients and may progress to BKV-associated nephropathy. We aim to determine the incidence of BK viremia during the first year post-KTx and the risk of adverse outcomes related to BKV in a large cohort of KTx recipients in a setting with regular screening.
Methods: We prospectively included all adult KTx recipients transplanted from 2012 to 2020 at our center. Recipients were screened with quantitative PCRs on serum samples at 60, 90, 179, and 270 days post-KTx. BK viremia and severe BK viremia were defined as a PCR of >1,000 copies/mL and two consecutive PCRs of >10,000 copies/mL, respectively. Data were retrieved from patient records, ScandiaTransplant, and the nationwide Danish Microbiology Database. Decreased graft function was defined as graft loss or >50 % decrease in eGFR. Graft loss was defined as return to permanent dialysis. The cumulative incidence of BK viremia was investigated using the Aalen-Johansen estimator with graft loss and death as competing risks and BKV as a risk factor for adverse outcomes post-KTx was investigated in time-updated Cox models.
Results: In total, 601 KTx recipients were included. Prior to BKV screening at day 60, 31 recipients were censored due to death or graft loss, resulting in a cohort of 570 recipients (*Table*). A total of 3,577 BKV PCRs were performed during the first year post-KTx, of which 24% were positive. The cumulative incidence of BK viremia and severe BK viremia was 21% (CI: 18-25) and 13% (CI: 11-16) within the first year post-KTx, respectively (*Figure*). Within 2 years post-KTx, 24 recipients had decreased graft function, 14 recipients experienced graft loss, and 16 recipients died. Recipients with BK viremia were at increased risk of decreased graft function (HR: 2.5, CI: 1.1-5.6, p = 0.03), whereas recipients with severe BK viremia were at increased risk of graft loss (HR: 3.5, CI: 1.2-10.4, p = 0.03). BK viremia was not associated with risk of death.
Conclusions: BK viremia is prevalent post-KTx and is associated with decreased graft function. Furthermore, the majority of KTx recipient with BK viremia had severe BKV viremia that was associated with increased risk of graft loss. Collectively, these findings highlight the importance of close BK monitoring and clinical management post-KTx.

Figure: Cumulative incidence curves



BK viremia: 601 572 532 490 481 464 458 456 443 440 434
Severe BK viremia: 601 573 565 527 512 505 497 496 486 483 481

Table: Cohort characteristics

KT characteristics		All n = 570	BK viremia n = 129	Severe BK viremia n = 80
Age at KT, median (IQR)		50 (41 - 61)	54 (44, 63)	56 (45, 65)
Sex, male (%)		366 (64)	91 (71)	60 (75)
Kidney number, n (%)	1st	497 (87)	112 (87)	70 (88)
	2nd	64 (11)	15 (12)	8 (10)
	≥3rd	9 (1.6)	2 (1.6)	2 (2.5)
Disease leading to KT, n (%)	Glomerulonephritis	149 (26)	30 (23)	19 (24)
	Cystic	98 (17)	18 (14)	12 (15)
	Diabetes	48 (8)	11 (9)	6 (8)
	Vascular & Hypertension	25 (4)	7 (5)	4 (5)
	Chronic Interstitial	7 (1)	0 (0)	0 (0)
	Systemic	33 (6)	8 (6)	3 (4)
	Other[1]	143 (25)	38 (29)	28 (35)
	Unknown	67 (12)	17 (13)	8 (10)
Donor type, n (%)	Deceased	323 (57)	68 (53)	44 (55)
	Living	247 (43)	61 (47)	36 (45)
Donor age at KT, median (IQR)		55 (44, 64)	57 [46, 64]	58 (45, 67)
ABOi (%)[2]		65 (11)	16 (12)	8 (10)
Cold ischemia time, median (IQR)		11 (3, 18)	10 (3, 19)	11 [3, 19]
Immunosuppression at discharge, n (%)	Tac-MMF-Pred[3]	549 (96)	126 (98)	79 (99)
	Other combination[4]	21 (3.7)	3 (2.3)	1 (1.3)

[1] Other diseases leading to KT included: Reflux nephropathy, pyelonephritis, hereditary and congenital urethral anomalies, Alport syndrome, etc.; [2] ABOi, ABO incompatible donor; [3] Tac, Tacrolimus. MMF, Mycophenolate Mofetil. Pred, Prednisolone; [4] Other immunosuppression regimens included Cyclosporine, mTOR and Azathioprine.

P616 DISEASE COURSE, MANAGEMENT AND OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS WITH SARS COV2 INFECTION DURING THE OMICRON WAVE: A SINGLE-CENTER EXPERIENCE

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Background: Since December 2019, kidney transplant recipients (KTRs) have experienced a great impact of coronavirus disease 2019 (COVID-19) pandemic, with a higher risk of morbidity and mortality compared to the general population. Preliminary data in KTRs suggest that the Omicron variant, which has been dominant as of December 2021, is more infectious than the previous ones but is associated with a reduced risk of severity and low lethality rates. The purpose of our study was to assess the disease course and clinical outcomes of SARS-CoV-2 infection in KTRs during the Omicron surge.
Methods: This single-center retrospective study included 451 KTRs who suffered from SARS-CoV-2 infection between December 1st,2021 and September 30th, 2022. Demographic and clinical characteristics of the patients at the time of infection, vaccination data, treatment, clinical course and outcomes were recorded and analyzed.
Results: Mean age of the study population was 51.8±13.7 years with a male predominance (61.2%). The majority (76.1%) were vaccinated with at least three doses of the available mRNA vaccines, although serology revealed low anti-SARS-CoV-2 antibody titers before infection (33 [3.3-1205] AU/ml). Only 6% of the patients experienced moderate and severe disease. Accordingly, there was a low prevalence of adverse outcomes related to COVID-19, such as SARS-CoV-2-related hospitalization (11.3%) and death (0.9%). Multivariate analysis revealed that only age significantly increased the risk of SARS-CoV-2-related hospitalization.
Conclusions: During the Omicron wave, clinical course of SARS-CoV-2 infection in KTRs has drastically changed, with lower rates of moderate and severe disease and a low prevalence of adverse outcomes. Prospective clinical trials are warranted to further elucidate the evolving pathogenesis, management and long-term outcomes of COVID-19 in such high-risk populations.

P617 PREOPERATIVE CONTINUOUS GLUCOSE MONITORING DEVICE CAN REVEAL HIGH RISK PATIENTS FOR NEW-ONSET DIABETES POST KIDNEY TRANSPLANTATION

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Background: New-onset diabetes after kidney transplantation (NODAT) is a common and significant complication that negatively impacts graft and patient survival. Preoperative continuous glucose monitoring (CGM) devices have been proposed as a means to identify patients at high risk for NODAT.
Methods: The patients enrolled in our prospective observational SNU KT CGM study, who had greater than 3-months follow-up post-transplantation and were non-diabetic pretransplant were selected for analysis. Of the 105 patients enrolled in SNU KT CGM study, a total of 73 patients were analysed. Univariate and multivariate analysis were performed to identify preoperative risk factors associated with NODAT.
Results: A total of 18 (24.6%) patients developed NODAT. The NODAT patients compared to non-NODAT patients were older (56.9 years vs. 46.2 years; p<0.001), had a greater BMI (24.7 vs. 22.8; p=0.042), larger waist circumference (91.18 cm vs.84.63 cm; p=0.016), and higher baseline HbA1c (5.6% vs. 5.1%; p<0.001). Preoperative CGM showed that NODAT patients had higher overall mean glucose levels (106.9 mg/dL vs. 95.6 mg/dL; p=0.003) and higher daily peak glucose levels (174.2 mg/dL vs. 149.7 mg/dL p<0.001). Multivariate showed that preoperative risk factors for NODAT were age (OR=1.17, 95% CI 1.02-1.34; p=0.017), baseline HbA1c level (OR=25.75, 95% CI 1.77-373.97; p=0.017), and preoperative daily peak glucose levels above 160mg/dL (OR=33.5, 95% CI 1.75-639.66; p=0.02).
Conclusions: The use of preoperative CGM devices may be useful in identifying patients at high risk for NODAT. Patients with high daily peak glucose levels above 160mg/dL showed increased risks for NODAT. Further research is needed to confirm the utility of CGM in predicting NODAT risk and to determine the best strategies for reducing the risk of NODAT in this population.

P618 EARLY OUTCOMES OF LIVER TRANSPLANTS AFTER NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) has been increasingly used in liver transplantation. Our aim was to assess the early outcomes of liver transplants after NMP.
Methods: In February 2023, we retrospectively reviewed our database of liver grafts perfused on the OrganOx metra machine in a period of 39 months (April 2019 – July 2022) to allow for a follow-up period of at least 6 months. We collected data about donor and recipient characteristics, as well as primary non-function (PNF), early allograft dysfunction (EAD), hepatic artery thrombosis (HAT), biliary complications, retransplant and mortality within the first 6 months after the liver transplant.
Results: 136 liver grafts [75 (55.1%) from donors after brain death (DBD), 61 (44.9%) from donors after circulatory death (DCD)] underwent NMP during the aforementioned period, out of which 116 (85.3%) were transplanted [68 (58.6%) from DBD, 48 (41.4%) from DCD], whereas 20 (14.7%) were discarded [7 (35%) from DBD, 13 (65%) from DCD] due to poor function during NMP. There were 2 cases (1.7%) of PNF and 39 cases (33.6%) of EAD. HAT occurred in 2 cases (1.7%). 51 recipients (44%) had at least one form of biliary complications. In particular, anastomotic leak occurred in 8 patients (6.9%), anastomotic stricture was evident in 34 patients (29.3%), ischaemic cholangiopathy was detected in 18 patients (15.5%), while there were 5 cases (4.3%) of other biliary complications (biliary cast, leak from disconnected duct, non-anastomotic bile leak). There were 4 retransplants (3.4%) and 9 deaths (7.8%) during the first 6 months after liver transplant.
Conclusions: High rates of biliary complications and EAD rates are noted in marginal liver grafts after NMP. Bile duct anastomotic stricture is the predominant biliary complication. NMP enables better assessment of marginal liver grafts and decreases the risk of PNF.

P620 PHOSPHATIDYLETHANOL AS A MARKER FOR THE DIAGNOSIS OF ALCOHOL RELAPSE AFTER LIVER TRANSPLANTATION: SINGLE CENTRE EXPERIENCE

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Background: Alcohol-related liver disease (ALD) is the most common indication for liver transplantation in Slovakia. The aim of this study was to determine the proportion of ALD patients who underwent liver transplantation (LT) who were diagnosed with alcohol relapse using phosphatidylethanol (PEth), to determine risk factors for relapse, to compare the effect of indirect markers of relapse and PEth.
Methods: A prospective study of consecutive patients with ALD after LT between May 2008 and May 2021. We included adult patients after LT due to ALD in which were PEth investigated between July 2020 and May 2021. We excluded those who died <1 month after LT. We recorded demographic and clinical characteristics, indirect and direct biomarkers, overall mortality and compared them between relapsers and abstainers.
Results: During the study period, we reviewed 298 cases of LT in 284 patients. We excluded 143 patients for non-ALD etiology and 37 patients by predefined criteria. The final analysis was carried out in 104 patients. We diagnosed relapse in 37 patients (35.58%), mean aged 55 years; 23.1% were female. The independent risk factor associated with relapse was: cigarette smoking (OR=2.24, P=0.025). Comparison of ROC curves in ALD relapse prediction with PEth and indirect biomarkers demonstrated the high specificity of PEth. Cox's regression analysis for biochemical parameters in the prediction of alcohol relapse confirmed PEth positive>0.05 (OR=6.28, P<0.0001) as an independent factor. The diagnostic performance of positive PEth values > 0.05 and > 0.3 at any time during the alcohol relapse prediction follow-up had specificity of 92.5 and 98.5, respectively. Overall survival between both cohorts was unaffected.
Conclusions: Our results suggest PEth might be tool of choice for diagnosis of relapse

P621 ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING TO PREDICT FUNCTIONAL OUTCOME OF THE ARTERIOVENOUS FISTULAE IN A PATIENTS WITH END-STAGE RENAL FAILURE

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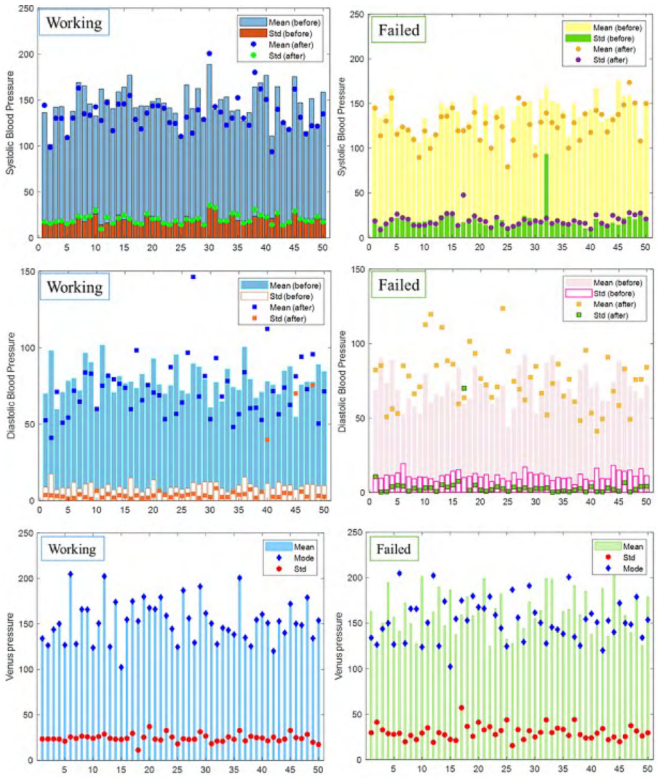
Background: Native arteriovenous fistulae (AVF's) are the gold standard haemodialysis (HD) access modality for patients in end stage renal failure. AVF failure may result in much patient morbidity and mortality as a significant proportion resort to dialysis with central venous catheters with its associated risks. Herein we present an AI-enabled approach to model prediction of AVF failure using continuous clinical measurements derived from HD machines.
Methods: We included 100 patients between Apr 2013-Aug 2019. 50 had a working AVF & 50 had a failed AVF at latest follow up. Demographic and comorbid data (e.g. diabetes, hypertension, thrombophilia) as well as machine parameters were collected. Originally 14 variables accumulated were from the HD machine, however, after feature selection process analysis only 3 were included - litres of blood processed, arterial & venous pressures. We employed feature engineering on static & temporal data, with Bayseian optimisation to train our AI model utilising random subspace methods for discrimination of AVF failure and identification of at-risk patients. We further introduced a survival-aware machine-learning-based system for the prediction of time-to-AVF failure.
Results: We found the 10-fold cross-validated discriminant subspace-based ensemble algorithms attained 79.8 ± 0.39 classification accuracy to predict the functionality of the fistula. Validation area under the receiver operating characteristic curve was 90.08 ± 0.27 which is the best performing predictive accuracy of fistula failure using routinely collected clinical data with readily available features from the dialysis machines. Using the 95% confidence interval, the sensitivity & specificity found to be found to be 87.33 ± 0.6 and 78.67 ± 0.6, respectively. Using concordance index (c-index) as a measure of performance, our Gradient boosting machine (GBM)-based survival model achieved maximum performance values of 0.76 ± 0.07 whilst establishing a connection between the variables and the time of an AVF failure.
Conclusions: We demonstrate the potential of AI to predict fistula failure in real world example. This model can be used to trigger a specialist access review when the algorithm suggests high risk of future fistula failure leading to pre-emptive interventions.



P623 LIVER TRANSPLANTATION FOR ECSTASY INDUCED FULMINANT HEPATIC FAILURE: THE NEED FOR GUIDELINES

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Background: Acute hepatic failure is the rapid development of acute liver injury with loss of liver function affecting individuals without any pre-existing hepatic condition. Approximately 10% of acute hepatitis cases among adults are drug induced with 15-20% of these cases attributed to recreational drugs. We present a case of emergency liver transplantation to a young patient due to MDMA induced fulminant hepatic failure and we discuss the available data on the subject.
Methods: We conducted a systematic review using MEDLINE, Scopus and CENTRAL databases. Case presentation**:** A 17-year-old patient lost consciousness after ingesting 3,4-methylenedioxymethamphetamine (MDMA). He was transferred to the emergency department of a regional hospital. The patient developed a rapid deterioration of liver function with coma, multi-organ failure and haemodynamic instability with a MELD score of 40. As he did not respond to any therapeutic intervention and because he remained comatose (GCS 3), he was placed in the emergency transplant list for liver transplantation. He underwent emergency orthotopic liver transplantation receiving a cadaveric whole liver graft from a 24-year-old deceased donor. The pathology examination of the native liver indicated massive hepatic necrosis.
Results: We identified 31 manuscripts, most of them case reports and cases series. Of 67 patients totally reported. liver transplantation was performed in 18 patients (26.9%). 2 patients were treated with a molecular adsorbent recirculating system (MARS®) and the rest of them with conservative treatment.
Our young patient fully recovered and was discharged from our institution 6 weeks after the transplantation.
Conclusions: Recreational drugs are widespread among young people and adolescents. MDMA fulminant hepatic failure is a rare but potentially fatal complication. Although Liver transplantation is a last-line therapeutic option, there are no specific guidelines that facilitate the selection of the patients that would benefit from this treatment. Consequently, it is essential to recognize MDMA induced fulminant hepatic failure as a distinct category in order to establish more precise guidelines.

P624 ASSOCIATION OF VESSEL-SPECIFIC CORONARY ARTERY STENOSIS WITH MAJOR ADVERSE CARDIO-VASCULAR EVENTS IN RENAL TRANSPLANT CANDI-DATE COHORT

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Background: Coronary artery stenosis is a key risk factor of major adverse cardiovascular events (MACE). Left anterior descending (LAD) artery stenosis is regarded to be the most severe vessel-specific coronary artery stenosis as depicted by its appellation *widow-maker*. We hypothesised that right coronary artery (RCA) stenoses may present poorer or similar outcomes to LAD. This study sought to understand the association of vessel-specific coronary artery stenosis using computed tomography coronary angiogram (CTCA) with MACE in a renal transplant cohort.
Methods: This was a single-centre retrospective study of all end-stage renal disease (ESRD) patients eligible for kidney transplantation who underwent CTCA between 2012 to 2014. MACE occurrences (heart failure, AMI, unstable angina, CVA, PVD and TIA) were recorded within a 9-year follow-up period. CTCA data-sets were assessed by 2 independent specialists, visually grading stenosis severity into 2 classifications (<50% or >50% coronary diameter reduction).
Results: Of 106 patients in our study, a total of 419 coronary arteries (106 RCA, 104 LAD, 104 circumflex (CX), 104 left mainstem (LM)) were graded by CTCA. 43 patients (40.6%) experienced at least one MACE within the time-frame. Statistical significance in MACE was observed when stratified by RCA stenosis severity (p=0.022) while no statistical significance in MACE observed when stratified by LAD (p=0.904), CX (p=0.472) & LM (p=0.222).
Conclusions: This challenges the conventional wisdom on individual vessel-specific coronary artery stenosis, suggesting that RCA stenoses is asso-ciated with MACE in the transplant cohort. This also offers the possibility of RCA stenosis as a prognostic tool in predicting MACE in ESRD patients.

P625 NORMOTHERMIC REGIONAL PERFUSION REDUCES APOPTOSIS MARKERS IN CONTROLLED DONATION AFTER DETERMINATION OF DEATH

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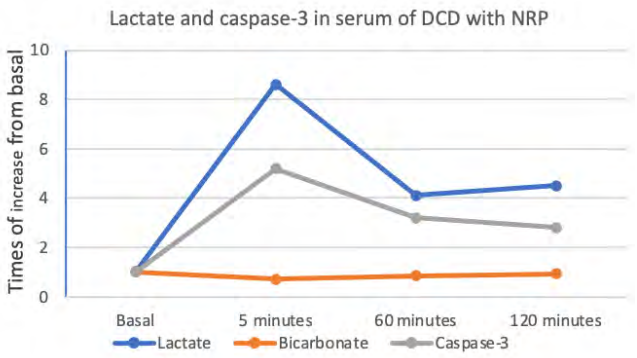
Background: Normothermic regional perfusion (NRP) rescues organs for transplantation in controlled donation after circulatory determination of death (DCD), however little is known about the damage molecules that are playing a role in this recovery. Our aim is to address if there is any role of markers of apoptosis in this process.
Methods: We performed a prospective longitudinal study of a cohort of 17 controlled DCD donors with NRP from February 2020 to October 2021. Demographic characteristics was recorded. Standard protocol for DCD were performed. Serum samples were collected at theater entrance, 5 minutes after determination of death, and 60 and 120 minutes of NRP, they were processed and stored at -20ºC until analysis. Multiplex analysis of caspase-3 was performed. Biochemical and data of NRP were recorded as standard protocol. Quantitative variables were expressed as mean o median and qualitative as percentage. IBM Statistics 24 package was used.
Results: The mean age of donors was 57 years old; the main cause of death was anoxic encephalopathy in 58,8%. All the DCD was performed with pre-mortem cannulation. The total warm ischemia time (TWIT) was 18 minutes ± 4,6, and the functional warm ischemia time (FWIT) was 12 minutes ± 5 whereas the preservation time was 127 ± 25 minutes (Table 1). Lactate was 1,06mmol/L ± 0,8 previous initiation of DCD protocol, increases at 5 minutes until 6,9mmol/L ± 1,78 and then decreased progressively to 4,45 ± 1,8; 4,0 ± 1,7; 3,6 ± 1,5 and 3,53 ± 1,1 at 30, 60, 90 and 120 minutes during the NRP. The median caspase-3 levels were 833 pg/mL (277- 2494) basal, increase 4407 pg/mL (519 – 7643) at 5 minutes and then decreased progressively to 2745 (1019 – 7933) and 2355 (946 – 5483) at 60 and 120 min of NRP (Figure 1).
Conclusions: There is an increase of caspase-3 and lactate levels after deter-mination of death, and this is reduced progressively during NRP. Further studies are needed to know the mechanisms of this reduction and to determine if this has any impact in the organ function after transplantation.

Demographic characteristics of DCD donors with NRP n=17		
Sex (Female %)	29%	
Age	57,2 ± 10,7	57 (33 – 73)
BMI	25,8 ± 2,7	26,2 (18,6 – 29,6)
Smoker (yes)	29,5%	
Alcoholism	17,6%	
Drugs	11,8%	
Hypertension	35,3%	
Diabetes mellitus	23,5%	
Dyslipemia	35,3%	
Cardiopathy	4%	
Cause of death		
Anoxic	58,8%	
Stroke	17,6%	
Traumatic	23,5%	
Cannulation	Pre-mortem	
TWIT	18:03 ± 4:46	18 (9:59 – 28:59)
FWIT	12:31 ± 5:27	11:59 (4:49 – 24:59)
Preservation time	127 ± 25	136 (72 – 163)



P626 PEDIATRIC LUNG TRANSPLANTATION ON EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT WITH PERIPHERAL CANNULATION: A SINGLE CENTER EXPERIENCE

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Background: No specific recommendations about mechanical circulatory support in pediatric lung transplantation (LT) exist. Data from small series suggest that the benefits of extracorporeal membrane oxygenation (ECMO) in adults may also apply to the pediatric setting. At our institution, the use of mechanical circulatory support is selective, and ECMO with peripheral cannulation has become the preferred strategy. We reviewed our experience, focusing on the feasibility and safety of this approach.
Methods: Prospectively collected data regarding a single center series of pediatric LT performed on ECMO support with peripheral cannulation were retrospectively analyzed.
Results: Between 2012 and 2023, 9 LT, including 1 early retransplantation, were performed using ECMO with peripheral cannulation. 7/9 (78%) LT were bilateral, sequential; 2/9 (22%) LT were monolateral, including 1 living donor LT. 5/9 (56%) grafts were lobar. The median (range) recipients' age and weight were 11 (6-15) years and 27 (20-37) Kg. Intraoperative ECMO was: veno-arterial in 5/9 (56%) cases, including 2 cases of preoperative bridging with veno-venous (VV) ECMO; veno-arterial-venous in 3/9 (33%) cases; VV in 1/9 (11%) case with preoperative VV ECMO. Arterial cannulation was surgical (carotid artery) in 5/8 (62.5%) cases and percutaneous (femoral artery) in 3/8 (37.5%) cases. Venous cannulation was percutaneous in 7/9 (78%) cases and surgical in 2/9 (22%) cases. ECMO was maintained after LT, and the median (IQR) duration of intra- plus postoperative ECMO was 25 (16-51) hours. Cannulation-related complications (3 arterial thromboses after percutaneous cannulation and 1 jugular thrombosis after dual-lumen cannula insertion) were successfully treated. The rates of bleeding, requiring reoperation, and acute kidney injury, necessitating renal replacement therapy, were 22%. In-hospital mortality was 12.5%: 1 patient, bridged to LT and retransplantation with VV ECMO, died of multiorgan failure. 6/8 (75%) patients are alive, with a median (IQR) follow-up of 38 (10-55) months.
Conclusions: Our experience suggests that ECMO with peripheral cannulation may be safe and effective also in the pediatric setting. Peripheral cannulation was not associated with permanent morbidity, and proved convenient for ECMO maintenance after LT.

P627 LONG TERM EFFECTS OF COMPOSITE WARM AND COLD ISCHAEMIC TIME IN DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: Cold (CIT) and warm ischaemic time (WIT) are independent predictors of poor outcomes in kidney transplantation. However, their combined effect has not been studied in large cohorts. We aimed to determine if a composite measure of combined WIT and CIT is a predictor of kidney transplant outcomes.
Methods: We analysed 26,583 adult kidney transplants from 2000-2018 using the UK Transplant Registry. CIT and WIT were assessed separately, and as a combined factor. The WIT threshold was 35 minutes, and CIT threshold was 12 hours for DCD and 15 hours for DBD transplants. Univariate and multivariate analyses were performed comparing outcomes based on WIT or CIT alone, and as a combined factor, adjusting for donor and recipient factors including age, sex, ethnicity, primary renal disease, dialysis modality and cRF. The main outcomes were 3, 12, and 60 month creatinine, delayed graft function (DGF), primary non function (PNF), and graft survival.
Results: Increased CIT or WIT alone were associated with poorer early graft function. DGF or PNF rates were generally higher, although this was not consistently observed across all groups. When analysed as a composite factor, there was a more consistent effect in grafts with increased CIT and WIT compared to either factor alone, with poorer 3 and 12 month creatinine, and increased risk of DGF and PNF (Table 1). Graft survival was also poorest in grafts with both raised CIT and WIT, while low CIT and WIT grafts performed best.
Conclusions: Longer composite times have stronger effects on graft outcomes compared to WIT or CIT alone. While it may not always be possible to reduce both CIT and WIT, reducing just one of these factors can significantly improve outcomes.

Table 1: Composite WIT/CIT outcomes

*Regression estimate **Hazard Ratio. Baseline group for comparison: Low CIT/Low WIT.

	3m Cr*	P-value	12m Cr*	P-value	60m Cr*	P-value	DGF**	P-value	PNF**	P-value
DBD										
High WIT/ High CIT	1.05	<0.001	1.03	<0.001	1.037	0.002	1.67	<0.001	1.80	<0.001
Low WIT/ High CIT	1.04	<0.001	1.04	<0.001	1.049	<0.001	1.29	<0001	1.23	0.31
High WIT/ Low CIT	1.01	0.155	1.00	0.978	1.016	0.21	1.18	0.015	1.50	0.031
DCD										
High WIT/ High CIT	1.07	<0.001	1.07	<0.001	1.031	0.103	1.48	<0.001	2.01	0.005
Low WIT/ High CIT	1.04	0.002	1.06	<0.001	1.034	0.096	1.17	0.052	2.20	0.002
High WIT/ Low CIT	1.01	0.511	1.02	0.127	1.003	0.898	1.21	0.028	1.54	0.121

P628 30 YEARS OF SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION: AN APPRECIATION OF ITS SURVIVAL BENEFIT OVER KIDNEY TRANSPLANTATION ALONE

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Background: Simultaneous pancreas-kidney (SPK) transplantation has revolutionized the management of type 1 diabetes mellitus (T1DM) patients with end-stage kidney disease (ESKD) as it provides a physiological means of achieving normoglycemia while rendering patients free of dialysis. However, the procedure is associated with more operative risks compared to kidney transplantation alone for frail patients.
Methods: Over 30 years (1992-2022), 141 SPK transplantations were performed at this single center, compared with 77 kidney-only transplantations in T1 DM patients (2 living, 75 deceased donors). We wanted to evaluate graft and recipient outcomes in both groups, adjusted for baseline demographics in a multivariable model.
Results: SPK recipients had significantly better graft and patient survival compared to kidney-only transplant recipients (5-year kidney graft survival 96% vs. 87%, P=0.039 and 5-year recipient survival 92% vs. 70%, P<0.0001, respectively). Especially recipient survival was inferior in kidney-only transplant recipients (10-year survival 38%), who were more frail (older donor and recipient age, longer dialysis vintage, higher donor and recipient BMI) compared to SPK recipients. However, also when correcting for these confounders and for the effect of increased expertise and diabetes management over the years, SPK had clear survival benefit (HR 2.47, 95% CI 1.32-4.61). Overall outcome (recipient survival and kidney graft survival) in kidney-only transplants did not improve significantly with years of expertise and expected better diabetes management in more recent years, even when adjusting for extended donor and recipient criteria (HR 0.98, 95% CI 0.94 – 1.02, P=0.23 per year of expertise).
Conclusions: SPK transplantation represents the preferred treatment for T1DM patients with ESKD. Even with improved diabetes care in recent years, transplantation of kidneys alone in T1DM patients has poor recipient survival, which is probably related to diabetes-related complications and comorbidities of these patients who seemed ineligible for SPK transplantation. Therefore, early referral of T1DM patients with ESKD for SPK, before macrovascular complications accumulate should not be forgotten.

P630 LEFT LOBE LIVER VOLUME CALCULATION USING REALITY CAPTURE HARDWARE VIA LIGHT DETECTION AND RANGING (LIDAR) 3D TECHNOLOGY

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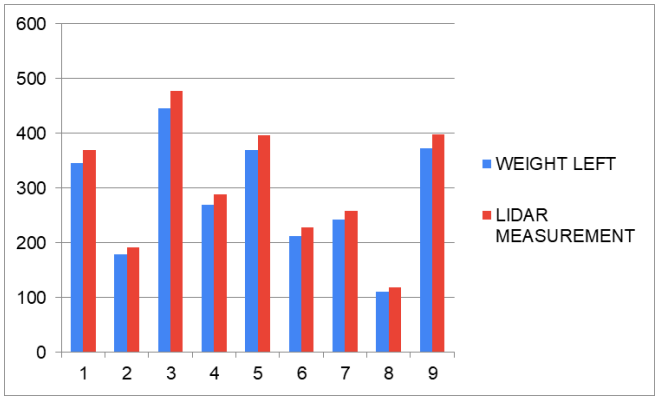
Background: Liver transplantation (LT) remains the golden standard in the treatment of end-stage liver disease, and limited graft availability remains a problem. The Split-liver technique offers a potential solution to this problem, although there is no reliable and recognized method for calculating ex-vivo graft volumes. Evaluate the use of LiDAR technology to calculate the volume of cadaveric organs (liver) and evaluate the method for application in transplantation.
Methods: A post-mortem examination was performed by the forensic team. After the hepatic graft was removed from the abdomen, it was grossly examined, including weight and volume calculation using the water immersion technique. Using a special 3D portable LiDAR camera, the graft was photographed, and a 3D digital model of the liver was created by the relevant software. Subsequently, an analysis was run to calculate the volume of the left lobe before a transplant surgeon divided the organ into two lobes. Actual left lobe weight and volume were then calculated using the same techniques as above. All relevant calculations were completed by the software.
Results: Nine liver grafts were assessed post-mortem for actual weight and estimated weight using a LiDAR camera. Due to normal distribution, the student t-test was used to compare the two sets. The mean total weight was 1647.3g, and the mean estimated weight was 1576.9g; the two groups had no statistically significant difference (P=0.744) with a 95% confidence interval (-378, 519). Furthermore, the same comparison was performed for the left lobe graft. The mean left lobe weight was 283.1g, and the mean estimated weight was 264.3g; the two groups had no statistically significant difference (P=0.708) with a 95% confidence interval (-86, 123).
Conclusions: Preliminary findings suggest that LiDAR photography scanning could be a potential tool for the calculation of the actual volume of liver cadaveric organs. Moreover, calculating the left lobe weight from the total graft volume using LiDAR photography and software produced a similar result compared to the actual measured weight. Validation of these findings with a larger sample is necessary.



P631 TOWARDS THE DEVELOPMENT OF A REGIONAL PEDIATRIC DCD NETWORK MODEL: A PREPARATORY SURVEY

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Background: The shortage of available organ donors is a significant problem worldwide, and among the pediatric population the problem has even wider ranges, mainly because of the peculiarity of the donation scenarios and the difficulty of matching between donors and recipients. Various efforts have been carried out to increase the donor pool, such as living donation and split liver techniques, but the possibility of pediatric DCD has not been exploited in Italy yet. In order to develop a Regional network to facilitate the development of shared protocols and guidelines, to define the epidemiological context and practices about end of life care in PICUs, a Regional survey has been carried out.
Methods: A simple questions survey has been proposed to the 5 pediatric Intensive Care Units of the Italian Northern Region Lombardy. The survey explored through 21 closed questions the number of PICU beds, the availability of WLST registry and institutional programs, the availability of an in-site NRP facility and the willing to elaborate or collaborate to a shared educational program.
Results: 4 out of the 5 Lombardy PICUs have similar pediatric demographic characteristics, except for one PICU, which is mainly dedicated to post operative patients. Traumatic pediatric patients are centralized in one center with few exceptions. All the participant centers hospitalize together more than 2000 patients/year, ranging from 40 days to 18 years of age, with roughly 1% mortality mostly due to genetical pathology complications. In all the hospitals DBD and tissue donation programs are active, 2 of them have pediatric transplant programs. Three centers have currently no formalized institutional WLST procedure, 4 out of 5 participate to a shared National registry. The main cause of WLST is post-anoxic cerebropathy, followed by cardiocirculatory disease, chronic pathology complications, half of the patients undergoing WLST develop MOF. Educational programs focused on pediatric DCD has not started in any of the institution, yet.
Conclusions: The preliminary survey draws the picture of 5 Regional Italian PICUs that could possibly create a shared network of competences and professionals for pDCD.

P632 EFFECT ON HUMORAL SENSITIZATION OF DUAL TARGETING APPROACH WITH ANTI-CD38 MAB AND COSTIMULATION BLOCKADE IN HIGHLY SENSITIZED PATIENTS (COMBAT STUDY)

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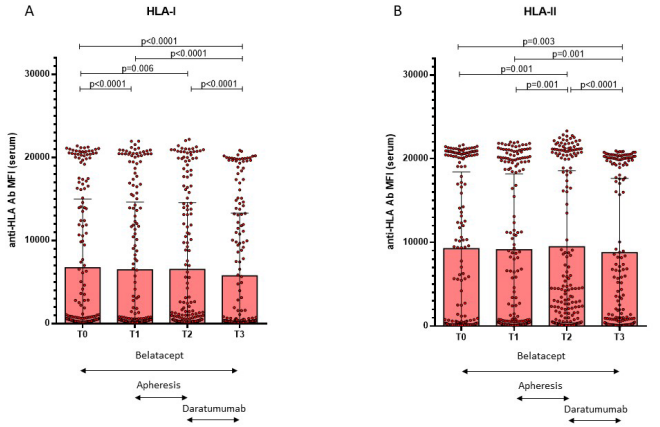
Background: Current desensitization therapies have shown very poor success to decrease anti-HLA antibodies in highly sensitized patients. Besides central bone marrow-residing long-lived plasma cells (LLPC), peripheral memory B cells (mBC) with their T Follicular Helper Cell (TFH) counterparts contribute to antibody formation. We designed a prospective, phase-II, exploratory trial (COMBAT; NCT05145296) based on a dual-target approach with co-stimulation blockade with belatacept and the anti-CD38 mAb daratumumab to abrogate these alloimmune compartments.
Methods: 10 patients with cPRA≥99% on the deceased donor kidney transplant waiting list, without a compatible donor offer for >3 years despite being on a national prioritization program, will be included. The first phase of the strategy consists on belatacept 10mg/kg administered on days 1, 5, and end of weeks 2, 4 and 8 (T0-T1), followed by 4 sessions of apheresis (T1-T2), and subsequent 4 doses of daratumumab (8mg/kg) every two weeks until week 17 combined with belatacept (5mg/kg) (T2-T3), ending with two doses of belatacept until week 24. Changes on serum anti-HLA antibodies, frequencies of circulating IgG-producing HLA-specific mBC, TFH and Bone Marrow-residing LLPC are assessed.
Results: We describe the preliminary results of the first 3 patients included in the trial, we expect to present the full data of the study by the ESOT congress. 1 patient discontinued the trial after 3 belatacept doses because of a colitis episode. 2 other patients completed the scheduled therapy. Notably, a progressive significant reduction of serum anti-HLA antibodies has been observed over time at each time point (Figure 1A and B). This reduction is observed for both class I (mean MFI at baseline 6706 ± 8279 vs 5725 ± 7564 at T3, p<0.0001) and class II HLA antigens (mean MFI at baseline 9243 ± 9177 vs 8772 ± 8878 at T3, p=0.003). No safety concerns were observed. All cellular assays and data of the remaining patients of the study are undergoing and will be presented at the congress.

Conclusions: Dual targeting of central and peripheral humoral alloimmune compartments with daratumumab and belatacept may be an effective strategy to reduce the sensitization burden of highly sensitized patients waiting for kidney transplantation eventually facilitating access to kidney transplantation.



P633 DUAL INDUCTION WITH ANTI-THYMOCYTE GLOBULIN AND RITUXIMAB IN SENSITIZED KIDNEY TRANSPLANT PATIENTS

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Background: The secondary immune response that is expected to occur in sensitized kidney transplant(KT) recipients having memory cells is characterized by the development of donor-specific plasmablasts and subsequently circulating secondary-memory B cells during a short-time frame of days to weeks after transplantation. Rituximab (RTX) can deplete plasmablasts, which retain CD20 on surface before the full maturation to long-lived plasmacytes and memory cells. Rabbit antithymocyte globulin (rATG) can abrogate T cell help for germinal-center B response and may diminish the genesis of secondary memory cells and plasmacytes. Peritransplant administration of both of these depleting-induction agents may be a reasonable way to efficiently reduce the number of donor-specific clonal cells, albeit not abolish the clones.
Methods: We use both rATG and RTX as induction agents in 30 KT patients having pretransplant donor specific anti-HLA antibodies (DSA). To reduce the infectious risk, rATG dose was limited to 3 or less (median 2 doses) daily dose of 1.5mg/kg. RTX dose was 100~300mg/body (median 200). CDC- and flowcytometry (FC)- crossmatch (XM) was positive in 10 patients, CDCXM negative but FCXM positive in 4, and pre-KT DSA without positive XM in 16. Twelve patients also had ABO incompatibility. Both class I and II DSAs were detected in 8 patients. class I only in 13, and class II only in 9. Pre-KT plasmapheresis was implemented in all but one patient.
Results: Six (20%) patients developed acute clinical AMR, which were all recovered by standard of care treatment. DSA, measured by single bead assay, became undetectable after KT in 18 patients, and persisted although significantly reduced in MFI (immunodominant, 7,481±4,612 to 1,810±2,321) in 12 patients. Seven patients developed infections that required hospitalization. No patients developed CMV disease or BKV nephropathy. There was no patient death. Two patients lost graft due to chronic antibody-mediated rejection.
Conclusions: Although our study lacks control patients, we feel that the dual induction with a moderate dose of rATG and RTX is a safe and effective strategy for sensitized KT patients, and worth for further studies.

P634 DE NOVO UPPER TRACT UROTHELIAL CARCINOMA AFTER RENAL TRANSPLANTATION

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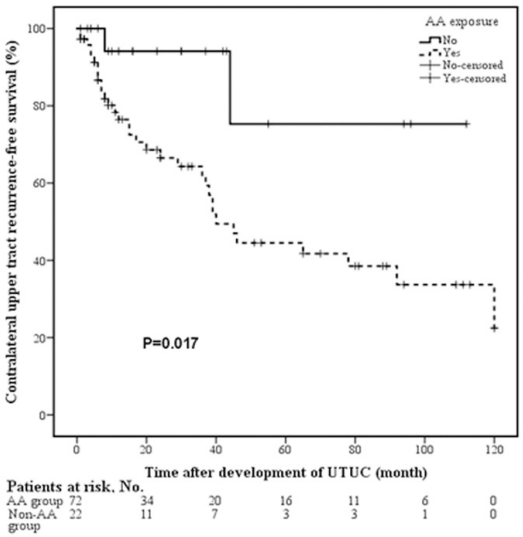
Background: Long-term prognosis and risk factors of de novo upper tract urothelial carcinoma after renal transplantation were rarely studied. Thus, the aim of this study was to investigate the clinical features, risk factors, and long-term prognosis of de novo upper tract urothelial carcinoma after renal transplantation, especially the impact of aristolochic acid on tumor, using a large sample.
Methods: 106 patients were enrolled in retrospective study. The endpoints included overall survival, cancer-specific survival, bladder or contralateral upper tract recurrence-free survival. Patients were grouped according to aristolochic acid exposure. Survival analysis was performed using Kaplan-Meier curve. Log-rank test was used to compare the difference. Multivariable cox regression was conducted to evaluate the prognostic significance.
Results: Median time from transplantation to development of upper tract urothelial carcinoma was 91.5 months. Cancer-specific survival rate at 1, 5, 10 years was 89.2%, 73.2%, 61.6%. Tumor staging (≥T2), lymph node status (N+) were independent risk factors for cancer-specific death. Contralateral upper tract recurrence-free survival rate at 1, 3, 5 years was 80.4%, 68.5%, 50.9%. Aristolochic acid exposure was independent risk factor for contralateral upper tract recurrence. The patients exposed to aristolochic acid had more multifocal tumors and higher incidence of contralateral upper tract recurrence.
Conclusions: Both higher tumor staging and positive lymph node status were associated with a worse cancer-specific survival in patients with post-transplant de novo upper tract urothelial carcinoma, which highlighted the importance of early diagnosis. Aristolochic acid was associated with multifocality of tumors and higher incidence of contralateral upper tract recurrence. Thus, prophylactic contralateral resection was suggested for post-transplant upper tract urothelial carcinoma, especially for patients with aristolochic acid exposure.



P636 A NOVEL APPROACH TO ADDRESS MASS MEDIA CAMPAIGNS FOR ORGAN DONATION PROMOTION. THE REGIONAL EXPERIENCE OF A 5-MILION INHABITANTS AREA OF ITALY

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Background: The availability of organ donors still represents the major limiting factor to tackle the gap between of demand and offer of organs for transplantation. Although many efforts have been done in order to expand the actual donors' pool both in terms of organ procurement and selection for transplantation, the will to donate is a clue. In Italy we have a soft opt-in system, where, in case no declaration in life is found, we ask permission to donate to the next- of – kin. Unfortunately only a small proportion of potential organ and tissue donors is found to have expressed their will to donate at the moment of organ donation. In such a context, fostering in-life declaration about donation will is of paramount importance and can be obtained by specific mass media regional campaigns to promote organ donation.
Methods: In order to have a targeted and effective communication we experienced a novel bottom-up approach trying to understand the sentiment of the citizens of Veneto Region, a 5-million inhabitants area in north-eastern Italy. In September 2021, we created a research panel of 500 citizens living in Veneto of all ages and genders who were interviewed with a funnel questioning approach, In order to explore their knowledge and propensity towards organ donation and to focus on their needs both in terms of contents and the "tone of voice" to be adopted.
Results: After data collection and analisys, we went back to the panel with different communication proposals. The most voted proposal was used as the main layout and claim of the regional campaign, that was launched in 2022.
Conclusions: promotion of subscription to donors' registries still remains a critical issue , especially in opt-in systems. Media and web campaigns can be a useful tool to promote organ donation. Targeted promotion, especially in this era where social media are a powerful tool to increase to culture of organ donation, can be of great support.

P638 VOLUMETRIC ASSESSMENT OF HEPATIC GRAFTS USING LIGHT DETECTION AND RANGING (LIDAR) TECHNOLOGY

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Background: Liver transplantation is the most effective the gold standard for treating end-stage liver disease. Due to continuous advances in the field, there is an increasing paucity of grafts. This means that thousands of adults and, mainly, pediatric patients are impacted by the scarcity of liver grafts. There is a need in both liver transplantation and liver resection to be able to accurately estimate liver volume. The LIDAR 3D technology could help address this need: A study has been designed to allow us to use a LIDAR camera to estimate liver volume. The main aim of the study is to examine whether hepatic graft volume can be estimated using the LIDAR camera. The safety and accuracy of measurements were two of the main study pylons.
Methods: Hepatic grafts were used. All demographic characteristics of donors were recorded, namely age, weight and height, while body mass index was also calculated. The cause of brain (stem) death was also recorded. A biopsy of all hepatic grafts was performed. The volume of hepatic grafts suitable for transplantation was estimated. Back-table preparation was completed before weighing the graft on precision scales and then taking a picture with a special LIDAR camera. The entire process lasted 2.5-3 minutes, and in no case were grafts left outside the preservation solution for long. From 06/2021 to 12/2022, a total of 23 hepatic grafts were assessed. The graft weight, the camera-estimated graft volume, the graft volume estimated based on the Vauthey formula, the transformation of the volume measured to estimated volume, and their difference in grams and percentile deviation were all recorded on the database.
Results: Data were recorded, followed by statistical analysis, initially assessing demographic data and finding mean values for the parameters recorded. T-test of related samples followed to calculate the p-value for statistically significant differences among samples. The mean total weight was 1521.2 g, and the mean estimated weight was 1627.7 g; the two groups had no statistically significant difference (P=0.314) with a 95% confidence interval (-354, 535).
Conclusions: The results of this study indicated that using a LIDAR camera to estimate total liver volume is feasible and safe. The method offers hopes for estimating partial liver volume.

N	Graft Weight (gr)	LIDAR volume (ml)	Vauthey volume (ml)	LIDAR Estimated Graft mass (gr)	Difference (gr)	Difference (%)
1	1202	1179	1275,04	1 261,53	59,53	4,95
2	1623	1490	1590,52	1 594,30	-28,70	-1,77
3	2201	2090	1781,61	2 236,30	35,30	1,60
4	1332	1248	1440,86	1 335,36	3,36	0,25
5	1227	1141	1818,15	1 220,87	-6,13	-0,50
6	1074	1040	2266,36	1 112,80	38,80	3,61
7	1623	1482	1680,03	1 585,74	-37,26	-2,30
8	1450	1318	1930,97	1 410,26	-39,74	-2,74
9	1505	1297	1475,51	1 387,79	-117,21	-7,79
10	848	680	1601,25	727,60	-120,40	-14,20
11	1838	1687	1789,30	1 805,09	-32,91	-1,79
12	1223	1113	1459,93	1 190,91	-32,09	-2,62
13	1150	1067	1459,93	1 141,69	-8,31	-0,72
14	1463	1194	1284,29	1 277,58	-185,42	-12,67
15	1489,5	1206	2062,83	1 290,42	-199,08	-13,37
16	1617	1227	1704,69	1 312,89	-304,11	-18,81
17	1846	1599	1519,31	1 710,93	-135,07	-7,32
18	1355	1179	1275,04	1 261,53	-93,47	-6,90
19	1989	1688	1716,27	1 806,16	-182,84	-9,19
20	1525,5	1346	2039,31	1 440,22	-85,28	-5,59
21	1589,5	1321	1550,34	1 413,47	-176,03	-11,07
22	1581	1321	1570,14	1 413,47	-167,53	-10,60
23	2237	1937	2121,17	2 072,59	-164,41	-7,35

N: Donor number; gr: grams; ml; milliliters %: percentage, [Estimated graft mass (gr) = (LIDAR volume ml x 1.07 gr/ml)]. The difference is calculated by subtracting the LIDAR estimated liver from the grafts' actual mass (weight).

P639 SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION IN OLDER RECIPIENTS

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Background: Improved therapeutic advances in diabetes mellitus care, has resulted in a higher number of older diabetics on dialysis. The majority of centers use an age cut-off 50 years for Simultaneous Pancreas Kidney transplantation (SPKT) for concern for poor graft survival and complications. This study aimed to compare the long-term outcomes of older (>50 years and ≤50 years) diabetic patients who received SPKT.
Methods: We retrospectively evaluated 317 deceased SPKT transplants at our center from July 2003 to March 2021. Median follow-up was 7 (3.9,11) years.
Results. There were 101(32%) subjects above 50 years and 216 (68%) subjects aged </= 50 years who received SPKT. Table 1 provides differences in recipient and donor characteristics. Mean age was 56.5 in >50 years and 39 in the younger cohort. Duration of diabetes was higher in the older cohort (31.6 vs. 25). Donor characteristics were similar between the 2 groups.
Results: Incidence of delayed graft function, length of stay, readmission, serum creatinine, Hba1c, and C-peptide post-transplant were similar (Table 2). Incidence of acute rejection of the kidney and pancreas by 1 year (including the for cause, protocol biopsy, and subclinical rejection) were also similar. Estimated 3-year death-censored pancreas (82% vs. 87%) and kidney graft survival (94% vs. 96%) were similar between the two cohorts. Patient survival was lower as expected but acceptable at 3 years in older groups (92% vs. 96.5%). Death-censored pancreas (log-rank 0.67) and kidney survival (log-rank 0.43) were similar between the 2 groups.
Conclusions: Carefully selected subjects older than 50 years have non-inferior pancreas and kidney graft survival compared to the younger cohort receiving SPKT.

	< 50 (216)	> 50 (101)	P value
Delayed graft function	19(9%)	10% (10%)	0.8
Length of stay (days)	8.5(9.3)	8.2(4.5)	0.58
Readmissions 30 days (0/1/2/3/4 times)	49%/37%/12.5%/1%/0.5%	50%/40%/6%/ 4%/0%	0.15
Creatinine at time of discharge	1.8(1.5)	1.6(0.9)	0.14
Serum creatinine at 1 year	1.3(0.6)	1.2(0.5)	0.9
Serum creatinine at 2 years	1.2(0.3)	1.2(0.6)	0.13
Hba1c at 1 year	5.6(1)	5.8(1.3)	0.82
Hba1c at 2 year	5.5(0.9)	5.7(1.3)	0.43
C-peptide at 1 year	3.9(1.9)	3.9(1.7)	0.45
C-peptide at 2 year	3.7(2)	4.2(3.7)	0.16
Kidney rejection within 1 year	15%	11%	0.57
Pancreas rejection within 1 year	35%	32%	0.2

P641 POST-TRANSPLANT DONOR SPECIFIC ANTIBODIES DYNAMICS CAN BE PREDICTED USING C3D ASSAY IN ASSESSMENT FOR HLA-INCOMPATIBLE KIDNEY TRANSPLANTATION

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Background: HLA-incompatible kidney transplantation outcomes can be variable. Pre-transplant/ pre-desensitisation diagnostic tests can help predict behaviours of donor specific antibodies post-transplantation and associated worse outcome. This study explores value of C3d assay in prediction of post-transplant dynamics of DSA.
Methods: 134 patients were transplanted against donor-HLA-specific antibodies (DSA). 93 cases had post-transplant DSA dynamics classified by unsupervised machine learning into five distinct DSA response groups and of these 92 had C3d assay performed on samples before desensitisation.
Results: C3d positive DSA was detectable in 1 out of 20 cases that had no DSA responses following transplantation (Group 0). Modulation group (Group 1 and 2) (N=41 cases) where DSA rose rapidly and then fell within first month post-transplantation had 7 cases with C3d positive DSA whilst the Sustained dynamic group (Group 3 and 4) (N=31) where antibody levels stayed high and did not fall had 19 cases with C3d positive DSA. This was statistically significant (p =0.0002).
Conclusions: Our analysis suggests using solid phase assay on pre-desensitisation treatment for HLAi transplant can predict post-transplant dynamics of DSA that are associated with rejection and poor graft survival long term. Thus the use of this assay for delisting and risk stratification is suggested.

P642 LATE NON-CATHETER-RELATED VENOUS THROMBOTIC EVENTS IN LUNG TRANSPLANT RECIPIENTS

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Background: Deep venous thrombosis (DVT) is a common complication in lung transplant recipients (LTRs) and is associated with higher 1-year mortality rates. Even within our population of LTRs, the majority of thrombotic events occur shortly after surgery and are generally related to the use of central venous catheter (CVC) or extracorporeal membrane oxygenation (ECMO). Instead, we hereby present a report focusing on thrombotic events that occurred at least 60 days after surgery and in sites that weren't used for CVC or ECMO application.
Methods: This study is a retrospective analysis from a tertiary-care, university-affiliated referral centre based in Milan, Italy. Clinical records of all lung transplant recipients between January 2014 to August 2022 were reviewed for thrombotic events. Demographic information and preoperative patient characteristics including age, sex, indication for transplantation, immunosuppressive therapy at the time of the event and risk factors for thrombophilia were reported. Follow-up was obtained until Jan 15, 2023. Thrombotic events in sites of CVC or ECMO and/or occurring within 60 days from transplant were excluded.
Results: The study comprised 13 patients (see image 1), 9 of which were men (69%). Indication for transplant: 5 cystic fibrosis, 4 COPD, 4 interstitial lung disease. Median age was 56 (24, 67) years. 3 patients (23%) had a history of venous thrombosis and 2 patients (15%) had a history of pulmonary embolism; these same 2 patients were also the only ones to have genetic coagulopathy (hyperhomocysteinemia and factor V Leiden). See table 1 for other risk factors. Median time of first-time thrombotic event occurrence from transplantation was 134 days (74, 1757). Of all events in this group of patients, 7 (54%) were DVTs of lower extremities. We also recorded 3 cases of pulmonary embolism, 2 of them were concomitant with DVTs.
Conclusions: Lung transplantation is a pro-thrombotic condition and DVT can be a relevant problem not only in the postoperative period. Approximatively 18% of LTRs of our patients with a diagnosis of thrombosis had a late event, i.e. in a period of time when surveillance for thrombosis is usually low, as the majority of lung transplant centers are only screening for thrombosis shortly after ICU discharge.

Image 1

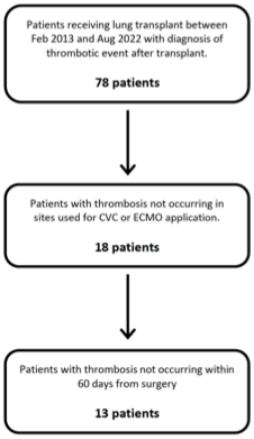

Table 1 – Risk factors for VTE

Risk factors	
EVEROLIMUS as part of maintenance immunosuppressive regimen	2 (15%)
Major orthopaedic surgery	0
Lower-extremity paralysis due to spinal cord injury	0
Fracture of the pelvis, hip or long bones	0
Multiple trauma	0
Cancer	1
Previous history of VTE/PE	2 (15%)
Age > 40 yrs	11 (85%)
Obesity	2 (15%)
Immobility	0
Oral Contraceptives or estrogen treatment	1 (8%)
Family history of VTE	2 (15%)
Physical inactivity	1 (8%)
Genetic blood conditions that affect clotting	2 (15%)

P643 DONATION AFTER CIRCULATORY DEATH IN INTESTINAL TRANSPLANTATION: THE PATH TO PROVE ITS VALIDITY IN BOTH EXPERIMENTAL AND CLINICAL MODELS

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Background: DCD (donation after circulatory death) has been precluded as a valid alternative for intestinal transplantation (IT).
Our aim was double: to test the viability of the intestinal grafts using normothermic regional perfusion (NRP) in an experimental model and to assess ischemic-reperfusion injury (IRI) of the small bowel in human DCD.
Methods: We used an experimental porcine model with 8 donor-recipient pairs (25.5 ± 2.5 kg). Donors were supported using NRP. The small intestine was heterotopically transplanted into the recipients and they were followed-up for two weeks. Blood and intestinal samples were obtained throughout the procedure and 1, 2, 7 and 14 days after. IRI was evaluated using the Park-Chiu score (PCS) in samples taken during NRP and up to 48 hours after IT. Samples from 7 and 14 days were analyzed to assess rejection and GVHD. The absorptive function was tested at the endpoint. Glycemia from the draining veins of the graft was compared with that from the native small bowel and peripheral blood 15, 30 and 60 minutes after intra-graft glucose administration. The intestines from 26 human DCDs were sampled for histological analysis while other organs were procured with NRP after 30 and 60 minutes.
Results: All the intestines were successfully procured. One case was excluded due to venous stenosis. 6 animals (86%) reached the endpoint in good conditions. Grafts conserved architecture during NRP. The highest PCS was observed 1h after reperfusion, with PCS-4 in 3 samples (43%). All grafts recovered, with no or very subtle alterations after 48h. Five recipients (71%) did not show rejection signs at any time. 2 cases (29%) expressed mild rejection after 7 days. At the endpoint, one of them had recovered but the other had progressed to severe acute cellular rejection (14%). Grafts' glycemia reached its maximum 30 minutes after glucose administration. All intestines from human donors appeared macroscopically normal. 80% did not show any significant IRI. PCS was 1.23 [0-3] and 1.65 [0-4] after 30 and 60 minutes.
Conclusions: This experimental model postulate DCD under NRP as an alternative source of organs for IT. Its results appear to be comparable to those of other organ procurement techniques. The analysis of the human samples suggests that this approach could be successfully translated to the clinical setting.

P644 TRANSPLANT RENAL ARTERY STENOSIS – SURGICAL INTERVENTION: TIME IS GFR

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Background: Transplant Renal Artery Stenosis (TRAS) is a well-recognised complication following kidney transplantation. Along with clinical suspicions of rising creatinine, elevated blood pressure, prolonged acute tubular necrosis (ATN) without rejection, the diagnosis is typically confirmed through a CT/MR angiograms or catheter angiography. Percutaneous Transluminal Angioplasty (PTA) is usually the initial treatment modality where possible. Surgical revascularisation is reserved for cases in which PTA is unsuitable and/or unsuccessful. We present our experience of reimplants highlighting common pitfalls and ways to improve function by mitigating them.
Methods: A single centre retrospective study was performed on all transplants between Jan 2019 and Jan 2023. Data on donor and recipient characteristics, operative findings, radiological and histological results, and biochemistry pre- and post-revascularisation was collected.
Results: Out of the 571 patients who underwent kidney transplantation during this time period, 7 were diagnosed with TRAS requiring surgical reimplantation All (3 DBD, 1 DCD and 3 LD) had rising creatinine levels, and those with serial biopsies had evidence of progressively worsening Remuzzi scores. 2/7 patients were reported to have a normal departmental ultrasound. The average time for reimplantation was 85 days post transplantation. 4/7 patients had a prior angioplasty (with half being initially successful - table 1). One reimplant failed to improve GFR and patient became dialysis dependent and there was one patient death due to perioperative cardiac event. 5/7 (71%) had a functioning allograft at the last follow up (4.8 years). The patients with the longest time from diagnosis to definitive treatment (82 days) had the worse graft outcomes (graft failed).
Conclusions: Surgical revascularisation is a complex major procedure, with significant morbidity and mortality, but if performed in the timely manner offers the greatest chance of better graft function and survival. High index of suspicious for TRAS in the face of clinical signs or prolonged ATN without obvious cause should trigger definitive investigations to prevent irreversible damage and worse outcomes
Table 1:

Patient	Donor type	Time from diagnosis & reimplant (days)	Allograft working (Y/N)	Diagnosis of TRAS	Creat 1/12 (µmol/L)	Creat near time of diagnosis (µmol/L)	Most recent Creat (µmol/L)	Remuzzi score pre-op	Remuzzi score post-op	Angioplasty (Y/N)	Cause of failure of the Angioplasty	Reason for surgical revascularisation
1	DBD	75	Y	US 18/02/19, angioplasty 17/03/19, reimplantation 15/03/19	587	504	333	4	5	Y	Inability to pass guidewire through stenosis	Angioplasty unsuccessful
2	DBD	82	N- HD	CT Angio 10/01/19, Angioplasty (10/01/19) 2nd angioplasty (19/03/19) reimplantation (02/04/19)	229	438	HD	3	4	Y	Successful	Re-stenosis
3	DCD	26	Y	CT Angio 18/04/19, angioplasty (01/05/19) reimplantation (14/05/19)	171	405	328	0	N/A	Y	Successful	Re-stenosis
4	LD	4	N- Dead	CT Angio 03/09/21, angioplasty and reimplantation (07/09/21)	274	337	Perioperative death	0	1	Y	Dissection of renal and external iliac artery	Dissection
5	LD	10	Y	CT Angio 19/04/22, reimplantation (29/04/22)	107	182	173	2	5	N	N/A	Tortorous/ kinked- angioplasty unsuitable
6	LD	26	Y	CT Angio 14/04/22, reimplantation (10/05/22)	216	213	140	0	2	N	N/A	Kink- angioplasty unsuitable
7	DBD	1	Y	CT Angio 01/11/22, reimplantation (02/11/22)	146	871	131	0	N/A	N	N/A	Too soon for angioplasty

P645 THE IMPACT OF LIVE KIDNEY DONATION IN A KIDNEY EXCHANGE PROGRAMME ON THE HEALTH-RELATED QUALITY OF LIFE OF THE DONOR

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Background: Kidney exchange programmes (KEP) were introduced as a solution for HLA- or blood group incompatible living donor-recipient pairs. Studies have been conducted to assess the quality of life (QoL) of donors after transplantation but few focused on differences between direct and indirect donation through KEP. This is important because in KEP, a living donor donates to a different person than their intended recipient, who is anonymous to them. In our national KEP, donors (and not kidneys) travel to the recipient center. In this study we analysed the difference in HRQoL between donors who donated directly or indirectly through the KEP. We hypothesize that the HRQoL of donors participating in a KEP is not significantly different compared to donors who directly donated a kidney to their intended recipient.
Methods: All living kidney donors in our centre from 2014 to 2022 were included. Standardized RAND-36 questionnaires were sent at 3-, 6- and 12-months after donation to assess physical and mental health on 8 domains. From these 8 domains the physical- (PCS) and mental component summaries (MCS) were calculated. Higher scores indicate higher HRQoL. Means and 95% confidence intervals were computed. Differences between groups were assessed by nonparametric statistics.
Results: 732 donors were included in the study of which 162 (22%) donated through KEP. At 3-months post-donation, we found a difference in the PCS, with a mean in KEP of 89.2 (95% CI: 86.5 - 91.9) and 84.6 (95% CI: 82.9 - 86.4, $p < 0.01$) in non KEP. The MCS was also higher at 3-months in KEP with a mean of 86.9 (95% CI:83.8 - 89.9) and 82.8 (95% CI: 81.8 - 84.5, $p < 0.03$) in non KEP. Donors who donated through KEP scored better in the domains of limitations due to physical health problems, energy level, mental health, and general health. At 6- and 12-month post-transplant we found that the PCS and MCS were not significantly different.
Conclusions: Living kidney donors who donated via KEP in general have similar quality of life compared to donors who donated directly to their intended recipient. The fact that there appears to be a small but significantly higher HRQOL in the KEP donors at 3-months and no difference after 12-months is another important advantage of KEPs and takes away another level of reluctance to further develop KEPs.

P646 LIVING DONOR NEPHRECTOMY: COMPARISON OF LEARNING CURVES AND SURGICAL OUTCOMES OF ROBOTIC VS LAPAROSCOPIC TECHNIQUE FROM TWO EUROPEAN CENTERS

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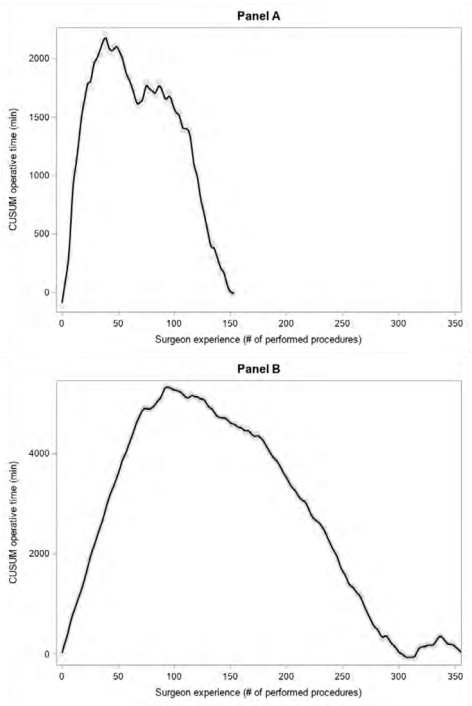
Background: Although laparoscopic donor nephrectomy (LDN) represents the gold-standard technique for kidney living donation, robotic donor nephrectomy (RDN) settled as another appealing minimally-invasive technique over the last decades. A comparison between LDN and RDN outcomes was carried out.
Methods: RDN and LDN outcomes were compared, focusing on operative time and perioperative risk-factors affecting surgery duration. Learning curves for both techniques were compared through spline regression and cumulative sum (CUSUM) models.
Results: The study analyzed 512 procedures (154 RDN and 358 LDN) performed from 2010 and 2021 in two different high-volume transplant centers. RDN group presented a higher prevalence of arterial variations (36.2 vs. 22.4%; p=0.001) compared to LDN cohort. No open conversions occurred; operative time (210 vs. 195 minutes; p=0.011) and warm ischemia time (230 vs. 180sec; p<0.001) were longer in RDN. Postoperative complication rate was similar (8.4% vs. 11.5%; p=0.49); RDN group showed shorter hospital stay (4 vs. 5 days; p<0.001). Spline regression models depicted a faster learning curve in RDN group (p=0.0002). Accordingly, CUSUM analysis highlighted a turning point after about 50 procedures among RDN cohort and after about 100 procedures among LDN group. Higher BMI resulted as an independent risk factor for longer operative time for both techniques; multiple arteries significantly prolonged operative time in LDN, while RDN was longer in right kidney procurements; both procedures were equally shortened by growing surgical experience.
Conclusions: RDN grants a faster learning curve and improves multiple vessels handling. Incidence of postoperative complications was low for both techniques.

Figure. The cumulative sum (CUSUM) analysis of operative time (min) among RDN (Panel A) and LDN (Panel B)



P647 TRENDS AND COST OF HEART TRANSPLANTATION AND VENTRICULAR ASSIST DEVICES IN GREECE-A LOW ORGAN DONATION ENVIRONMENT

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Background: Patients with heart failure (HF) are increasing on a global scale,and the burden in terms of money, labour, and other resources on national health systems continues to grow heavier.Orthotopic heart transplantation(OHTx) is the gold standard treatment for HF but is still reserved due to the shortage of donors.New technologies in the form of durable ventricular assist devices(VADs) or temporary assist devices such as intraaortic balloon pumps (IABPs) and ECLS have emerged to support HF patients.
Methods: Our study used the database of the only HTx centre in Greece to examine the impact of various types of intervention comparing patients transplanted directly to those bridged to transplant with a device and the associated healthcare costs for those patients, along with patient survival rates, and mean waiting times till transplant.
Results: Analysis of the results shows that while 1 year survival rates are similar for both VAD-implanted and HTx patients,VADs quadruple healthcare costs,causing overall care costs to balloon dramatically.
Conclusions: In this analysis of outcomes and costs associated with all the treatment modalities for the end-stage HF, VADHTx and HTx both resulted in excellent one-year survival rates but the use of VAD pre-transplant quadrupled the cost.

P648 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: DIFFERENCES IN PRE-TRANSPLANT RADIOLOGY VERSUS EXPLANT PATHOLOGY REPORTS AND IMPACT ON SURVIVAL

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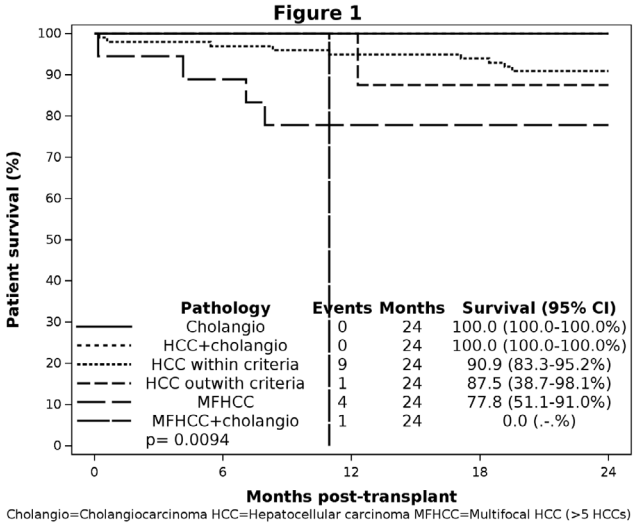
Background: Suitability for liver transplantation in patients with hepatocellular carcinoma (HCC) is based on strict imaging criteria. We sought to establish the accuracy of pre-transplant imaging by cross-referencing explant liver pathology reports and examined the impact on survival.
Methods: Pathology reports of all explant livers from transplants performed for HCC at our centre (January 2015 to December 2020) were compared with pre-transplant imaging reports and UK transplant criteria. Two-year survival outcomes were analysed using Kaplan-Meier estimates.
Results: 140 patients were included. Based on pathology reports, 99(70.7%) patients were within transplant criteria, 35(25%) were outwith criteria, 1(0.7%) had an unclassifiable lesion and in 5(3.6%) no malignancy was identified. 19(13.6%) livers contained >5 HCCs. 9(6.4%) livers contained cholangiocarcinoma. Median interval between imaging and transplantation was 46 days. Of 203 HCCs identified on explant pathology, 122(60%) were definitively identified on imaging, 28(14%) were reported as indeterminate and 53(26%) were missed. 54% of HCCs <10mm were missed on imaging. Overall 2-year survival was 91% and 83% for patients within and outwith transplant criteria respectively (p= 0.174). Patients outwith transplant criteria with >5 HCCs had the poorest survival at 77.8% (p= 0.009) (Figure 1).
Conclusions: In a significant proportion of patients undergoing liver transplantation for HCC, pre-operative imaging failed to accurately identify the pathology, resulting in transplantation outwith transplant criteria. Current pre-operative imaging has suboptimal sensitivity, particularly for lesions under 10mm. Patients with multiple small HCCs have significantly poorer survival and there is a need to accurately identify this cohort to ensure optimal use of liver transplantation. Patients with cholangiocarcinoma did not have poorer outcomes, however numbers were small and further work is required to explore whether transplant criteria should be revised.

Figure 1



Cholangio=Cholangiocarcinoma HCC=Hepatocellular carcinoma MFHCC=Multifocal HCC (>5 HCCs)

P650 REVIEWING CARDIAC STRESS TESTING AS PART OF KIDNEY TRANSPLANTATION WORK-UP

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Background: Cardiovascular events are a leading cause of morbidity and mortality in people with significant chronic kidney disease. Cardiac stress testing can guide risk stratification for transplantation, in addition to identifying people who may require invasive coronary intervention, although the benefit of this versus conservative strategy is contentious. We aimed to look at our practice locally, and review cardiovascular outcomes after a 3 year period.
Methods: We identified all patients we referred for a dobutamine stress echocardiogram (DSE) in 2019 in Nottingham University Hospitals as part of kidney transplantation work up. From this cohort, we reviewed their chronic kidney disease status, indication for referral for the DSE, results of the DSE, whether a cardiology referral was required and whether they required coronary intervention. We also looked for any cardiovascular events for at least a 3 year period since the DSE. We used online hospital patient databases and clinic letters to retrieve this information.
Results: In 2019, 54 patients had DSE performed. The majority had Chronic Kidney Disease Stage 4 or 5 (35/54) and the rest being dialysis and failing transplant patients. Diabetes was the most common reason for DSE request (48%). The average wait time between DSE request and result was 56 days. 33/54 patient had normal DSE results. 12 had inconclusive studies, but 10 of these patients did not require an angiogram or cardiology referral. 8/54 patients had evidence of inducible ischaemia – of these, all were referred to cardiology. 3 patients required diagnostic angiograms and 1 of them had a CABG. The average wait time to see cardiology was 165 days. Of these 8 patients, 3 have died, 2 are not listed as angiogram was suggested once commenced on dialysis, 1 moved, 1 was listed as unfit and 1 was transplanted. After 3 year period, 14/54 of these patients received a kidney transplant and 10 had died. There were 4 cardiovascular events (2 myocardial infarctions, 2 had heart failure).
Conclusions: Cardiovascular events and death rates are significant in CKD population. DSE is a useful tool in predicting cardiovascular outcomes, but research on effects on transplantation listing and longer-term outcomes is needed.

P651 POST-TRANSPLANTATION LYMPHOPROLIFERATIVE DISORDERS: A FOCUS ON OUTCOMES OF LIVING DONOR AND EXTENDED CRITERIA RECIPIENTS

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Background: The increased numbers in living donor (LD) and extended criteria deceased donor (ECD) kidney transplants were two major developments over the last 20 years in most European countries. Post transplantation lymphoproliferative disorder (PTLD) is an aggressive malignancy which carries a lifetime development risk of up to 2.5% for kidney transplant recipients. Aim: To conduct a narrative review related to the effect of PTLD on LD vs deceased donor (DD) recipients, and ECD vs standard criteria deceased donor (SCD) kidney transplant recipients.
Methods: Two searches on databases MEDLINE and EMBASE were conducted for PTLD outcomes on each of LD and ECD transplants, yielding 210 and 125 results respectively. 10 studies were included in the LD category, and 3 studies included in the ECD category following screening.
Results: Within cohort studies, the incidence of PTLD in LD and DD recipients is 0.49% and 2.50% respectively. With a median follow up period of 52 months from transplant, all-cause mortality for PTLD patients was similar at 60% for LD and 61% for DD recipients. For ECD recipients, a higher incidence of PTLD is recorded (HR 2.72, 95% CI 1.38-5.37) when compared to LD, and SCD recipients in a large Australasian analysis, but this result is not fully supported in smaller European studies. In these studies, incidence of PTLD in the ECD group range from 1.60-14.10%, while it is 0-8.20% in the SCD group. No conclusion can be made on mortality. In both study groups, EBV serological mismatch and induction using T-cell depleting agents seem to be associated with higher risk of PTLD.
Conclusions: Efforts to minimising PTLD risk should focus on applying T-cell depleting treatment in a tailored and targeted way, screening for EBV status and providing prophylaxis for CMV, while enabling shared decision-making during counselling when choosing kidney donor types and individualised risk are equally important.

P652 DETERMINING PREVALENCE OF NON-HLA ANTIBODIES IN NON-SENSITIZED BLOOD DONORS. IMPLICATIONS FOR CLINICAL PRACTICE

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Background: The diagnosis of antibody-mediated rejection (ABMR) is limited by the requirement to detect circulating anti-HLA antibodies. In the absence of anti-HLA antibodies, ABMR can be attributed to non-HLA antibodies and determining the sensitivity of current autoantibody detection assays is key to future correlation with pathological and outcome studies. We aimed to identify prevalence of non-HLA antibodies in male blood donors to determine assay testing sensitivities and thresholds, and gain insights on the pre-transplant prevalence of autoantibodies and their most common targets.
Methods: We performed this cross-sectional study using the LABScreen™ Autoantibody solid-phase assay (OneLambda, Thermo Fisher, USA) to test male blood donors (n = 92) for prevalence of 33 known non-HLA antigens.
Results: We observed significant variability between the assays performed and when comparing them to manufacturer-established cut-offs (Figures 1 and 2). The response to positive controls was significantly different between antigens, however this did not affect median MFIs based on control ratio groupings. Within assays, ratios between positive and negative controls ranged from 0.17 to >100, indicating varying degrees of antibody binding to the solid-phase assay. Further, despite being from unsensitized patients, mean fluorescence intensities (MFIs) of antigens varied by significant magnitude. There was further variability when applying manufacturer-established cut-offs to our population. 12/33 antigens had >50% of their samples above the 75th percentile established by the manufactured, while 5/33 antigens had >50% of their samples above the 95th percentile and 12/33 antigens had >25% of their sera samples above the manufacturer-established 95th percentile.
Conclusions: Autoantibody testing, in its current format, is limited by variability in the sensitivity for different antigens, with a large proportion of samples being above manufacturer-established thresholds. Caution should be exercised when interpreting results of non-HLA solid-phase assays, as demonstrated in these unsensitized male blood donors. While further refinement is required in our diagnostic methods, the longitudinal comparisons could be helpful but difficult to interpret in acute presentation.

Figure 1: Ratio of Manufacturer provided positive and negative controls for multiplexing non-HLA antigens demonstrating significant variation in identification of different target antigens. Log10 Transformed

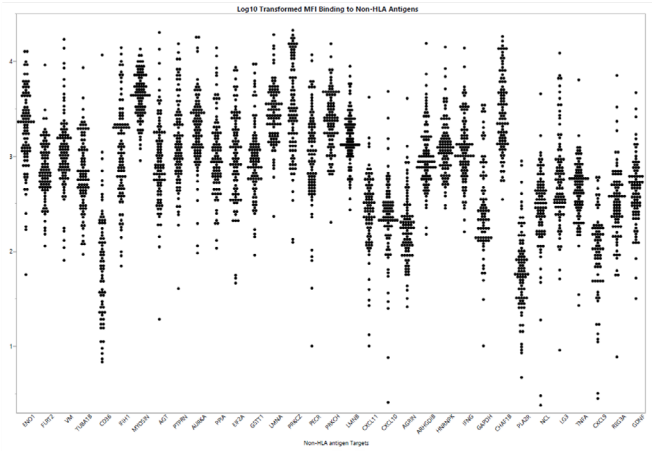
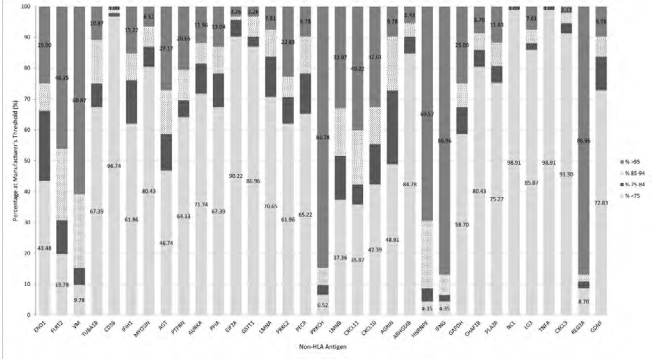


Figure 2: Response of Testing Male Blood Donors using Manufacturer's Threshold cutoffs demonstrated a large proportion of testings being within the <75% MFI and above 95% MFI thresholds



P653 PREDICTION OF GRAFT SURVIVAL PRIOR TO ACCEPTING AN OFFER FOR DECEASED DONOR KIDNEY TRANSPLANT: AN ARTIFICIAL INTELLIGENCE APPROACH

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Background: The current available models for evaluation of outcomes of deceased donor kidney transplant **before** accepting an offer are poorly developed, reported, validated and have small sample sizes. Aim: We aim to use Artificial Intelligence to build a model that can accurately predict overall graft survival for deceased donor kidney transplant prior to accepting an offer
Methods: All deceased kidney transplant patients who were: registered in the UNOS database between 1/1/2007 and 1/6/2021, maintained on TAC/MMF immunotherapy were included in our analysis. We excluded patients with age<18 years old and ABO incompatible transplant. We divided the data randomly into training and testing dataset with ratio 80:20. We performed recursive feature elimination to select the important ones for prediction. Features were selected based on their Gini impurity scores. We performed Artificial Neural Network analysis (ANN). We evaluated the model using dynamic AUC (for discrimination), and Integrated Brier score (for calibration).
Results: 128,409 deceased donor kidney transplant patients were included in the study. Dynamic AUC were 0.70 at 10-years post-transplant, and 0.73 at 13 years post-transplant, indicating very high discrimination power. Integrated Brier Score was 0.15, indicating very high calibration score for our model.
Conclusions: The ANN model had high discrimination, calibration, and performance indices for predicting overall graft survival prior to transplant. It can aid the clinical decision for management of the transplant patients. We are currently developing a user-friendly web application that can be used to apply the ANN model for prediction. Our model can help ranking potential deceased kidney donors based on graft outcomes. Therefore, our model can help improve current outcomes of kidney allocation schemes.

P654 AVAILABILITY OF PRE-DONATION CLINICAL DATA AND OUTCOMES OF KIDNEY TRANSPLANT ALLOGRAFTS FROM DECEASED DIABETIC DONORS

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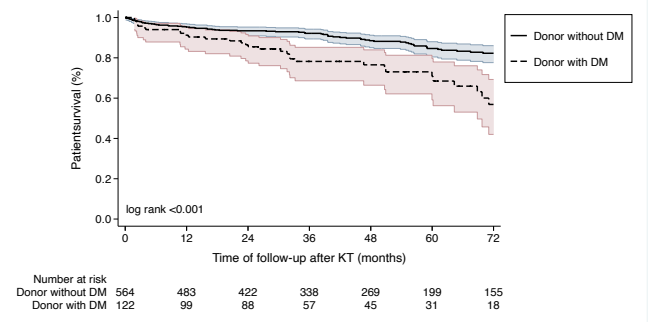
Background: Recipients of deceased diabetic donor kidneys (DM-D) have shown worse graft and patient survival outcomes than non-diabetic donors (N-D). However, pre-transplant information availability of diabetic donors concerning their disease with potential renal involvement is usually limited. We aimed to evaluate the availability of pre-donation clinical data of DM-D vs. N-D to improve our understanding of KT outcomes from DM-D.
Methods: Retrospective single-center study including kidney transplant (KT) patients transplanted from DM-D and N-D (2011-2020). A total of 699 recipients were included, with a mean follow-up of 41.7 (21.7-71.9) months after KT.
Results: We registered 123 (17.6%) DM-D KT and 576 (82.4%) N-D recipients. DM-D were older (67.70 vs. 49.83 years), more comorbid, and had a longer cold ischemia time than N-D (**Figure 1A**). Historical and pre-donation clinical data (creatinine, albuminuria, proteinuria, HbA1c, and fundoscopic examination) were only available in 16.8% of DM-D and 13.1% of N-D. DM-D were assigned to older recipients (66.8 vs. 58.83 years) with more history of cancer. DM-D recipients presented worse creatinine and higher proteinuria in all the studied periods (nadir, 6 months - 5 years). There were no differences in death-censored graft survival between groups. However, patient survival in DM-D recipients was worse (Kaplan-Meier, log rank<0.001) (**Figure 1B**). The multivariate analysis confirmed that an older recipient's age (HR 1.08 [1.07-1.10], p<0.001) and receiving a DM-D graft (HR 1.72 [1.08-2.75], p=0.023) were independent risk factors for mortality.
Conclusions: Pre-transplant information availability of DM-D concerning their disease (HbA1c and renal damage) is scarce. KT from DM-D are associated with higher recipient mortality, regardless of age. The improvement of pre-transplant information availability from DM-D could improve characterizing the impact of these donors on our KT recipients' outcomes.
(Figure 1A)

	Overall cohort (n=699)	Donors without DM (n=576)	Donors with DM (n=123)	p-value
Recipient characteristics				
Age at transplantation, years, mean ± SD	60.11 ± 13.19	58.83 ± 13.42	66.08 ± 13.19	**<0.001**
Female sex, N (%)	240 (34.33)	200 (34.72)	40 (32.42)	0.641
Hypertension, N (%)	664 (94.99)	549 (95.31)	115 (93.50)	0.402
Diabetes mellitus, N (%)	231 (33.05)	184 (31.94)	47 (38.21)	0.180
Diabetes mellitus treatment (insulin), N (%)	190 (82.97)	152 (83.52)	38 (80.85)	0.665
DM microvascular complications[a], N (%)				
None	87 (38.33)	68 (37.57)	19 (41.30)	
Retinopathy	47 (20.70)	41 (22.65)	6 (13.04)	0.111
Neuropathy	11 (4.85)	11 (6.08)	0 (0)	
>=2	82 (36.12)	61 (33.70)	21 (45.65)	
Coronary artery disease, N (%)	109 (15.59)	88 (15.28)	21 (17.07)	0.618
Cerebrovascular disease, N (%)	74 (10.59)	57 (9.9)	17 (13.82)	0.199
Peripheral vascular disease, N (%)	127 (18.17)	99 (17.19)	28 (22.76)	0.145
History of cancer, N (%)	108 (15.45)	76 (13.19)	32 (26.02)	**<0.001**
Cause of ESKD, N (%)				
Glomerulonephritis	112 (16.02)	98 (17.01)	14 (11.38)	
PKD	73 (10.44)	63 (10.94)	10 (8.13)	
Reflux/obstructive nephropathy	40 (5.72)	30 (5.21)	10 (8.13)	
Hypertension	36 (5.15)	32 (5.56)	4 (3.25)	0.358
Diabetes	101 (14.45)	80 (13.89)	21 (17.07)	
Other	52 (7.44)	43 (7.47)	9 (7.32)	
Unknown	285 (40.77)	230 (39.93)	55 (44.72)	
Type of KRT, N (%)				
Hemodialysis	505 (72.25)	408 (70.83)	97 (78.86)	
Peritoneal dialysis	149 (21.32)	129 (22.4)	20 (16.26)	0.299
None (pre-emptive transplant)	41 (5.87)	36 (6.25)	5 (4.07)	
KT	4 (0.57)	3 (0.52)	1 (0.81)	
Time on dialysis, years, median (IQR)	1.9 [1 – 3.3]	1.90 [1 – 3.2]	2.07 [1 – 3.5]	0.566
Donor characteristics				
Donor age, years, mean ± SD	61.22 ± 16.42	49.83 ± 17.01	67.70 ± 11.34	**<0.001**
Donor sex, N (%)	314 (44.99)	261 (45.39)	53 (43.09)	0.641
History of hypertension, N (%)	377 (54.64)	276 (48.68)	101 (82.11)	**<0.001**
History of coronary artery disease, N (%) (n=218)	20 (9.17)	12 (6.32)	8 (28.57)	**<0.001**
History of cerebrovascular disease[c], N (%) (n=325)	241 (74.15)	206 (73.31)	35 (79.55)	0.380
History of peripheral vascular disease, N (%) (n=216)	15 (6.94)	9 (4.76)	6 (22.2)	**0.001**
Donor type, N (%)				
DBD	479 (68.53)	401 (69.62)	78 (63.41)	0.179
DCD	220 (31.47)	175 (30.38)	45 (36.59)	
Cold ischemia time, hours, mean ± SD	14.36 ± 5.66	14.05 ± 5.60	15.83 ± 5.77	**0.002**
Immunosuppression at KT				
Thymoglobulin as induction therapy, N (%)	106 (15.21)	85 (14.81)	21 (17.02)	0.526
Maintenance with CCT + CNI + AMF, N (%)	3 (0.44)	2 (0.36)	1 (0.82)	0.484
Kidney function and Outcomes				
Nadir creatinine, mg/dl, mean ± SD	1.40 ± 0.62	1.37 ± 0.61	1.53 ± 0.66	**0.010**
Creatinine 1 year after KT, mg/dl, mean ± SD	1.71 ± 0.71	1.66 ± 0.68	1.94 ± 0.83	**0.009**
Albuminuria 1 year after KT, mg/g, median (IQR)	65.7 [20 – 216]	48.9 [17.4 – 187]	147.15 [67.9 – 331.7]	**<0.001**
Creatinine 3 years after KT, mg/dl, mean ± SD	1.72 ± 0.82	1.68 ± 0.82	1.97 ± 0.75	**0.016**
Albuminuria 3 years after KT, mg/g, median (IQR)	44.1 [13.6 – 167.8]	38.1 [12.9 – 130.5]	153.07 [35.4 – 351.2]	**0.002**
Delayed graft function, N (%)	209 (32.06)	169 (31.5)	40 (34.48)	0.537
Acute rejection, N (%)	99 (15.23)	82 (15.30)	17 (14.91)	0.917
Post-transplant DM[d], N (%)	115 (16.45)	91 (15.80)	24 (19.51)	0.313
Need of follow-up care from an endocrinologist[e], N (%)	307 (47.38)	242 (45.49)	65 (56.03)	**0.039**
Coronary artery disease, N (%)	62 (9.67)	47 (8.88)	15 (13.39)	0.143
Stroke, N (%)	23 (3.59)	20 (3.78)	3 (2.70)	0.579
Peripheral arterial vasculopathy, N (%)	41 (6.42)	28 (5.30)	13 (11.71)	**0.012**
Cancer, N (%)	90 (14.04)	75 /14.18)	15 (13.39)	0.828
Primary non-function, N (%)	50 (7.15)	42 (7.29)	8 (6.50)	0.758
Death-censored graft failure, N (%)	126 (18.03)	102 (17.71)	24 (19.51)	0.637
Mortality, N (%)	121 (17.31)	85 (14.76)	36 (29.27)	**<0.001**

1B.



P655 EVALUATION OF KIDNEY DONOR RISK INDEX / KIDNEY DONOR PROFILE INDEX AS PREDICTOR TOOLS OF DECEASED-DONOR KIDNEY TRANSPLANT OUTCOMES IN A GREEK COHORT

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Background: Kidney Donor Risk Index (KDRI)/Kidney Donor Profile Index (KDPI)have been developed as predictive tools to assess deceased-donor graft quality, although validation of their utility outside the USA remains limited.The present study evaluated the ability of KDRI,KDPI to predict transplant outcomes in a Greek cohort.
Methods: A single-center retrospective cohort study, included all deceased-donor kidney transplantations between 1st/2008 and 12th/2018. Donors were assessed with KDPI/KDRI scores. Additionally, they were categorized according to Standard Criteria Donor (SCD)/Expanded Criteria Donor(ECD) classification. The efficacy of KDPI and donor age in predicting death-censored graft failure was primarily assessed. Secondary endpoints included delayed graft function (DGF), kidney allograft function and patient survival. Statistical analysis was performed by fitting multivariable linear regression and Cox proportional hazards models. The median follow-up period was 6.3 years [3.6-10].
Results: A total of 394 kidney donors with a median age of 53 years [39.3-61] were included. The recipients' median age was 52 years (43-59). Donors had a median KDRI of 1.02 (IQR: 0.78 to 1.34) and a KDPI of 54 (IQR: 25 to 79). Death-censored graft survival was significantly worse with higher KDPI (Hazard Ratio-HR:1.01, 95% confidence intervals-CI: 1.00-1.02) and donor age (HR: 1.03, 95% CI: 1.00-1.05). The unadjusted discriminative ability was similar for KDPI (C-statistic: 0.54) and donor age (C-statistic: 0.52). The KDPI threshold of 85 was not predictive of graft failure (p-value: 0.19).Higher KDRI, KDPI values were linked to delayed graft function (DGF) and lower eGFR in the 1st, 3rd, and 5th post-transplant year, but not among ECD transplantations. No significant correlation was found between KDRI, KDPI and patient survival.
Conclusions: In our population higher KDPI, KDRI values were linked to worse graft function, as well as to DGF. However, their ability to discriminate long-term graft failure was limited. Donor age had similar prognostic value to KDRI, KDPI indexes.

P657 THE FALL OF A MYTH: THE FIRST THREE CASES OF DONATION AFTER CIRCULATORY DEATH IN INTESTINAL TRANSPLANTATION

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Background: The universal shortage of organs has prompted the growing use of donations after circulatory death (DCDs). Nonetheless, the use of DCD as a source of intestinal grafts has been denied due to concerns regarding their ischemic susceptibility. This belief has been widely accepted for years. Now this myth is over: we present the first three DCD cases in intestinal transplantation in the world.
Methods: We reviewed the cases of intestinal transplantation after DCD performed at our center. Technical, demographic and clinical data relating donors and recipients were collected. Recipients were also studied in detail during their clinical and histological follow-up.
Results: Three DCD multivisceral transplants (MVT) were performed at our institution between June 2022 and January 2023. Donors (3M) had a mean age and weight of 3 months (1-6) and 5.3 kg (4-8). Their death was declared after their cardiac arrest and a 5-min "no-touch period". Then, a rapid laparotomy was performed and a normothermic regional perfusion (NRP) was established. Warm-ischemia time was 25 minutes (23-29). Recipients were 3 patients (2F/1M) with short bowel syndrome (jejunal atresia and meconium cyst, Hirschsprung's disease, multiple intestinal atresia with severe combined immunodeficiency). Their mean age and weight were 19 months (9-36) and 4.9 kg (3.88-6.8). They all received a MVT leaving an ileostomy. Cold-ischemia time was 383 minutes (340-420). After MVT, biopsies showed a complete recovery of the architecture of the intestinal epithelium in all cases. After a mean follow up of 3 months (0-7), two patients have done exceptionally well with only a mild self-limited cutaneous GVHD in one case and a humoral sensitization perfectly controlled in the other. Ileostomy could be taken-down in one 8 months after MVT. The third patient is being treated for enterocolitis and has needed a proximal jejunostomy.
Conclusions: DCD in intestinal transplantation is feasible as demonstrated by our world-leading series. The ischemia-reperfusion injury in these grafts seems to be transient and reversible. Although experience is limited, their use could address the mismatch between the waiting list for intestinal transplantation and the scarcity of donors, especially in situations of need such as pediatric transplantation.

P658 PREFORMED DONOR-SPECIFIC ANTIBODIES IN DECEASED-DONOR KIDNEY TRANSPLANTATION: A SINGLE-CENTER STUDY

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Background: The prognostic value of preformed HLA Donor-Specific Antibodies (pre-DSAs) detected by sensitive solid-phase assays on the long-term outcomes in Deceased-Donor (DD) Kidney Transplantation (KT) has not yet been fully elucidated. The aim of this study was to evaluate the effect of pre-DSAs on long-term patient and kidney allograft outcomes in a single-center cohort.
Methods: A retrospective, matched (1:1), cohort analysis of 110 DDKT recipients, between 1st/2011 and 12th/2021 was conducted. In total, 55 patients (21 males), with a median age of 49 years and pre-DSAs at the time of DDKT, were matched for recipients' demographics, time on dialysis and follow-up period with 55 patients without pre-DSAs (control group-CG), at the time of DDKT. Patients' blood samples were analyzed for IgG DSA using a SAB assay (One Lambda). Mean Fluorescence Intensity (MFI) values >1000 were considered positive for DSA. All patients were transplanted with negative CDC and T/B Flow Cross-match (FCM). There were no significant differences in immunosuppression regimens between the two groups, whereas 26/55 patients with pre-DSAs received the anti-CD20 monoclonal antibody Rituximab. The median follow-up period was 48 [12-145] months.
Results: Detected HLA-DSAs were class I, with a median MFI 1965 [1011-4305] in 31/55 patients (56%), and class II, with a median MFI 3012 [1095-24719] in 24/55 patients (44%). Sixty-five% of pre-DSAs patients had cPRA>70%. There was a significant difference in DGF occurrence between the two groups (76% vs 51% in the CG, p=0.005). Patients with pre-DSA had a higher incidence of early transplant biopsy-proven acute rejection (BPAR) (20% vs 9%, p=0.09), mainly Acute Cellular Rejection (ACR) (68.5%) and mixed ACR-Antibody Mediated Rejection (18.5%) within 30 days post-transplant. There was no significant difference in *de novo* DSA development between the study groups (11% vs 5.5%, p=0.49). The eGFR was comparable in both groups during the entire study period (p>0.4). Death-censored graft survival rates and patient survival rates were not significantly different between the groups.
Conclusions: DDKT recipients with circulating pre-DSA are at an increased risk of BPAR, which doesn't seem to influence the long-term outcomes.

P659 IMPLEMENTATION OF NEW M-HEALTH TOOL TO MONITOR IMMUNOSUPPRESSION ADHERENCE AND VITAL PARAMETERS IN KIDNEY TRANSPLANT PATIENTS

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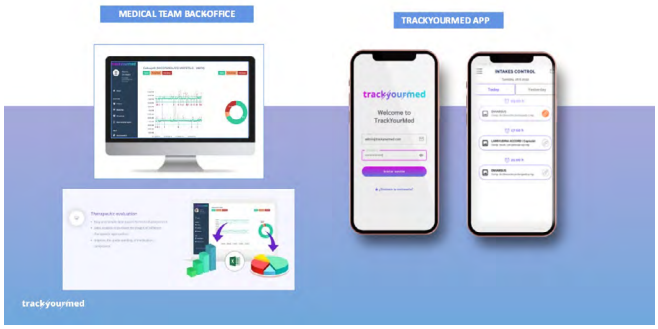
Background: Current management of immunosuppression adherence is based on unreliable and ineffective tools, which do not allow any understanding of the degree of medication adherence. Also, main vital parameters such blood pressure, glycemia or weight are key variables to understand the proper evolution of a kidney transplant patient. We developed a novel digital m-Health tool in which the medical team can perform an accurate follow-up and monitorization of transplant patients through a digital platform who receives in real-time all the feedback from patient's behaviour through a smart mobile App (Trackyourmed®; TYM).
Methods: From November 2021 until December 2022, 208 consecutives kidney transplants from our transplant centre, were proposed to actively use TYM, based on a novel App directly interconnected with a back-end platform used by the medical team. The aim of the study was to describe the lifespan of this new tool, both from the physician and patient's perspectives. We recorded main reasons for not accepting its use, for stopping its use and for its active usage during the 12-month study follow-up. We analyzed main clinical and demographic variables, also degree of medication adherence and interval of times of medication in-takes.
Results: In 68%, TYM was given right before being discharged after receiving a kidney transplant and in 42% TYM was offered at the out-patient clinic in patients with a functioning graft for more than 2 years. Out of these 208, 64% were male and 36% female, with a mean age of 54.9 (range: 18-90). Six percent did not accept TYM because of no or lack of use of a smart phone, 28% because they already had a different tool to guide medication adherence and 66% accepted its use. At current mean time of follow-up (10+/-5 months), 49.5% were actively using TYM, with 54% (23/44) patients with more than 12 months of active use. Notably, the physician with the highest recruitment and active use, showed very low rates of withdrawal (25/73 [34%]). Mean optimal adherence to immunosuppression in-takes during the previous 2 months was 61%, erratic adherence (in-takes out of time) was 10.1%, whereas 41% showed absence of some medication in-takes.
Conclusions: Implementing m-Health technology for improving immunosuppression adherence may be an excellent option for an important percentage of transplant patients.



P660 GENE EXPRESSION PROFILES OF PERITUBULAR CAPILLARITS IN CHRONIC ANTIBODY-MEDIATED REJECTION

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Background: Chronic antibody-mediated rejection (ABMR) is a significant cause of late allograft loss. Diffuse ptc (extent >50%) was associated with worse graft survival independent from the ptc score. Nevertheless, current ptc thresholds are arbitrarily defined and may not reflect pathophysiological phenotypes accurately. We hypothesize that re-assessment of ABMR biopsies with the Nanostring-NCounter based gene expression analysis allows the definition of novel thresholds of ptc extent, reflecting molecular ABMR phenotypes more accurately.
Methods: We retrospectively analyzed 25 patients with ABMR/chronic ABMR and presence of donor specific antibodies, treated at two centers (Medical University of Vienna and Ordensklinikum – Elisabethinnen Linz). PTC was re-evaluated by an experienced external nephropathologist (M.M.) and included the ptc score as well as the ptc extent (focal ptc: 10-50%, diffuse: >50%). We performed Nanostring nCounter Gene expression analysis with a customized gene set corresponding to the recommendations in Banff 2017 guidelines. Gene expressions above the first quartile ($ABMR^{Q>1}$) were considered as positive values for ROC analysis.
Results: Biopsies with diffuse ptc had significant higher gene expressions with the ABMR gene set [63/55-83 vs. 32/27-52; (median/IQR); p=0.012], the ABMR exhaust gene set (390/245-609 vs. 245/128-358; p=0.022), the Eculizumab gene set (180/143-339 vs. 65/57-133; p=0.0027) and the TCMR gene set (48/40-75 vs. 25/19-35; p=0.001). Sensitivity analysis revealed improved AUCs for predicting biopsies with ABMR gene expressions over the 1st quartile with a ptc cutoff of 35% compared to ptc cut-off of 50% [$ptc^{>35}$: AUC 0.76/0.61-0.90 (95% CI), p=0.013; $ptc^{>50}$: AUC: 0.71/0.54-0.88, p=0.039].
Conclusions: With the application of gene expression-based Nanostring platform we were able to identify a new threshold of ptc extent. The newly proposed cut off >35% may reflect molecular phenotypes of ABMR more accurate than the current one and could improve early diagnosis of ABMR.

P662 TRANSPLANTATION OF EXTENDED CRITERIA DECEASED DONOR KIDNEYS TO EXTENDED CRITERIA RECIPIENTS: A CHALLENGING COHORT

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Background: Extended criteria deceased donor kidneys have become an accepted option in order to increase the donor pool, decrease waiting times and increase the number of transplants. The objective of the study was to compare outcomes of deceased donor kidney transplants from extended criteria donors to extended criteria recipients vs. standard criteria donors to standard criteria recipients.
Methods: Retrospective single-centre study of 88 recent deceased donor kidney transplants performed between 1 January 2022 and 1 July 2022. Extended criteria were defined as donors or recipients with one or more of the following: age>60, BMI>30, hypertension, diabetes, coronary artery disease, pre-retrieval donor creatinine> 2.0 mg/dl.
Results: 46.5 % of the kidneys were retrieved from donors after circulatory death, while 53.4% from donors after brain death. 25% of the grafts came from standard and 75% from extended criteria donors. 8% of recipients were standard and 92% of extended criteria. Of all transplants, 4.5% were of standard criteria recipients who received organs from standard criteria donors, and 69.3% of extended criteria recipients who received organs from extended criteria donors. Graft survival rates, with a mean follow-up of 6 months, were better in the standard criteria group (p<0.05). Rates of surgical complications (bleeding, hernia and surgical site infection) were higher in the extended criteria group (p<0.05). There was no significant difference in the e-GFR values between the two groups at 6 months' post-transplantation (p=0.66).
Conclusions: Extended criteria transplantation is "here to stay" considering the increasing prevalence of kidney failure and the aging donor and recipient populations with the relevant co-morbidity. Stratification of risk for the allocation of extended criteria kidneys to extended criteria recipients as well as mitigating modalities such as organ reconditioning are crucial for improving outcomes.

P663 PREEMPTIVE KIDNEY TRANSPLANTATION: EXPANDING TO ALL KIND OF DONORS AND RECEPTOR

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Background: Preemptive kidney transplantation without prior dialysis initiation improves patient and graft survival compared to remaining on dialysis or undergoing transplantation after initiation of dialysis. Despite its advantages, mainly due to organ shortage, starting kidney replacement therapy (KRT) with a preemptive kidney transplant occurred only in 4.5% of patients in 2021(6.8 pmp).
Methods: Single center descriptive study of patients who received isolate or combined preemptive kidney transplants performed and followed up in our center from the start of the program on 7/2/1979 to 7/12/2022. Clinical-demographic variables of donors/recipients/transplant as well as glomerular filtration rates (GFR) were collected.
Results: From a total of 2057 kidney or combined transplants, 105 of them (5.1%) received a preemptive kidney graft. 72.4% (N=76) were males with a mean age of 46.6±14.6 years and received a renal graft from donors of 45.2±16.1 years. From those 105, 58 were isolated kidney transplants (55.2%) and 47 combined transplants: 32, simultaneous pancreas-kidney transplant (30.5%); 13, liver-kidney transplants (12.4%); 1 heart-kidney transplant and a liver-pancreas-kidney transplant. In the isolated kidney transplant group regarding the type of donation, the majority were from living donors, 53.4% (N=31); 36.2% (N=21) were from brain-dead donors and only 6 were circulation-dead donors. Regarding ABO blood group, 74.1% (N=20) were group A, 14.8% (N=4) group AB, 2 cases were group B, and only one transplant belonged to group 0.
Patients were included on the preemptive waitlist with an average creatinine of 4.9±1.21 mg/dl, with a corresponding CKD-EPI eGFR of 12.75±3.57 ml/min/m^2.
Conclusions: Despite preemptive kidney transplantation is the best option for KRT, the proportion of patients in this modality remains low (5.1% of the total transplants). This modality seems to be limited to living donor and to combined transplantation with other organs, however, 26% of our transplants were procured from deceased donors belonging the majority of them to group A recipients receiving brain-dead donors. As organ shortage and waitlisting times change, this modality should be expanded to a greater number of donor/recipient pairs.

P664 DECEASED ORGAN DONATION ACTIVITY, IN THE CRITICAL CARE UNIT OF A GREEK UNIVERSITY HOSPITAL, DURING 2022

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Background: Despite the strategies to increase organ availability, the rate of organ donation in Greece remains low, especially during COVID-19 pandemic. The current study is aimed to describe the deceased organ donation activity during 2022, in a medical-surgical critical care unit of a Greek University Hospital.
Methods: We retrospectively studied the deceased organ donation activity during 2022, in the 2nd Department of Critical Care of ATTIKON University Hospital of Athens. This is a 40-bed medical – surgical intensive care unit, in which ten COVID-19 and 30 non COVID-19 patients are hospitalized. Donors' demographic characteristics, cause of death and bacterial colonization data were recorded. Days of mechanical ventilation, time of organ procurement after brain death and number of organs and tissues procured were also provided.
Results: During the study period, there were eleven actual deceased organ donors after brain death, 4 females and 7 males. The mean (±SD) donors age was 51.3 (±16) yo, while the most common cause of death was intracerebral or subarachnoid haemorrhage (8 donors). The mean duration of mechanical ventilation until donation was 16 (±5) days, while the time frame between death (confirmed by brain death tests) and donation was 3 (±0.6) days. Bacterial colonization was observed in four donors, who respectively developed *Staphylococcous aureus, Klebsiella pneumoniae, Acinetobacter baumannii* and *Enterobacter clocae* in bronchial secretions. All the strains were susceptible to commonly used antibiotics, while the donors did not demonstrate any signs of infection. Thirty-seven solid organs were procured, among which, 18 kidneys, 8 lungs, 2 hearts, 8 livers and one pancreas.. 64% were multiorgan retrievals and 95% of the harvested organs were transplanted in Greek patients. Moreover, 18 cornea procurements have been performed.
Conclusions: Organ donation procedure requires devoted healthcare personnel, to preserve the opportunity of potential organ donation before the death and to ensure actual donation after death, after consent has been obtained from the relatives. The study indicates a deceased donation activity which is reaching the prepandemic rate. However, there are measures that should be taken to maximize the availability of organs and satisfy the transplantation needs.

P665 LONG TERM OUTCOMES OF COMBINED LIVER KIDNEY TRANSPLANTATION

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Background: Combined liver kidney transplant (CLKTx) is the mainstay of treatment for concurrent liver failure and end stage renal failure. The use of CLKTx has increased markedly since the introduction of the MELD (Model for End Stage Liver Disease) score for liver allocation. In this study we examined the long-terms outcomes of 25 years of cLKTx in our centre with a specific attention on patient and liver/kidney graft survival.
Methods: From a database of all transplants for the 25-year period from 1997 – 2022, 158 recipients of CLKTx were identified. Primary outcomes of interest were mortality and graft failure. Data was analysed in R studio and GraphPad prism.
Results: Overall patient survival was 89% at 1 year, 87% at 2 years, 81% at 5 years, 72% at 10 years and 50% at 20 years. The 20 year patient survival with a pre-transplant MELD of <20 was 52%, with a PreTx MELD of >20 associated with significantly lower 20 year patient survival of 26% (P<0.05). Death censored (dc) liver graft survival was 99% at 1 year, 98% at 2 years, 97% at 5 years and ten years, and 88% at 25 years. A donor age of <40 showed 20 year liver graft survival (dc) of (100%), which was significantly greater than the donor age >40 group (72%, P<0.05). Death censored kidney graft survival was 96% at 1 year, 95% at 2 years, 95% at 5 years, 92% ten years and 84% at twenty years post Tx. There was no statistically significant impact of donor age on kidney graft survival. The acute kidney rejection rate was 16%, with a chronic rejection rate of 1.4%. The liver acute rejection rate was 4% and no chronic rejection events observed in our cohort. Stratification by indication revealed a better kidney survival in patients with hepatorenal polycytosis compared to other indications (97% v 83%, P<0.05). No difference in liver graft survival or patient survival was observed based on transplant indication.
Conclusions: We report favourable long-term outcomes following 25 years of CLKTx. Predictors for better long term patient and graft survival include pre transplant MELD score and donor age.

P666 ESTIMATING TIME TO LIVER TRANSPLANTATION USING PROGNOSIS SCORES IN PATIENTS WITH LARGE-DUCT PRIMARY SCLEROSING CHOLANGITIS

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Background: Primary sclerosing cholangitis (PSC) is a chronic progressive cholestatic disease with poor prognosis and high need for liver transplantation (LT). Estimating prognosis of the disease is challenging due to disease heterogeneity and insufficient biomarkers. Magnetic resonance cholangiopancreatography (MRCP) is used for the diagnosis and follow-up of individuals with PSC and can be also associated with outcome. The aim of our study was to assess the need for LT in patients with large-duct PSC.
Methods: The following scores: revised Mayo Risk Score (rMRS), Amsterdam Oxford Model (AOM), UKPSC, PREsTo, MELD-Na score, FIB-4 and APRI scores, Majoie endoscopic retrograde cholangiopancreatography classification applied to MRCP studies were analysed in 48 patients with large-duct PSC. Univariate and multivariate Cox proportional hazards model was used to identify the need for LT in this cohort of patients.
Results: There were included 58.3% females and 41.7% males with a median age at diagnosis of 40.5 years. 27.1% of patients had associated inflammatory bowel disease. The median period of follow-up was 7.7 years since diagnosis. LT was performed in 20.8% of cases, 12.5% developed cholangiocarcinoma and 12.5% of patients died during follow-up. The following prognosis scores were associated with the need for performing LT in PSC patients in the univariate Cox regression analysis: higher AOM score at diagnosis (p=0.006), higher negative short-term UKPSC score (p=0.04), higher score of intrahepatic ducts changes at MRCP classification (p=0.01), higher Meld-Na score (p=0.01), higher FIB-4 score (p=0.009), a higher serum bilirubin at diagnosis (p=0.02). A higher score of extrahepatic ductal changes at MRCP reached only a marginal significance in predicting the need for LT (p=0.06) in our cohort. Multivariate Cox regression analysis identified the following single independent prognostic factor related to the need of performing LT was the higher score for the intrahepatic ductal changes (p=0.02).
Conclusions: More severe intrahepatic ductal strictures at MRCP classification is strongly associated with a negative outcome and lower transplant free survival, indicating its prognostic value for our PSC patients in clinical practice.

P668 EVALUATING THE BIDIRECTIONAL IMPACT OF KIDNEY TRANSPLANTATION AND HIV CONTROL

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Background: Kidney transplantation is now a viable option for patients living with HIV who have progressive end-stage renal disease and well controlled HIV, with resultant good clinical outcomes. However, kidney transplant recipients living with HIV (KTRLHIV) are found to have increased rates of graft rejection and studies suggesting immunosuppression variably impacting HIV control.
Methods: A retrospective analysis of electronic health records was preformed from 1998 to 2022 for key metrics correlating with HIV control in the KTRLHIV cohort (n=29). Kidney function metrics were also extracted and compared to a 1:1 matched HIV-negative KTR cohort. Patients were matched for age (55 years, range [43,74]), sex (66% male), ethnicity (72% black), and years since KT (7.4 years, range [0.7,23.8]).
Results: Average years since HIV diagnosis was 20.2years (95% CI [16.6, 23.7]), with all but 1 patient having an undetectable HIV viral load (1 patient with 166 copies/ml). Comparing pre and post-transplant averages, the CD4 count reduced by 30cells/mm3 (p=0.18), the total lymphocytes reduced by 144cells/μL (p=0.12), and the CD4:CD8 ratio increased by 0.029 (p=0.32). Average eGFR in the KTRLHIV was 34 (95% CI[26.8, 41.6]) vs 43 (95% CI[35.7, 50.1]) in the matched HIV-negative KTRs (p = 0.045). Average creatinine in the KTRLHIV was 247 (95% CI [164.9, 329.4]) vs 159 (95% CI[126.9, 192.4]) in the matched HIV-negative KTRs (p = 0.023). Higher rates of graft rejection were seen in the KTRLHIV (38% vs 10%, p=0.014). Majority of these cases in the KTRLHIV were T-cell mediated rejection (21%), followed by anti-body mediated rejection (10%), and mixed acute rejection (7%).
Conclusions: There is no statistically significant difference in key HIV control metrics when comparing pre-transplant and post-transplant levels. Significantly worse overall kidney function and higher rates of acute rejection is noted in the KTRLHIV when compared to a matched HIV-negative KTR cohort

P669 EPH RECEPTOR SIGNALLING AND CELL MIGRATION IN 3 D CELL CULTURES THROUGH EPHRIN MIMETIC PEPTIDES

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Background: The end-stage liver failure is a key challenge in regenerative medicine because of the ageing society and the severe shortage of suitable donor organs. Tissue engineering is emerging as a novel technology using cells with regenerative capacity, 3D scaffolds or synthetic materials, growth factors and morphogens to induce tissue regeneration. The aim of our study was engineering of extracellular matrix (ECM)-mimicking scaffolds for effective growth factor and morphogen delivery that can act as an inductive template for functional 3D tissue and organ reconstruction after recellularization with autologous stem cells or differentiated cells.
Methods: Plasmid transformation and DNA miniprep and maxiprep preparation, Mammalian cell culture, Calcium phosphate transfection, microscopy, SDS-PAGE and Western Blot, RNA isolation and cDNA synthesis, PCR, qPCR, Construction of vectors for ephrinA1 secreation, Fibrin and thrombin preparation, Hepatocyte isolation and preparation of cell spheroids, cell 3D engineering in hydrogels were performed. The resulting DNA/Ca/HBS solution was incubated for 20 min at room temperature and then distributed onto the cells. Transfected cells were incubated for 12 h in 5 % CO_2 incubator at +37 °C and transfection medium was replaced with fresh DMEM++ medium and cells incubated fir additional 24 h. Results were evaluated using an inverted fluorescent microscope. The same methodology was used for cloning ephrin genes into pFUSE and pC4W vectors for eukaryotic gene expression in Expi293 cells.
Results: Protein bands visible in coomassie gels are indeed His tag expressing ephrins. Their expression is not detected in the absence of IPTG treatment and was visible upon treatment with IPTG. Our data indicate that Expi293 cells are suitable for production of engineered TG ephrin A1, ephrin A1 TG proteins. This might be due to the fact that pFUSE vectors have a hybrid LTR/E1-Fα promoter which is not strong enough in comparison with other viral promoters (CMV, SV40).
Conclusions: Our data demonstrate that we produced functional TG-ephrinA1 and ephrinA1-TG molecules that could be incorporated into fibrinogen hydrogels and induce migration of human hepatocyte non parenchymal cells and also chondrocytes.

P670 CHRONIC ALLOGRAFT NEPHROPATHY IS AGGRAVATED IN AGED DONORS BY THE EXACERBATION OF AGE-RELATED LOSS OF PROTECTIVE FACTORS

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Background: Kidneys are crucial for homeostasis and overall survival, and the prevalence of kidney disease increases with age. The age classification of donors and recipients is a way of expanding the group of donors. Kidneys from elderly donors have a higher risk of developing chronic allograft nephropathy (CAN). Mechanisms contributing to CAN have been linked to cellular senescence, a process implicated in regeneration failure and progression to fibrosis. However, the molecular and pathological basis of the age-related increase and its relation with iron homeostasis is not completely understood.
Methods: Experimental renal transplant model in rat were used. Young (3mth) and old (10mth) donors and recipients were used to perform isogenic and allogenic group without immunosuppressive treatment into 3 groups old-to-old, old-to-young and young-to-young donor/recipient groups. Tubular damage score, and proinflamatory chemoquines, regulated necrosis, ferroptosis, necroptosis, apoptosis, senescence, age-related loss of protective factors and production of senescence-associated secretory phenotype components (SASP) were evaluated by Real Time. In parallel biochemical parameters of iron metabolism were determined on blood and tissue.
Results: From all processes evaluated we could not elucidate significant differences between old and young grafts independently from the recipient's age, although a slight increase (not statistically significant) of these processes was observed in the old grafts. The analysis of the gene expression levels of SASP components Tgfβ1, Il6, Ctgf, PAI-1, showed that Tgfβ1 were over-expressed all grafts independently of age; IL6 and PAI1 were over-expressed in old grafts compared to the young ones, and CTGF were down-expressed in old grafts compared to the young ones. The senescent cell apoptosis resistance factor BCL-2 was evaluated. Bcl2l1 gene was conserved on isogenic grafts, but in all allogenic grafts independently from age was down-regulated. None of the blood parameters showed differences between groups.
Conclusions: In conclusion, our model did not show statistically significant results but indicates that the expression of renal protective factors are decreased in old grafts evidencing the need of further studies with older donors (20mth).

P671 MI-EDON STUDY: THE ROLE OF RESPIRATORY PHYSIOTHERAPY AS TOOLS FOR THE OPTIMIZATION OF THE LUNG DONOR

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Background: Mechanical Insufflation-exsufflation (MIE) is a non-invasive device to simulates a cough and thus favoring the elimination of secretions. There is no evidence regarding its use in the maintenance/optimization of solid organ donors. We intend to assess whether the use of MI-E in eligible donors is safe and improves oxygenation parameters.
Methods: This is a preliminary safety analysis of a prospective multicenter study conducted in 4 national centers. 10 eligible donors offered in 1month have been included. After completing national maintenance oriented towards pulmonary optimization (OTP) MI-E cycles were implemented. Blood gas monitoring (Pa/FiO2) (FiO2 1 and PEEP 5) was performed: initial, post MPO, 10 min and 60 min post MI-E. Complications derived from the technique were recorded.
Results: Five donors were eligible lung donors (PaFi>300, ELD) and 5 did not were eligible (PaFI<300, NELD). ELD maintained PaFi>400 after the MI-E. Four of 5 NELD increased 25.4% the PaFi and it was maintained 1h after (Table 1). No one had complications during or after MI-E.
Conclusions: MI-E seems to be a safe technique who use could be useful to increase the lung donor pool.

Table 1

		Initial	Post-OTP	Post-MIE	Post-MIE 60´	Δ1(%)	Δ2(%)	Δ3(%)
ELD	pH (SD)	7,45 (0,04)	7,44 (0,09)	7,48 (0,06)	7,44 (0,1)			
	PaO_2mmHg (SD)	428,2 (65,94)	447 (72,44)	436,8 (84,18)	406 (32,39)	18,8 (8%)	-10,2 (-0,4)	-30,8 (-5,05)
	$PaCO_2$mmHg (SD)	34,5 (2,95)	39,22 (12,32)	32,5 (4,52)	34,8 (6,41)			
	HCO_3mmHg (SD)	24,46 (1,97)	25,58 (1,96)	24,56 (3,04)	24,14 (2,5)			
NELD	pH(SD)	7,47 (0,08)	7,46 (0,05)	7,47 (0,09)	7,45 (0,13)			
	PaO_2mmHg (SD)	255,8 (36,43)	307,4 (26,6)	334,2 (56,22)	302,4 (93,10)	51,5 (21,6)	26,8 (25,48)	31,8 (11,24)
	$PaCO_2$mmHg (SD)	39,68 (6,49)	38,56 (2,84)	37,84 (7,18)	36,64 (8,49)			
	HCO_3mmHg(SD)	28,08 (2,49)	27,24 (2,41)	28,04 (1,71)	27,24 (1,38)			

P672 LAPAROSCOPIC LIVE DONOR NEPHRECTOMY AND VASCULAR ANATOMICAL VARIATIONS: A CHALLENGE FOR THE TRANSPLANT SURGEON

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Background: Laparoscopic live donor nephrectomy is a widely accepted procedure for the most transplantation centers worldwide. However, choosing the suitable donor side for kidney retrieval, is a very challenging task for the performing surgeon, which is principally affected by the donor's vascular anatomy and complexity. As a result, CT angiography is necessarily performed in all cases. There is scarce data regarding the variations of the renal vessels and its implications to their recipients, consequently it is constantly a debatable subject.
Methods: In our center, 267 laparoscopic live donor nephrectomies were performed from October 2018 until December 2022. In all cases CT angiography was performed preoperatively. We analyzed the data, where the cases with single renal vessels were excluded. As a result, a total of 107(40%) cases were included in this research.
Results: Anatomical variations were present in 40% of the cases. Concomitant different anatomical variations were observed in 31 of 107 cases (28%). Regarding the left kidney, double artery was present in 35 out of 107 cases, 5 cases had double renal vein and 12.2% of the patients had retroaortic course of the renal vein in general. On the other hand, dual right renal artery was observed in 28 patients while 18 patients had dual right renal vein (16.8%). Rest of the vascular variations are concluded in Table 1. Operation Time and warm ischemia was slightly higher in these cases, but that fact was not clinically significant neither to the donor nor to the recipient. Blood transfusion was not needed in these patients. In addition, complication rate was very low with only 2 cases (1.87%) presenting chylous ascites postoperatively, which have been treated conservatively with dietary modification. Hospitalization length was similar to the patients with single renal vessels.
Conclusions: Vascular anatomical variations regarding live donor nephrectomies are pretty frequent and represent a challenge for the surgeon pre- and intraoperatively. CT angiography should not be neglected preoperatively. Through our experience, multiple renal vessels do not constitute a negative impact to the donor and the recipient. In addition, implications were rarely observed, thus we recommend harvesting kidneys with multiple vessels, but not more than 2 arteries

TABLE 1. RENAL VESSELS VARIATION

ANATOMICAL VARIATION	Number of cases	Donor Implications	Recipient Implications
DUAL LEFT ARTERY	12	-	-
DUAL LEFT ARTERY (LOWER POLE)	11	-	-
DUAL LEFT ARTERY (UPPER POLE)	8	-	-
DUAL LEFT VEIN	5	-	-
LEFT VEIN BIFURCATION	1	-	-
RETROAORTIC LEFT VEIN (JOIN IVC AT L4-5 LVL)	13(8)	2 (chylous ascites)	-
LEFT ARTERY BIFURCATION	10	-	-
TRIPLE LEFT ARTERY	5	-	1 (renal artery Thrombosis)
DUAL RIGHT ARTERY	19	-	
DUAL RIGHT ARTERY (LOWER POLE)	5	-	-
DUAL RIGHT ARTERY (UPPER POLE)	4	-	-
DUAL RIGHT VEIN	11	-	-
RIGHT VEIN BIFURCATION		-	-
RIGHT ARTERY EARLY BIFURCATION	3	-	-
TRIFURCATION RIGHT ARTERY	1	-	-
TRIFURCATION RIGHT VEIN	5	-	-
DUAL LEFT ADRENAL VEIN	1	-	-
DUAL INFERIOR VENA CAVA	1	-	-
	107 (100%)	2 (1.87%)	1(0.93%)

P674 MEDIAN ARCUATE LIGAMENT COMPRESSION-AN ACHILLEAS KNEE FOR HEPATIC ARTERY FLOW DURING LIVER TRANSPLANTATION

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Background: Median arcuate ligament can induce the narrowing of the celiac trunk, either by the insertion of muscular fibers or by fibrous bands of the celiac nervous plexus. Significant celiac artery compression is revealed in 10-50 % in angiographic CT examination. The presence of celiac trunk compression is a risk factor for hepatic artery thrombosis after liver transplantation, and subsequently for the graft loss. Several surgical procedures have been advocated to overcome its effect in liver transplantation, but their impact is still on debate.
Methods: The aim of our study is to retrospectively review 8 cases of celiac artery compression by median arcuate ligament, who were preoperatively identified by celiomesenteric angio-CT and underwent orthotopic liver transplantation, between September 2016 and September 2022.
Results: In three cases standard hepatic artery reconstruction was performed during liver transplantation, followed by median arcuate release whereas the flow in the reconstructed hepatic artery was insufficient. In 2 other cases we preserved the additional flow coming from the gastroduodenal artery and the hepatic artery reconstruction was performed on the recipient proper hepatic artery bifurcation. In three other cases in whom the arterial flow didn`t recover after ligament release, an arterial aorto-hepatic jump graft was undertaken. In all the 8 cases, an excellent hepatic artery flow was restored.
Conclusions: Our presentation highlights the importance of overt diagnosis and management of median arcuate ligament in liver transplant recipients during transplant surgery.

P675 PHOTOPROTECTION AND SKIN CANCER AWARENESS IN KIDNEY TRANSPLANT RECIPIENTS LIVING WITH HIV: A SINGLE-CENTRE CROSS-SECTIONAL STUDY

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Background: Kidney transplant recipients (KTRs) are up to 65 times more likely to develop non-melanoma skin cancers when compared to age-matched general populations. HIV has also been associated with increased skin cancer rates. However, to date there has been no study evaluating photoprotection and skin cancer awareness in KTRs living with HIV (KTRLHIV).
Methods: Using validated photoprotection and skin cancer awareness questionnaires we evaluated knowledge and practices in KTRLHIV and an HIV-negative KTR cohort, matched for age, sex, ethnicity, and years since transplant.
Results: n=27 KTRLHIV and n=25 matched HIV-negative KTRs completed the questionnaires. Of those n=34 (65%) were male and n=37 (71%) were Black. Average age was 56 years (43-74 years). On average patients were 7.3 years post-transplant (range years). N=22 (81%) KTRLHIV compared with n=15 (60%) matched HIV-negative KTRs had not seen a Dermatologist in the last year. Only n=14 (52%) KTRLHIV had received sun protection advice, compared to n=20 (80%) of the matched KTRs (p=0.033). There were statistically significant lower rates of overall sunscreen use in KTRLHIV compared to matched HIV-negative KTRs (33%vs60%, p=0.054). Only a small proportion used sunscreen daily (22%vs27%), of a factor >25 (78%vs100%). A strongly positive Tetrachoric correlation coefficient of 0.77 indicated that providing photoprotection advice correlates to sunscreen use. Significantly lower rates of photoprotection behaviours were seen in the KTRLHIV compared to HIV-negative KTRs, particularly never avoiding direct sunlight (59%vs16%, p = 0.001), and never dressing to protect from the sun (52%v 12%, p = 0.002).
Conclusions: We have identified statistically significant lower knowledge of photoprotection and skin cancer awareness in KTRLHIV compared to matched HIV-negative KTRs. Lower rates of skin cancer protection advice may have resulted in lower rates of sunscreen use, and poorer photoprotection behaviours in KTRLHIV. Dedicated skin cancer awareness education to promote patient-led skin cancer prevention alongside formal Dermatology referral is recommended.

P676 THE DEVELOPMENT OF REJECTION IS ASSOCIATED WITH A MORE AGGRESSIVE PATTERN OF POST-TRANSPLANT NEOPLASIA

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Background: A relation between immunosuppressive status and the development of post-transplant malignancies (PTM) is already published. Our objective is to evaluate the impact of the development of rejection and its treatments with the incidence and behavior of PTM.
Methods: Retrospective single-center study of adult kidney transplants recipients (KTR, 2003-2015, follow-up till december of 2020). Different statistical tests and survival analysis were used according to the type of variable used collected from the different databases of the center. The study was approved by the Ethics Committee of our Institute.
Results: 169 (11.2%) of 1,505 KTR developed some type of neoplasia (60.5% men and 17% diabetics) with a mean follow-up of 62.78 +/- 158.01 months. The patients with PTM were older (p = 0.000; Exp(B) 1.042; univariate: 62.8 +/- 11.1 years vs 54.7 +/- 14.3 years, p = 0.000), with worse survival of the patient (p = 0.000 Exp (B) 2.427; K-M: 73.4% vs 88.7%, Log-rank 0.001), less incidence in those who wore CNI plus mTORi (p = 0.01; Exp (B) 0.314) and who developed rejection (p = 0.003; Exp (B) 0.521) in the multivariate analysis (binary logistic regression). Despite this unexpected lower incidence of PTM in those who developed rejection, being age (p = 0.061; Exp (B) 1.024) and the use of CNI (p = 0.016; Exp (B) 0.233) the factors in the multivariate analysis, we evaluate the aggressive patterm, and the patients who rejected and developed neoplasia, this was more aggressive with more metastases (4.8% vs 3.8%, p=0.006) and higher patient mortality associated with the tumor (5.7% vs 1.37%, p=0.002)
Conclusions: In long-term follow-up, patients with rejection developed a more aggressive neoplasm with higher tumor-associated mortality. Rejection types and treatments are being analyzed as potential factors associated with tumor behaviour.

P677 BEST PRACTICES ALONG THE KIDNEY TRANSPLANTATION CLINICAL JOURNEY: A QUANTITATIVE SURVEY TOOL

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Background: This study designs and tests a survey tool to assess the implementation of best practices recommendations and guidelines along the kidney transplantation clinical journey, from chronic kidney disease (CKD) prevention to long-term post-transplant care.
Methods: Best practice recommendations and guidelines were analysed to identify the key themes and elements of the clinical journey. The most recent version of three sets of guidelines were chosen as the main sources (KIDGO guidelines, European Commission's CD-P-TO's "Guide for Quality and Safety in Organ Transplantation", British Transplantation Society clinical practice guidelines). Topics were identified and a comprehensive survey was created to collect data on how current practice relates to best practices. The survey was validated by a selected group of experts and stakeholders, including living organ donors, transplant patients, nephrologists, transplant coordinators, and transplant surgeons, across five countries (France, Germany, Italy, Spain, United Kingdom). Questions with divergent answers in repeated survey responses were analysed and rewritten.
Results: The main themes of the final version of the survey are: 1) Chronic kidney disease (definition and classification, prevention, progression, complications, referrals and models of care); 2) Kidney donation and transplantation (identification of deceased organ donors, determination of death, consent, management after brain death, donor selection criteria, organ procurement, living donation, biovigilance, quality management, measuring outcomes); 3) Transplant recipients (post-operative care, prevention of infectious diseases, graft failure, long term care, quality of life); and 4) Management of donation and transplantation service (funding, governance, decision making). The final survey tool has 80 questions, and takes on average 30 minutes to complete.
Conclusions: This survey tool can be used to assess conformity of clinical practice with best practices. Preliminary survey responses from 56 respondents (patients, transplant surgeons, nephrologists, and transplant coordinators) from Italy and France indicate a wide range of practices and perceptions along the kidney transplantation clinical journey.

P678 3D BIOPRINTING OF A BIONIC PANCREAS WITH A VASCULAR SYSTEM – RESULTS OF TRANSPLANTATION IN LARGE ANIMALS

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Background: The transplantation of the pancreas is recommended in diabetes with complications. The combination of cell biology and 3D-bioprinting can create organs with vasculature which should be functional. dECM derived biomaterials shoved superior functionality when bioprinted with pancreatic islets. In fully vascular organ or macro-device, there are issues to be solved: leakage, thrombosis, enhancement against high pressure, connecting organ to the recipient. The purpose of this study was to demonstrate 3D-bioprinting of bionic pancreas as a macro-device for stem-cell derived beta cells or knocked-out xeno-derived islets, with use of dECM-derived biomaterials with stable flow through the organ in vitro and in large animal studies
Methods: Mathematical analysis in the designed bionic pancreas was performed. The bionic pancreas was 3D bioprinted with 2 types of bioinks. The first tests were carried out in a bioreactor then organs were subjected to magnetic resonance and X-ray with contrast. Pressure endurance tests were performed. 14 pigs received 3D-bioprinted bionic pancreas transplantation. DCL-VESS-Group (n=5) received decellularized vessels as anastomosis. 9 pigs received bionic pancreas with vascular prosthesis as anastomosis - Prosthesis-Group. Pigs were observed up to 14 days. Hist-pat analysis of removed pancreas was performed.
Results: The tests carried out in the bioreactor showed the stability of the bionic organ and vascular system in MRI and X-ray examination for 5 days. No leaks beyond the bionic pancreas were observed up to 400 mmHg. Animals transplantation: In all 14 cases of transplantation there was stable flow throughout the organ after release of vascular clamp. DCL-VESS-Group - In all cases vascular cloth was observed. Prosthesis-Group - In 5 cases there were no complications influencing blood flow through the organ. 4 died to postoperative complications. Stable flow within a transplanted bionic organ was observed till 2 weeks post – surgery within ultrasound examination and radiology intervention in three animals. Histopatological showed the presence of CD31 / PECAM-1 (new blood vessels formation).
Conclusions: It is feasible to 3Dbioprint and transplant bionic organ in big animal model as a macro-device for stem-cell derived beta cells or knocked-out xeno-derived islets.

P679 THE BURDEN OF SKIN DISEASE IN KIDNEY TRANSPLANT RECIPIENTS LIVING WITH HIV: A SINGLE-CENTRE RETROSPECTIVE ANALYSIS

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Background: Kidney transplant recipients (KTRs) are at lifelong risk of immunosuppression-related cutaneous complications, in particular skin cancer. KTRs are up to 65 times more likely to develop non-melanoma skin cancers (NMSCs) when compared to age-matched general populations. Published evidence suggests skin disease occurs in over 90% of patients living with HIV. However, there is a paucity of published data on the prevalence and characteristics of skin disease in KTR living with HIV (KTRLHIV).
Methods: We performed a retrospective analysis of electronic health record data (between 1998-2022) to analyse the prevalence and characteristics of skin diseases in our KTRLHIV cohort (n=29) compared to matched HIV-negative KTRs (n=29) (matched for age, sex, ethnicity, and years since transplant).
Results: In each of our cohorts n=19 (66%) were male and n=21 (72%) were Black with a mean age of 55.5 years [range 43-74 years]. On average patients were 7.4 years post-transplant (range 0.7-23.8 years). The mean GFR in KTRLHIV compared to matched HIV-negative KTRs was 34 vs 43mL/min (p = 0.045). Having concomitant HIV increased the risk of skin disease in KTRs 1.6 times (p = 0.027). N=27 (93%) KTRLHIV experienced 120 episodes of skin diseases (4.4 episodes/patient). In comparison n=21 (72%) HIV-negative KTRs experienced 76 episodes (2.6 episodes/patient). Skin infections (especially genitourinary) were the most common (43% KTRLHIV vs 39% HIV-negative KTRs), followed by benign lesions (17%vs22%) and inflammatory skin disease (9%vs9%). Interestingly, pre-malignant or malignant skin cancers occurred more frequently in HIV-negative KTRs (4%vs11%). Most of these were actinic keratosis (n=4) and found only in patients with fair (Fitzpatrick Type 1) skin.
Conclusions: We have identified statistically significant higher rate of skin disease in KTRLHIV compared to matched HIV-negative KTRs. Further research to evaluate the reasons underpinning this increased burden of skin disease in this cohort is necessary.

P680 KIDNEY TRANSPLANTATION IN ALBANIA: A SINGLE CENTER EXPERIENCE

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Background: Kidney transplantation (KTx) is the treatment of choice in patients with end-stage kidney disease (ESKD), associated with improved quality of life, survival rates and cost-effectiveness. The aim of this study was to present an overview of the experience in kidney transplantation in our country.
Methods: This is an observational, retrospective cohort study comprising patients who underwent KTx between 2013-2022, in a single transplantation center in our country.
Results: In our country, we exclusively accept kidneys from living donors. Between 2010-2022 approximately 214 KTx have been performed nationally. Our transplant center first opened its doors in 2013, when we performed the first KTx and our experience has steadily grown, encompassing a total of 44 patients. In our institution, the donor kidney is harvested with a minimally invasive retroperitoneoscopic technique. In our cohort, 77.2% of recipients were male, 70.5% of the donors were female. The mean age of the recipients was 39.2±13.82, that of the donors was 50 ± 10.4. The BMI of the recipients and the donors were 24.5±4.1 and 26.9±3.3, respectively. In 43.6% of cases the donor was a sibling, in 34% a parent, in 20.4% a partner and in the remaining 2% the donor was a first-degree relative. The primary diseases leading to a KTx were glomerular disease in 25.71% of patients, chronic pyelonephritis and reflux nephropathy in 22.6%, HTN in 17%, DM in 14.2% and unknown etiology in 20.1%. A preemptive transplant was performed in 18.1% of the cohort. ATG was the induction therapy in 76.5% of patients, in the remaining 23.5% basiliximab was used. Maintenance therapy for all patients consisted of a triple immunosuppressant regimen. In our center, there were no cases of acute rejection. 2.2% developed DGF with no need for hemodialysis and 4.5% of patients developed chronic rejection. One patient lost his graft due to BK nephropathy. One patient died due to Covid-19 disease, at the time, his graft function was normal.
Conclusions: To the best of our knowledge, this is the first report of the kidney transplantation experience in our country. Despite our small cohort, our findings show excellent outcomes associated with kidney transplantation surgery and long-term follow-up.

P681 VALGANCICLOVIR PROPHYLAXIS IN HIGH-RISK TRANSPLANT RECIPIENTS: A DOUBLE-EDGED SWORD WITH IMPLICATIONS FOR NEUTROPENIA AND KIDNEY GRAFT SURVIVAL

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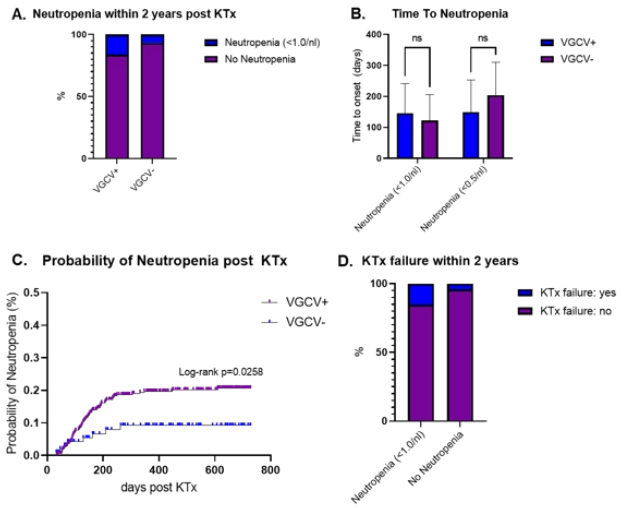
Background: Cytomegalovirus (CMV) infections constitute a significant condition in kidney transplant (KT) recipients with a major impact on morbidity, mortality and graft survival, with CMV negative recipients (R-) transplanted from a CMV positive donor (D+) at highest risk. The prevention of active CMV disease in KT recipients mainly relies on antiviral prophylaxis and preemptive therapy with virostatics, e.g., valganciclovir (VGCV). Although these strategies proved to be efficient, their use is limited due to substance related toxicities, especially myelotoxicity. This study aims to evaluate the effects of VGCV administration on the development of (severe) neutropenia and graft survival in CMV high risk KT.
Methods: A retrospective data analysis was used to analyze KT recipients with CMV high risk constellation, transplanted at Charité Berlin (Germany) between 2003-2019. The incidence of neutropenia (<1/nl), severe neutropenie (<0.5/nl) and KT survival within the first two years after transplantation was assessed for patients with and without a VGCV prophylaxis during day 0-200 after KT.
Results: 556 patients with CMV high risk constellation received a KT, including 437 (78.6%) and 119 (22.4%) with and without prophylactic VGCV administration, respectively. The mean age at KT was 50.6 ± 14.1 years. The likelihood of developing (severe) neutropenia was elevated in KT recipients with VGCV administration (log-rank 0.0289). The time to onset of neutropenia was 145.4 ± 96.4 days for recipients with VGCV prophylaxis and 122.1 ± 83.8 days for those without VGCV (p=0.062). The development of neutropenia was associated with an increased risk of graft failure within the first two years (p = 0.002). However, VGCV administration was not linked to reduced graft survival (p=0.482).
Conclusions: Our findings suggest that the use of VGCV as prophylaxis in CMV high-risk kidney transplant recipients is linked to an increased likelihood of developing (severe) neutropenia. However, the timing of the onset of neutropenia is not significantly altered by VGCV. Given the potential negative impact of neutropenia on transplant outcomes, it is crucial to closely monitor kidney transplant recipients who develop neutropenia. Further research may help determine if targeting neutropenia could lead to improved transplant outcomes.



A. KTx recipients with CMV high risk constellation (donor CMV +/recipient CMV-) and valganciclovir (VGCV) administration during the first 200 days after kidney transplantation (KTx) experience significantly more neutropenia (neutrophils <1/nl). **B.** The time to onset of neutropenia or severe neutropenia (neutrophils <0.5/nl) was not significantly different in the groups with VGCV intake (VGCV+) and without VGCV intake (VGCV-). **C.** The probablitiy of developing neutropenia within the first two years after KTx is singificantly higher in patients with VGCV+ and appears to occur predominantly within the first 120-150 days. **D.** Significantly more patients with neutropenia experience a KTx failure within the first two years after transplantation.

P682 GLOBAL BURDEN OF CYTOMEGALOVIRUS RESISTANCE TO ANTIVIRALS IN FRANCE

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Background: Refractory/resistant CMV infections are deleterious for graft survival. The global burden of resistance to anti-CMV compounds is surveyed since 2006 by the National reference Center for Herpesviruses.
Methods: Resistance genotyping indication was: viral replication persisting for more than 3 weeks on treatment (NRC recommendations) and since 2018: more than 15 days in a previously treated patient. Method: Sanger-sequencing of full-length genes *UL97*, *UL27*(ganciclovir/maribavir) *UL54* (ganciclovir, cidofovir, foscarnet), and since 2018, *UL56 UL89* and *UL51* (letermovir).
Results: 2006-2022: Out of 2928 genotypes performed at the CNR in Limoges, 931 (31,8%) showed the presence of resistance mutations, 732 in UL97 (77,5%), 240 in UL54 (25,78%), 13/181 (7,8%) since 2018 in UL56, 0 in UL89, 2 in UL51, 3 in UL27 and New UL54 mutations (CMV resistance data base cnr-herpesvirus.fr) 2017-2021: In 1159 patients whose pathology was known, the percentage of resistance in non-responders to treatment for whom a genotype was requested was 40% (29% in stem cell transplantation, in organ transplantation: kidney 48%, lungs 40%, liver 70%, heart 32%, multi-organ 41%). In 2019-2021 during Covid19, the number of genotypes was stable. Multidrug resistance was present in 31-35% of cases and 23-14% initiate resistance with UL54 mutation alone in 2017-2018 and 2019-2021.letermovir resistance between 2018 and 2021: 20 patients, 1 kidney recipient (curative treatment). In secondary prophylaxis 5,5% (4/80) of treated patients were resistant. maribavir resistance between 2021-2022 was found in 5/30 refractory patients, all kidney recipients; 3 other patients had primary resistance through C480F (1) or F342Y (2) selected under ganciclovir.
Conclusions: Virological resistance account for 40% of non-response. Mainly to ganciclovir but also early multidrug resistance. Genotype interpretation should also include primary resistance detection before maribavir treatment.

P684 INPATIENT REHABILITATION AFTER LIVER TRANSPLANTATION IN A DEDICATED REHABILITATION HOSPITAL IS FEASIBLE, SAFE, AND EFFECTIVE

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Background: Patients undergoing Liver Transplantation (LT) nowadays are increasingly sarcopenic and frail, conditions that often not only further deteriorate after LT but also compromise their survival. To improve and accelerate physical rehabilitation, we refer more and more medically stable but still physically unfit and frail LT recipients for subsequent inpatient physical rehabilitation in a dedicated rehabilitation hospital. Here, we report our first experiences of such rehabilitation program with specific attention to safety and efficacy.
Methods: In this single-centre cohort study, we included adult LT recipients transplanted between July 2020 and August 2022. Demographics, LT indication, Intensive Care Unit (ICU), LT centre and rehabilitation hospital admission time, as well motor function (6-minute walk test) and balance/stability perception (Tinetti test) before and after rehabilitation were analysed. Data are presented as mean and standard deviation
Results: 12/138 (9%) LT recipients (9 males/3 females, aged 57±11) were referred for subsequent inhospital rehabilitation. LT indications included ethyl cirrhosis (n=5), non-alcoholic steatohepatitis cirrhosis (n=2), primary sclerosing cholangitis relapse (n=1), polycystic liver disease (n=1), chronic intestinal and liver failure (n=1), post-ICU cholangiopathy (n=1) and cardiac cirrhosis (n=1). MELD score was 20±8 at moment of listing. ICU, LT centre and rehabilitation hospital admission time were 9±8, 41±31, 36±24 days, respectively. No serious adverse events were reported during the rehabilitation period. Two patients were re-admitted in the LT centre for medical reasons not related to the rehabilitation. The mean 6MWT increased from 126±98 to 362±126 meters ($p<0.05$). Balance/stability perception remained stable before and after rehabilitation (20±8 vs 24±8, $p>0.05$).
Conclusions: This study shows that referring medically stable but physically unfit LT recipients for intensive inpatient rehabilitation is feasible, safe, and well-tolerated with significant functional gains. Closer collaboration between LT centres and dedicated rehabilitation hospitals to improve physical fitness, not only after but also before LT, should be encouraged and explored to further improve outcomes after LT for very frail patients.

P685 OUTCOME OF KIDNEY TRANSPLANTATION IN PATIENTS WITH BALKAN ENDEMIC NEPHROPATHY

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Background: Balkan endemic nephropathy (EN) is a chronic tubulointerstitial aristolochic acid nephropathy with insidious presentation, slow progression to end-stage renal disease and the frequent development of urothelial cancer. Immunosuppressive treatment increases the risk for a poor outcome. To reevaluate our practice, we analyzed the incidence of urothelial cancer and treatment outcome in the group of kidney transplant recipients with EN.
Methods: We retrospectively evaluated the database, patient records and pathology results of 610 kidney transplant recipients treated at our institution during a 30-year period.
Results: From January 1993 until December 2022, 657 kidney transplants were performed in 610 adult patients at our institution. EN was diagnosed as the original kidney disease in 11 (1.8 %) of the recipients, based on medical history, clinical findings and laboratory results. All patients with EN received the first deceased donor allograft, patients' mean age at transplantation was 65 (range 36-76), 6 (54.5%) patients were male. None of the patients underwent a preventive nephroureterectomy. During the post-transplant follow-up (mean 5 years, range 1-13 years) urothelial cancer was diagnosed in 6 (54.5%) of 11 patients with EN, and resulted in the death in four patients.
Conclusions: Kidney transplant recipients with EN are at high risk for the development of urothelial cancer. Our data stress the need for careful urological evaluation and decision about pre-transplant preventive bilateral nephroureterectomy, close post-transplant follow-up and the individualization of immunosuppressive treatment.

P687 THE STRUCTURE OF THE SYSTEM OF TRANSPLANT COORDINATORS IN POLAND

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Background: In 2010, Poltransplant started to create a structure of transplant coordinators in Poland. Over the 12 years (2010-2022), the number of organ and tissue donation coordinators in Polish hospitals was increased from 35 (2010) to 168 (2022). Over the years, the network of coordinators has been expanded to include provincial coordinators increasing donation in a given area, coordinators in transplant centers, coordinators of living kidney donors and coordinators of hematopoietic cell collection and transplantation.
Aims: The aim of the work is to present the basics of functioning, the structure of the coordinator system, and the tasks of individual groups of transplant coordinators in Poland.
Results: At the end of 2022, Poltransplant in Poland employed a total of 254 coordinators (various tasks). From the group of all coordinators, 209 (82.1%) people were responsible for organizing the coordination of organs and tissues from deceased donors and increasing the donation potential. In this group, 168 (80.1%) coordinators were donation coordinators in hospitals reporting donors, 18 (8.6%) people were transplant coordinators in transplant centers, another 15 (7.8%) people were voivodeship coordinators, and the remaining 8 (3 .8%) central (national) coordinators. A separate group of 24 people (9.5%) out of 254 coordinators is made up of coordinators responsible for coordinating the collection and transplantation of kidneys from living donors, and 21 people (8.3%) are responsible for the collection and transplantation of hematopoietic cells in hematology centers.
Conclusions: The presentation of the creation and expansion of the network of transplant coordinators is aimed at showing good practices (know-how) proven in one country, for others, like Poland, which also has a problem with too few donors.Key words: transplant coordinators; deceased donors; living donation coordinators; coordinators of collection and transplantation of hematopoietic cells;

P689 INTRAPATIENT VARIABILITY AND TESTS ABOVE LOWER TACROLIMUS TRESHOLD ARE ASSOCIATED WITH ACUTE REJECTION IN PANCREAS TRANSPLANTATION

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Background: The immunosuppressive maintenance regimen in solid organ transplantation with tacrolimus is currently the gold standard in clinical practice. However, this drug has a narrow therapeutic window. There are multiple studies in which the tacrolimus coefficient of variation (CV) in heart, kidney, and lung transplantation has been associated with the incidence of graft rejection. This study aims to find the association between the CV and the percentage of tests above the lower tacrolimus threshold (TALT) with the incidence of rejection in simultaneous pancreas-kidney transplantation (SPKTx).
Methods: This is a retrospective study of SPKTx performed between April 2017 and February 2021. We calculated the tacrolimus CV and the TALT of included patients. The lower target trough level was defined as 10 ng/mL during the first 3 months, 8 ng/mL by 6 months, and 6 ng/mL thereafter. Biopsy-proven acute SPKTx rejections (BPAR) were registered.
Results: Thirty-four patients were analysed, 3 that were receiving mTOR inhibitors were excluded. Seventeen (43.6%) were males, 39 biopsies were performed (either per protocol or for-cause). There were 9 cases of BPAR. These were significantly associated with a TALT below 70% [PPV 38.1%, NPV 94.4%, OR 10.46 (1.2 – 94.5), p= 0.023], and with a CV greater than 60% [PPV 50%, NPV 83.3%, OR 5.5 (1.1 – 27.4), p= 0,.32].
Conclusions: This small pilot study suggests that CV and a new parameter, TALT, are potential tools that can help identify patients at risk of pancreatic graft rejection. Larger studies in time and number of cases are required to prove this hypothesis. Transplant physicians should be aware of their patients' tacrolimus CV and TALT and individualize the pattern and frequency of follow-up to optimize it and reduce rejections.

P690 THE IMPACT OF SURGICAL SITE INFECTIONS (SSI) ON OUTCOME AFTER DECEASED DONOR LIVER TRANSPLANT

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Background: Infections are a significant cause of morbidity and mortality after liver transplant (LT). The first period after LT is mainly characterized by the occurrence of deep and organ/space surgical site infections (SSI). Perioperative antimicrobial prophylaxis is aimed to prevent these SSIs. The objective of this study is to evaluate the incidence, etiology, timing, and outcomes of SSIs in LT.
Methods: All deceased donor LT recipients between 2016-2019 in the Erasmus Medical Center were included. All relevant donor and recipient parameters were collected. SSIs within the first 90 days after transplantation were scored according to the CDC definition.
Results: Of the 187 patients included, 43 patients (23%) experienced a total of 55 SSI events. Median time until first SSI was 9 (6-13) days after LT. The most common pathogen was *Enterococcus spp*. in 64% (35/55) of all OSSI events and in only 8% the pathogen was multi-drug resistant. In 60% the SSI was a peritonitis. Patient survival at 1 year was 84% for SSI vs 97% for no SSI (p<0.001). Graft survival at 1 year was 80% vs 96% (p=0.001). In patients with SSI, the median units of blood products transfused was higher (14 vs 6; p=0.002), the duration of anhepatic time was longer (50 min vs 45 min; p=0.005) and the incidence of early re-laparotomy was higher (19.1% vs 8.2%, p=0.011). Patients with SSI more often had a choledochojejunostomy in 29.5% vs 16.1% (p=0.48). Risk factors for SSI were re-laparotomy after LT OddsRatio OR 22.535(95%CI 3.406-253.475, p=0.002) and a choledochojejunostomy OR 2.516 (95%CI 1.044-6.062, p=0.040).
Conclusions: SSIs occur frequently after LT, and result in increased morbidity and mortality. In patients with SSI, *Enterococcus spp*. lead to even worse survival rates. Peri-operative antibiotic prophylaxis should target *Enterococcus spp*., if risk factors are present.

P691 NONCODINGRNA-BASED BIOMARKERS IN AFP NORMAL HEPATOCELLULAR CARCINOMA: LNCRNA SNGH1 PLAYS AN IMPORTANT ROLE IN RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Alpha-fetoprotein (AFP) is most commonly used as a biomarker for the diagnosis of Hepatocellular carcinoma (HCC). Increase in AFP is considered diagnostic value and AFP> 400 ng/mL is consider had poor prognosis in terms of Liver Transplantation. However, the AFP threshold for the diagnosis of HCC is still controversial. The alterations of non-coding RNAs (lncRNAs and miRNAs) are related to multiple diseases including cancer. In this study, we aimed to establish a diagnostic and prognostic ncRNA signature for AFP-normal HCC recurrence after LT.
Methods: Twelve LncRNAs were chosen as candidates on the basis of the literature to evaluate the diagnostic. The candidate lncRNAs were validated by qRT-PCR arranged in the training and validation sets. Twenty-two patients with normal AFP but HCC at biopsy diagnosis and 36 patients with high AFP were evaluated (This study was supported by Gilead Grant No:220075).
Results: SNGH16 and PVT1 were significantly up-regulated in plasma samples of AFP-normal HCC patients during training set and validation set (P=0.021, P=0.0001). Receiver operating characteristic (ROC) analysis showed that plasma SNGH16 exhibited significantly increased discriminatory power for differentiating patients with HCC from recurrent HCC patients with normal AFP.
Conclusions: Our results suggest that plasma levels of SNGH16 achieve a fine diagnostic accuracy in diagnosing ontogenesis and recurrence of HCC patients with normal AFP and may act as novel biomarkers for AFP-normal HCC patients.

P693 DESENSITIZATION IN KIDNEY TRANSPLANT RECIPIENTS WITH PREFORMED DSA AND A NEGATIVE CDC CROSSMATCH DOES NOT IMPROVES REJECTION RATE AND GRAFT SURVIVAL

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Background: A significant proportion of kidney transplants showed a high HLA sensitization and should be considered for transplantation across the HLA barrier. The best strategy to manage these patients is still a matter of debate and the benefits of desensitization based on apheresis techniques and rituximab have not been clearly delineated.
Methods: We review all kidney transplant performed at our center between 2009 and 2021 who showed donor-specific antibodies (DSA) at the time of transplant and a negative CDC crossmatch. All patients received induction therapy with thymoglobulin and maintenance immunosuppression with tacrolimus, MMF and steroids. According to the treating physician criteria patients also received treatment with apheresis (5-7 sessions of plasma-exchange or 5 sessions of immunoadsorption) and one single dose of Rituximab 375 mg/m2. We analyze main outcomes after transplantation in both groups.
Results: During the study period 101 out of 1525 kidney transplants performed at our unit had at least one DSA at the time of transplant. In 64 cases standard treatment was administered while in 37 cases treatment with apheresis and rituximab was added. Main donor and recipient characteristics are shown in table 1. Incidence of acute rejection (37.5% vs. 35%), renal function at 6 months and 5-year patient and death-censored graft survivals were not different between groups (table 1). The main cause of graft failure was chronic antibody mediated rejection in both groups. Infectious complications were not different between groups.
Conclusions: HLA incompatible kidney transplants are associated with a high rate of antibody-mediated rejection. Adding treatment with apheresis and rituximab during the peri-transplant period did not significantly modify main outcomes after transplantation.

N	64	37	
Donor age	55 ± 14	53 ± 16	0.523
Patient age	56 ± 13	47 ± 16	0.005
Dialysis time (months)	76 ± 93	77 ± 101	0.980
HLA A mismatches	1.3 ± 0.7	1.3 ± 0.6	0.889
HLA B mismatches	1.5 ± 0.7	1.4 ± 0.7	0.487
HLA DR mismatches	1.3 ± 0.6	1.2 ± 0.6	0.681
cPRA (%)	95 (65-100)	98 (85-100)	0.130
HLA class (I / II / I+II)	21 / 38 / 5	8 / 26 / 3	0.449
MFI iDSA	4950 ± 4990	6177 ± 6004	0.264
ABMR (n; %)	16 (25%)	7 (19%)	0.246
TCMR (n; %)	8 (12.5%)	6 (16%)	0.645
Serum creatinine 6 months (mg/dL)	1.7 ± 1.0	1.4 ± 0.4	0.125
Proteinuria 6 months (g/g creatinine)	0.62 ± 1.4	0.62 ± 0.68	0.985
5-year patient survival	82%	89%	0.153
5-year death-censored survival	61%	67%	0.147

P694 LONGITUDINAL ANALYSIS OF ANTIBODIES IMMUNE RESPONSES IN KIDNEY TRANSPLANT RECIPIENTS AFTER SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2

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Background: Evaluating the immune response of Kidney transplant recipients (KTRs) who recover from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the factors that may influence it, namely the role of immunosuppression, is crucial to understand the quality and durability of the immune response to natural infection. In this study we report the longitudinal antibody kinetics using two SARS-CoV-2 antigens, namely the nucleocapsid and the S1 domain of spike protein, anti-N and anti-S1 IgG ratio values, respectively.
Methods: All adult KTRs with primary infection SARS-CoV-2, in the absence of vaccination from March 2020 and March 2021, were included in this study. Patient demographic and clinical characteristics were retrospectively retrieved from the electronic medical records. Blood samples were collected according to schedule visits to hospital with the last sample for antibody testing collected on July, 2021.
Results: Seventy-seven KTRs with SARS-CoV-2 infection were analyzed. Mean (SD) age of KTRs was 57.1 (11.6) years, and 49 (63.6%) were male. Among the 77 KTRs, 52 (67.5%) were seropositive for anti-N and 64 (83.1%) were seropositive for anti-S1. Posterior mean estimates of anti-N values reached their peak by day 42 after infection with a maximum value of 3.92 (95% credibility interval (CrI), 3.10-4.99) followed by a decay with time, reaching the threshold of positivity of 1.4 (95% CrI, 0.64-2.31) by day 176. In these patients, severe disease, male sex, tacrolimus trough levels and dichotomized mycophenolate dose were significantly associated with changes in posterior mean values over time. Regarding anti-S1 values, posterior mean estimates peaked later, by day 56 after infection with a maximum value of 5.29 (95% CrI, 3.79-7.17), and then remained relatively stable over time, with minimal decline over the 7-month follow-up period. In these patients, disease severity was the only factor significantly associated with changes in posterior mean values over time.
Conclusions: This is the largest known longitudinal study describing the variability of memory of the immunosuppressive response of KTRs in a state of primary infection in the absence of vaccination.

P695 LAPAROSCOPIC LIVE DONOR NEPHRECTOMY AND SIMULTANEOUS LAPAROSCOPIC OPERATIONS. EVOLUTION OF MINIMAL INVASIVE LIVE DONOR NEPHRECTOMY

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Background: Laparoscopic live donor nephrectomy, represent a milestone in the history of transplant surgery. Since 1995, this procedure provides several benefits for the live donor, reducing the constantly increased disparity between organ supply and demand. During the preoperative evaluation, various asymptomatic or symptomatic pathologies may be discovered. Live donor nephrectomy and other concomitant laparoscopic surgical procedures are rarely reported in the world literature. According to our experience this kind of surgery could be performed with safety, without increased morbidity for the donor.
Methods: We prospectively collected data from 267 cases since November 2018 to December 2022 from our transplant center. Laparoscopic live donor nephrectomies with simultaneous other operations were performed in fifteen cases (5,5%). Donor demographics, art of concomitant surgery, operative time, intra- and postoperative complications and morbidity are presented in Table 1.
Results: In all cases nephrectomies were preceded the other surgical procedures. Mean operative time was 164.33 minutes (median time 160 minutes, range 130-240 minutes) Changing patient's position was done intraoperatively from lateral to supine in 13 cases, with no incidents. An extra 5mm trocar was inserted in only in 4 cholecystectomy cases below the right coastal margin. The mean hospitalization time was 3 days (range 3-4 days). The postoperative course in all cases was uneventful with no need of blood transfusion. No intra or postoperative complications have been noticed. No Surgical Site Infections (SSIs) were observed. Regarding the longterm complications, there are none to mention.
Conclusions: Laparoscopic live donor nephrectomy and simultaneous surgery for concomitant pathologies are very rare reported in the literature. Herein we report our experience with 15 cases. with is safe and feasible by an experienced surgical team. This uncommon practice is truly beneficial for the donor avoiding further anesthesia as well as surgical approach and their potential complications.

TABLE 1. Donor Characteristics- Concomitant surgery

Donor	Age	Gender	Prior surgeries	Simultaneous Surgery	OR time(to ip)	Position	Kidney retrieval (Laterality)	Complications (Intra/postoperative)
1	46	F	Y	Cholecystectomy	200	Supine	Left	None/None
2	46	F	Y	Cholecystectomy	180	Supine	Right	None/None
3	75	F	N	Left Groin Hernia	180	Supine	Right	None/None
4	55	M	Y	Umbilical Hernia Repair and Cholecystectomy	240	Supine	Right	None/None
5	51	F	Y	Cholecystectomy	180	Supine	Left	None/None
6	56	F	Y	Cholecystectomy	175	Supine	Left	None/None
7	76	M	Y	Umbilical Hernia Repair	170	Supine	Left	None/None
8	60	M	Y	Cholecystectomy	150	Supine	Left	None/None
9	59	F	N	Cholecystectomy	160	Supine	Left	None/None
10	58	M	N	Cholecystectomy	145	Supine	Left	None/None
11	62	M	N	Cholecystectomy	140	Supine	Left	None/None
12	57	F	Y	Left Ovarian Cyst Exclusion	140	Lateral	Left	None/None
13	58	F	N	Cholecystectomy	130	Supine	Left	None/None
14	50	F	Y	Cholecystectomy	130	Supine	Left	None/None
15	39	F	N	Unroofing Cyst of Left Liver Lobe	145	Lateral	Left	None/None

P696 IMPACT OF DELAYED GRAFT FUNCTION COMBINATION WITH OTHER COMPLICATIONS ON LATE POST-TRANSPLANT OUTCOMES

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Background: Kidney transplantation (KT) ensures better patient survival and quality of life compared with dialysis. Delayed graft function (DGF) is a relatively frequent complication in early posttransplant period, impacting both early and late posttransplant outcomes. The aim of this study was to evaluate association of DGF with donor, recipient and transplantation factors and graft losses (GL) and patient mortality (PM) in early and late posttransplant outcomes.
Methods: This retrospective study included results of all consecutive deceased donor (DD) KT from deceased donors (DD) performed in a single transplant center from 01.01.2004 till 31.12.2012, where patients were available for 10-year follow-up (n=521, 271 male, 250 female, mean age = 45,5 + 14,2 years). All cases were divided into 4 groups according to presence of GL: 1) presence of both DGF and GL, 2) presence of DGF and no GL, 3) no DGF and presence of GL and 4) no DGF and no GL. Groups were compared for donor, recipient and transplantation factors, and posttransplant outcomes.
Results: DGF was observed in 112 cases (21.5%) and was associated with higher recipient age, higher DD age and weight, presence of hemodynamic problems in DD prior to organ recovery operation ($p<.05$ for all), tendency towards higher creatinine, urea, erythrocyte and haematocrit levels and longer cold ischemia time. In posttransplant period DGF was associated with higher rate of acute rejections, development of vascular surgical complications and lymphocele ($p<.05$ for all), however failed to be associated with significantly higher GL or PM. Graft losses during 10-year follow-up were associated with younger age donor and recipient, higher serum creatinine level at discharge, re-transplantation cases, development of acute rejections and vascular, urologic or lymphocele complications in posttransplant period ($p<.05$ for all). Analysis of groups showed that patients with DGF had higher risk of GL in re-transplantation cases and when combined with vascular complications and acute rejections.
Conclusions: Presence of DGF in posttransplant period is a significant complication and need careful posttransplant evaluation and treatment to prevent development of vascular surgical complications and acute rejection, that may negatively impact graft survival.

P697 AFTER A STEPWISE METHODOLOGY TO SHAPE A NATIONAL ALLOCATION SCORING SYSTEM FOR LIVER TRANSPLANTATION, WHICH IS THE BEST METRICS TO EVALUATE RESULTS?

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Background: A stepwise methodology to create a liver allocation system in Italy was applied through a 4-year consensus conference process leading to a new liver allocation scoring system (ISO score) officially applied on July 1, 2019. An ideal system should regularly promote adaptive changes with the aim to equalize the risk of death/dropout while waiting among the candidates of the different etiologic groups.

Methods: as efficiency metrics of the system, we arbitrarily choose to measure the drop-out rate (defined as death on the waiting list (WL) or delisting due to clinical worsening) of the different etiologic strata of candidates to liver transplantation: liver cirrhosis (LC), hepatocellular carcinoma (HCC) and MELD exceptions (MELD-ex). We analyzed the differences between PERIOD1 (from July 1, 2018 to June 30, 2019) and PERIOD2 (from July 1, 2019 to December 31, 2020) after the introduction of ISO score. To adjust the burden of the waiting time related to previous allocation systems only incident cases in both periods were considered. To avoid the potential bias related to COVID-19 period, SARS-CoV-2 positive cases dropping out were censored. Drop-out probabilities were analyzed both as crude rates and as competing risk time dependent events.

Results: 3555 incident listings across the two periods were evaluated. They included 1185 (33.3%) LC, 1550 (43.6%) HCC and 820 (23.1%) MELD-ex. There were 727 (50.9%) LTs with 102 (7.1%) drop-outs in period1, and 1237 (58.1%) LTs with 175 (8.2%) drop-outs in period2 (p=0.000). Using HCC as reference group, competing risk of drop-out in period1 was significantly higher in LC (HR 2.54, p=0.003) and lower in MELD-ex (HR 0.50, p=0.114), whereas in period2 the difference between HCC and LC significantly decreased (HR 1.45, p=0.027). Consistently, the advantage of MELD-ex compared to cirrhosis reduced.

Conclusions: A stepwise methodologically solid development of allocation systems is mandatory to ensure transparency and efficiency of the processes. The intrinsic complexity and diversity among the various etiological candidate categories requires regular adaptive changes. Drop-out rate homogeneity among macrogroups seems to be the first relevant metric to improve equity in the distribution of organ scarce resource.

Table 1. Crude and competing risk values of drop-out probabilities in the two study periods.

PERIODS	Groups	LT	On WL	DROP OUT Other Causes	Drop-out	Competing risk
		Number (%)	Number (%)	Number (%)	Number (%)	HR (95% CI), p value
Period 1	HCC	355 (56,5%)	242 (38,5%)	0 (0,0%)	31 (4,9%)	Reference
	LC	300 (56,9%)	151 (28,7%)	11 (2,1%)	65 (12,3%)	2.54 (1.66-3.88), 0.003
	MELD-ex	72 (26,5%)	193 (71,0%)	1 (0,4%)	6 (2,2%)	0.50 (0.21-1.18), 0.114
Period 2	HCC	551 (59,8%)	299 (32,4%)	2 (0,2%)	70 (7,6%)	Reference
	LC	389 (59,1%)	177 (26,9%)	16 (2,4%)	76 (11,6%)	1.45 (1.04-2.01), 0.027
	MELD-ex	297 (54,2%)	216 (39,4%)	6 (1,1%)	29 (5,3%)	0.64 (0.41-1.00), 0.050

Abbreviations: HCC, hepatocellular carcinoma; LC, liver cirrhosis; MELD-ex, MELD exceptions; LT; liver transplantation; HR, hazard ratio; CI, confidence interval.

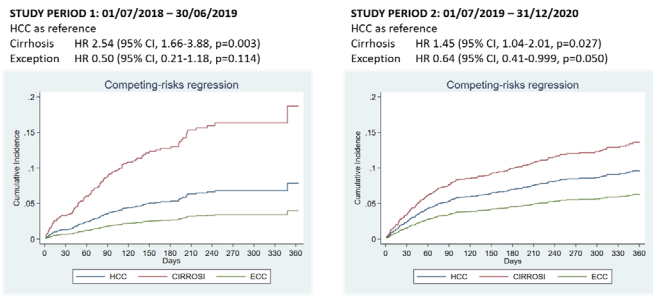

Figure 1. Competing risk analysis of drop-out probability comparing the three patient groups (i.e. HCC vs. LC vs. MELD-ex) in the two study periods.

P698 A SINGLE CELL TRANSCRIPTOMIC LANDSCAPE OF KIDNEY ENDOTHELIAL CELLS, FROM KIDNEY ORGANOIDS TO MATURE KIDNEY

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Kidney endothelial cells (KEC) are the main barrier between the circulatory system and the kidney graft. Targeting these cells holds potential as a therapeutic approach to mitigate the effects of inflammation, hypoxia, and drug toxicity. Kidney organoids (KO) provide a useful model to study KEC therapies and have the potential to serve as clinically transplantable auxiliary tissue. However, the structure of KO is immature and does not fully replicate that of the functional kidney. To fully utilize the potential of KO as a drug screening model and for tissue repair, it is crucial to thoroughly understand the molecular signatures of EC that drive further differentiation of the kidney's vasculature.

We dissected the heterogeneity of renal EC from different sources (human iPSC KO, implanted human iPSC KO, embryonic and adult kidney tissue) using single-cell RNA sequencing. We performed a trajectory analysis and checked transcription factor (TF) activity in KEC. By conducting differential gene and pathway analysis with a Wilcoxon rank sum test on all genes with a logFC of 1, we were able to identify alterations in injured KEC, whether caused by ischemia-reperfusion or upon immune response.

The transcriptome of the KEC from various sources/tissues created a heterogenous map where EC conserved features related to ion channels, nutrient transporters and some angiocrine growth factors were the common denominators. Nevertheless, angiogenesis, fibrosis and hypoxia related markers showed to be the main drivers of disparity among EC (pval<0.01). Trajectory analysis provided a global EC arrangement with iPSC KO as starting point, followed by embryonic, iPSC implanted KO, and finishing with adult EC, reflecting the path of KEC profiles over maturation. We also found specific TF sets for each of the KEC groups that switch upon development. Finally, we showed that KEC upregulate PKHD1, FHIT, WWOX, RUNX1 during relevant distress situations for the kidney, such as ischemia-reperfusion injury or allogenic immune cell exposure.

We present a comprehensive analysis of the transcriptomic changes in KEC across development and injury. Our findings highlight the activity of TF as potential targets for modulation, which could accelerate the maturation of KO and enable their use in exploring the underlying mechanisms of kidney disorders.

P699 TREATMENT OF RENAL CELL CARCINOMA IN RENAL GRAFT WITH NEPHRON-SPARING SURGERY OR ABLATIVE THERAPY

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Background: Renal cell carcinoma (RCC) in transplanted kidneys has been reported with an incidence of up to 0.5%. Conservative options such as nephron-sparing surgery (NSS) either enucleation or partial nephrectomy, and ablative therapy have been progressively used in selected recipients with early-stage allograft RCC (RCC T1, ≤7cm sec. AJCC 2018). We report our experience of 4 radiofrequency ablation (RFA) and 2 NSS occurred in our population of 1849 kidney transplant (KT) recipients.
Methods: The first 4 patients were treated with ultrasound-guided RFA, percutaneously in the first 3 cases and laparoscopic for case 4, using 14G electrode-needle mean exposure time was 3 minutes.Last 2 cases had NSS, the tumor was fully excised throughout a median umbilical-pubic laparotomy, in the last case there was an involvement of the renal calyx then indocyanine green was used for a better definition of the RCC surgical margins.
Results: No relapses were reported in both groups, and all patients remained with a stable renal function. Patient 5 and 6 had a complete RCC excision, PT1aG1 and PT1bG1 respectively.
Conclusions: Both RFA and NSS are valid options compared to radical nephrectomy for RCC T1 in KT patients allowing the maintenance of pre-treatment graft function and is associate with low morbidity. Considering the low grade of the RCC and the radical resection in the NSS group, the relapse risk is almost zero.
Table 1 patients' clinical features

	Gender	Age (year)	Months from KT	RCC size (mm)	Treatment
Patient 1	M	43	144	12x15	RFA
Patient 2	F	36	156	36x27	RFA
Patient 3	M	37	108	20x25	RFA
Patient 4	M	63	288	26x21	RFA
Patient 5	F	49	202	45x25	NSS
Patient 6	M	64	158	50x40	NSS

P700 ANTICOAGULANT AND ANTIPLATELET USE IN RENAL TRANSPLANTATION: IS PERIOPERATIVE BLOOD LOSS AND TRANSFUSION RATES A SIGNIFICANT CONCERN?

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Background: Renal patients often have multiple pathologies which necessitate anticoagulation. Renal transplantation remains the gold standard for patients with end-stage renal failure (ESRF). Major surgery poses increased risks of significant haemorrhage in the operative and perioperative period. Whilst reversal of agents such as warfarin is possible, the effect of antiplatelet therapies such as aspirin, clopidogrel, new oral anticoagulants (NOAC's), associated with surgical safety is less understood.
Methods: Electronic and paper records were accessed to investigate transplants occuring between 18/12/2019 and 30/11/2022. Preoperative anticoagulant/antiplatelet regimens were recorded, along with coagulation screens and Haemoglobin (Hb) levels. Sequential Hb's for 72 hours perioperative were collated along with transfusion rates and adverse outcomes.
Results: 12 transplants occurred during this period. International normalised ratios (INR) ranged from 0.9 – 2.4 preoperative. No preoperative blood products or reversal agents were administered. The average Hb drop was 16.2 g/dl at 72 hours. 1 patient required a 2-unit red cell transfusion (starting Hb 76 g/dl). No deaths were recorded. Salient findings are summarised below:
Conclusions: This small, yet focussed study suggests a blood transfusion rate of 8.4% in patients undergoing renal transplant taking concurrent anticoagulants. Hb fluctuations along with transfusion rates are comparable to those undergoing renal transplant in the absence of any anticoagulant. This would suggest that renal transplant is feasible under these circumstances. Further large scale studies are required.

Recipient no.	Agent	Type of Rtx	Hb Preop	Hb Postop	Hb D1	Hb D2	Hb D3
1	DAPT	LD	108	97	98	89	96
2	DAPT	LD	128	119	112	119	113
3	Warfarin	LD	121	106	94	93	104
4	Ticagrelor	LD	92	80	83	82	85
5	Warfarin	LD	120	113	108	109	107
6	Apixaban	Deceased	116	103	106	111	104
7	Apixaban	Deceased	121	98	104	96	92
8	Warfarin	Deceased	127	119	112	102	96
9	Warfarin	Deceased	146	122	119	103	94
10	Warfarin	Deceased	106	102	102	99	101
11	Clopidogrel	Deceased	120	107	108	106	99
12	Warfarin	Deceased	76	86	86	83	87
AVERAGE			114.4				98.2

P701 EVOLUTION OF MINIMAL INVASIVE LIVE DONOR NEPHRECTOMY:TECHNIQUES AND OUTCOMES FROM THE BUSIEST GREEK RENAL TRANSPLANT CENTER,IN LAIKO GENERAL HOSPITAL

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Background: Since its introduction in 1995, laparoscopic nephrectomy has emerged as the preferred surgical approach for living donor nephrectomy. Given the ubiquity of the surgical procedure and the need for favorable outcomes, as it is an elective operation on otherwise healthy individuals, it is imperative to ensure appropriate preoperative risk stratification and anticipate intraoperative challenges. The aim of the present study was to compare peri-and postoperative outcomes of living kidney donors (LD), who had undergone laparoscopic nephrectomy (LDN), with a control group of those who had undergone open nephrectomy (ODN).
Methods: Data from 409 LD from a single transplant center from March 2015 to January 2023 were analyzed retrospectively. In total, 274 donors in the LDN and 135 in the ODN groups were assessed. Demographics, type of transplantation, BMI, duration of surgery, length of hospital stay, peri- and postoperative complications, renal function at discharge were recorded and compared between the two groups.
Results: There was no difference in baseline characteristics, nor in the prevalence of peri-and postoperative complications, with a total complication rate of 10% (mostly minor, Clavien–Dindo grade II) in both groups, while a different pattern of surgical complications was noticed between them. Duration of surgery was significantly longer in the ODN group (median 240 min vs. 140 min in LDN, $p < 0.01$), warm ischemia time was longer in the LDN group (median 4 min vs.2 min in ODN, $p < 0.01$) and length of hospital stay shorter in the LDN group (median 3 days vs. 7 days in ODN). Conversion rate from laparoscopic to open surgery was 1.09%. There was a drop in estimated glomerular filtration rate (eGFR) at discharge of 36 mL/min in the LDN and 32 mL/min in the ODN groups, respectively ($p = 0.03$). No readmission or reoperation were recorded. One donor death has been occurred due to no surgical reasons.
Conclusions: This study provides evidence that minimally invasive surgery can be performed safely, with very good short-term outcomes, providing several benefits for the living kidney donor, thereby contributing to expanding the living donor pool, which is essential, especially in countries with deceased-donor organ shortage.

P702 WHEN MORE IS NOT BETTER — BIG DATA AND MACHINE LEARNING IN ASSESSING THE RISK OF COVID-19 INFECTION IN SOT RECIPIENTS AND PATIENTS ON WAITING LIST

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Background: We used big data from a single transplant center to machine learning experiments aiming to find best predictive model for COVID-19 incidence. This study's primary objective was to determine which parameters can predict if a patient will be infected with COVID-19. Secondary objective: to determine if the addition of immunogenetic data to the machine learning prediction model adds meaningful value
Methods: Big dataset (136 features) from 565 patients (274 were SOT recipients) underwent machine learning experiments. The characteristics of patients randomly assigned to the training or testing groups. Following factors formed input parameters (134 features): a) clinical (including comorbidities) and demographic characteristics, b) genetic HLA-A, B, C, DR, DQ, TNFRSF8 (rs2297729), BSG (rs4919859), TNFA (rs1799724), IFNG (T+874A, rs2430561), TNFA (G-308A, rs1800629), IL-17A (G-197A, rs2275913), IL-17F (T+7488C, rs763780), IL-6 (G-174C, rs1800795), ACE2 (rs210680, rs2074192, rs4240157), TMPRSS2 (rs12329761, rs2070788), c) presence of SARS-CoV-2 antibodies and vaccination status, d) inflammation related markers from peripheral blood: CRP, hemoglobin, albumin, BNP, NT-pro-BNP, suPAR, IL-6, IFN-gamma, TNF-alpha, complement functional activity), e) blood morphology derived parameters: NLR, PLR and MLR, f) immune cell phenotypes including T cells (regulatory T cells, Tc, Th1, Th2 and Th17), B cells (naive, memory, transitional, plasmablasts), NK and NKT and g) TTV viremia.

Results: Surprisingly, the best model obtained only 63% accuracy when all 134 characteristics were utilized as input data. The model using immunogenetics data without circulating biomarkers and cell phenotypes yielded the best performance (93.5%). Figure 1 depicts the neural network's weights, which are the real values associated with each input and which represent the contribution of that feature to the final prediction
Conclusions: Using immunogenetics data and machine learning, we were able to evaluate the risk of COVID-19 occurrence in SOT recipients with good accuracy. We have discovered that more data does not necessarily increase the accuracy of COVID-19 prediction, particularly when employing a single assessment of circulating biomarkers that are likely to change over time.

Weight	Feature
0.2587 ± 0.0247	SARS-COV2 variant (virulence based on pandemic time)
0.1444 ± 0.0252	mRNA vaccination status
0.0101 ± 0.0040	chronic kidney disease (yes/no)
0.0074 ± 0.0078	ACE2 polymorphism, rs4240157
0.0074 ± 0.0040	diabetes (yes/no)
0.0058 ± 0.0052	transplanted organ age (years)
0.0058 ± 0.0097	GFR below 60 ml/min/1.73m2
0.0048 ± 0.0040	renal disease vintage (years)
0.0042 ± 0.0042	IL-17A polymorphism, rs2275913
0.0042 ± 0.0026	liver transplant (yes/no)
0.0037 ± 0.0042	hypertension (yes/no)
0.0037 ± 0.0072	patient age
0.0037 ± 0.0042	BMI
0.0037 ± 0.0042	TMPRSS2 polymorphism, rs2070788

P703 IMPACT OF HEPATIC VEIN RECONSTRUCTION TECHNIQUE ON VENOUS OUTFLOW OBSTRUCTION IN VENA-CAVA SPARING (PIGGYBACK) DECEASED DONOR LIVER TRANSPLANT

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Background: Hepatic vein outflow obstruction (HVOO) is a rare but serious complication of deceased donor liver transplant (DDLT) using the vena-cava sparing piggyback technique (PGB). In this technique, there are many options for reconstruction of the hepatic veins. It is unknown which technique is the least likely to result in HVOO. This study analyzes a large number of liver transplants at a single center to determine if one type of reconstruction is superior.
Methods: Single center data were extracted using a retrospective review of all LTs between 2013 and 2022, including operative notes and any interventional radiology procedures. Anastomosis in all cases included the donor suprahepatic vena cava anastomosed to the recipient vena cava at the recipient hepatic veins. HVOO was diagnosed with venogram and/or pressure measurement, and/or the requirement for venoplasty and/or stent placement. Evaluation was indicated generally for persistent ascites or evidence of liver congestion. Vena cava reconstruction technique was based upon the recipient hepatic veins included in the anastomosis, right (R), middle (M), and left (L) hepatic veins. Primary outcomes included 1-year post transplant need for hepatic vein imaging/intervention, and 90-day and 1-year graft survival.
Results: There were 1179 LTs. HV drainage pattern included 688 R/M/L (58%), 377 M/L (32%), 77 R/M (6%), and 14 R only (1%). Less than 2% of the recipients underwent bicaval or cavocavostomy reconstruction. Any HV imaging was needed for 4% R/M/L, 5% M/L, 1% R/M, and 0% R only (p=0.03). Any posttransplant hepatic vein complication was identified in 2% R/M/L, 3% M/L, 1% R/M, and 0% R only (p=0.67). Ninety-day graft survival was 95% R/M/L HVs, 94% M/L, 99% R/M, and 100% R only (p=0.32). One-year graft survival was 93% R/M/L, 92% M/L, 95% R/M, and 93% R only (p=0.71).
Conclusions: In this cohort, recipients with right/middle and right only HV drainage patterns required less need for hepatic vein imaging compared to middle/left and right/middle/left HV drainage. The rate of post-transplant hepatic vein complications was not significantly different among the four groups.

P704 ROBOTIC SURGERY TO SOLVE URINARY TRACT COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

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Background: Complications of the urinary tract (UT) after kidney transplantation are described in 5-10% and represent significant morbidity. The treatment of choice is surgical repair with high success rate. Robotic surgery provides the benefits of minimally invasive surgery in complex cases. The objective of this study is to assess the efficacy and safety of robotic surgery for treatment of UT complications in kidney graft.
Methods: We conducted a retrospective study of transplanted patients undergoing robotic surgery for UT complication from January 2018 to December 2022. A total of 20 patients were collected. Clinical and surgical aspects, and follow up are described. Pre-surgical: With nephrostomy (NP) tube placed, a pyelography and CT-scan is performed. Surgical Technique: A modified robotic pelvic surgery protocol is used. NP is connected in the field for its manipulation. Robotic ultrasound (US) is a key tool. Double J stent is always placed. Post-operative: All tubes stay open for 24 hours, then NP tube is closed and removed at day 5-7. If reimplantation is done, bladder catheter stays 5-7 days. Double J stent is removed at week 4. Follow-up: US is done 1 month after Double J removal, and 3-6-12 month and then annually.
Results: There were 8 stenosis of the uretero-vesical anastomosis, 11 pyelo-ureteral junction stenosis and 1 ureteral fistula. For distal stenosis a robotic uretero-vesical reimplantation was performed (9 cases) and for upper UT stenosis a robotic anastomosis to the native ureter was performed (11 cases). One case was converted to open surgery due to adhesions. The surgical time was 150 minutes (IQR125-190). The hospital stay was 3 days (IQR 2-5.25). In 18/19 patients, all urinary drainage was removed with stable renal function, representing 94.74% success rate, with 10 months median follow-up (IQR 4-22). As complications, there were 6 pyelonephritis, 1 hematuria and 1 stricture recurrence after a systemic genito-urinary tuberculosis, including multiple ureteral stenosis, consider failure of the surgical technique.
Conclusions: Robotic surgery to manage UT complications after kidney transplantation is effective and safe in short and long term. It provides the benefits of minimally invasive surgery with greater surgical precision in complex cases.

P705 THE COMPASSIONATE MINDFUL RESILIENCE (CMR) PROGRAMME TO IMPROVE PSYCHOSOCIAL WELL-BEING IN PEOPLE WITH KIDNEY DISEASE

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Background: Kidney disease is a progressive condition, and patients experience difficult physical and psychological symptoms. In addition, the impact of the coronavirus (COVID-19) pandemic has brought many additional burdens for patients. Presently access to psychological and emotional support is not well provided or funded and the UK's leading patient support charity Kidney Care UK (KCUK) was keen to explore the feasibility of delivering mental health support via virtual means as a cost-effective way to support patient's wellbeing. The aim of the study was to support a new service development project in partnership with KCUK by implementing the four-session Compassionate Mindful Resilience (CMR) programme, developed by MindfulnessUK, and explore its effectiveness for patients with stage 4 or 5 chronic kidney disease or have received a kidney transplant.
Methods: Participants (n=19) and the Mindfulness Teacher completed online interviews, which were transcribed, coded and thematically analysed.
Results: Results: Three themes and ten subthemes were reported: benefits of participating in the CMR programme, participants lived and shared experiences and experience of participating in the CMR programme. All participants reported that they found participating in the CMR programme to be beneficial.
Conclusions: The programme was found to be acceptable, feasible and suitable for people living with kidney disease, and provided tools and techniques that support the mental health and wellbeing of this patient group.

P706 REAL-TIME ASSESSMENT OF PERFUSATE BIOMARKERS DURING EX SITU LIVER PERFUSION: A PILOT CLINICAL STUDY

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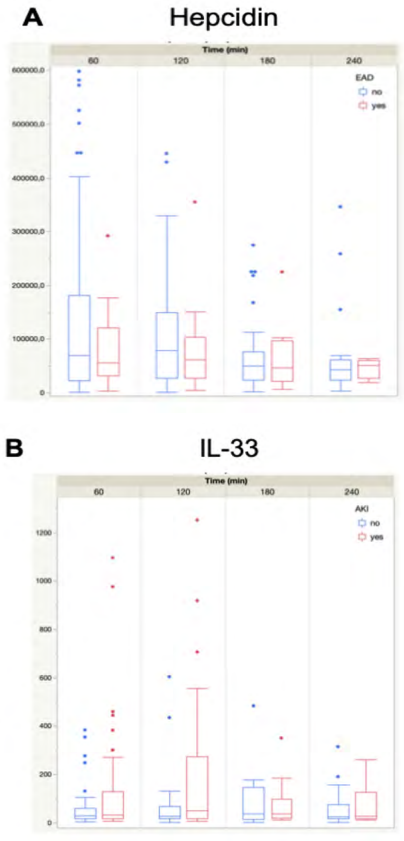
Background: The molecules released from the liver during ex situ perfusion can provide important information regarding graft function as well as the factual damage experienced by hepatocytes and cholangiocytes during the donation process. The present study investigated the use of a novel automated immunoassay platform to determine the concentration of perfusate biomarkers released by human livers subjected to Hypothermic oxygenated machine perfusion (HOPE).
Methods: The retrospective observational study includes HOPE procedures performed on DBD-ECD and DCD donor livers from 2017 to 2020 at Policlinico (Milan, Italy) and Molinette (Turin, Italy). Perfusate samples were collected hourly and stored at -80°C. Selected biomarkers relevant to inflammation, cell damage, and endogenous healing processed were assessed using the traditional approach (Enzyme-linked Immunosorbent Assay, ELISA) and the automated technology. Consistency between the 2 techniques was evaluated by Bland-Altman analysis.
Results: Eighty-nine donors were included, of whom 51 were DBD-ECD and 38 DCD. All grafts were successfully transplanted; 23 (26%) recipients developed early-allograft-dysfunction (EAD), while 52 (58%) developed acute-kidney-injury (AKI). All the evaluated molecules were consistent between the two analytical techniques. The automated technology provided the results within 90 min after the beginning of the assay. Analysis of the perfusates collected at 1 h of HOPE revealed a lower concentration of Hepcidin in the EAD-yes compared to the EAD-no group (79.65±52.37ng/g vs 137.24±21.03ng/g, p<0.050, Figure, panelA), while an increased concentration of IL-33 was detected in the AKI-yes relative to the AKI-no group (190.32±69.09pg/g vs 59.11±15.23pg/g, p=0.017, Figure, panelB).
Conclusions: Molecular profiling of the perfusate collected during MP could enable to obtain a precise evaluation of marginal grafts, while providing useful information for prediction of postoperative complications. This strategy could optimize the donor/recipient match, in line with the principles of personalized medicine.



P707 HEART TRANSPLANTATION IN RECIPIENTS OVER 60 YEARS-OLD: A SINGLE-CENTRE EXPERIENCE

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Background: For decades the selection of potential recipients for heart transplantation (HTx) was limited to the 60 year-old as the upper age limit because of an increased risk complications and comorbidities in the older group. However, throughout the years and in experienced transplant centers, HTx in older patients can achieve acceptable results. The aim of the study was to evaluate our experience of HTx in recipients over 60 year-old.
Methods: From 2010 to 2021 HTx was performed in 177 patients, 22 (12.4%) of them were over 60 year-old. We analyzed retrospectively results in aged transplant recipients group: early-term results, including 30-day mortality, and survival within 1 year after HT
Results: Recipients' mean age was 63±2 year-old (n=18 – male). Causes of heart failure (HF) were IHD (n=14), dilated cardiomyopathy (n=6), RHD (n=1) and isolated cardiac amyloidosis (n=1). LVEF was significantly decreased 23.9±12.3% while PASP (49.1±14.1 mm Hg) and PVR (3.1±1.5 W.U.) were elevated. Patients spent in a HTx waiting list 103±26 days (1 was bridged with an ECMO) and were classified by UNOS: 1A (n=4), 1B (n=3) and 2 (n=15). All recipients underwent HTx using the bicaval technique (369±39 minutes – duration of surgery. Results of early-term follow after HTx were: 5±2 days on respiratory support, 11±2 days – on inotrope support, 11±3 days – ICU stay. After HTx ECMO was implanted to 3 patients due to the development of right HF (RHF). During 1st month there were no episodes of allograft rejection but the following complications were diagnosed: urinary tract infection (n=6), pneumonia (n=5), acute kidney failure (n=1) and a sick sinus syndrome followed by pacemaker implantation (n=1). Early-term 3 recipients died: 1 – from stroke in 6 days and 2 – from RHF 25 and 40 days after HTx, respectively. In 9 months an allograft rejection (2R/3B) was diagnosed in 1 patient which was successfully treated by pulse steroid therapy and plasma exchange sessions. In 6 months and 1 year 2 patients died from infectious complications complicated with sepsis.
Conclusions: Transplant recipients over 60 year-old were characterized by the development of RHF but only 14% of them required an ECMO implantation. In our study, 30-day mortality was 9%. Both ealy and long-term after HTx infectious complications prevailed in this group.

P708 SEXUAL DYSFUNCTION AND KIDNEY TRANSPLANTATION: A SCOPING REVIEW TO INFORM BEST PRACTICE

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Background: Kidney transplantation is the gold-standard treatment for patients with end-stage kidney disease. Patients who receive a kidney transplant, experience an improvement in many aspects of daily life but often have poorer quality of life than the general population. Sexual functioning is a general component of health which can be affected negatively in patients with a kidney transplantation. However, the assessment of sexual functioning is not incorporated into standard practice in renal care. It is important to enhance quality of life for kidney transplant recipients, especially considering the many treatments available to successfully treat sexual dysfunction. The aim of this scoping review is to explore what is known about the management of sexual dysfunction in adult kidney transplantation to inform best practice.
Methods: A scoping review methodology was used.
Results: Results explored treatments, therapies, and interventions to treat sexual dysfunction in kidney transplantation. This included accommodative adjustment mechanisms, psychological support, medication/devices, spousal support, and healthcare professional support.
Conclusions: It is evident that sexual functioning is a complex multi-factorial, multi-faceted phenomenon. However, research is limited and there is an urgent need for high-quality evidence to inform the development of appropriate support strategies and interventions for this patient population. Healthcare professionals need to develop a better understanding of sexual dysfunction in kidney transplantation and remove challenges to the assessment and treatment in renal healthcare.

P709 STATE-OF-THE-ART LAPAROSCOPIC LIVE DONOR KIDNEY RETRIEVAL TWICE IN THE SAME PATIENT. A UNIQUE CASE IN THE WORLD LITERATURE

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Background: Living kidney donor transplantation has been a significant contributor to renal transplantations since its inception in 1954. Over a third of all kidney transplants in the USA are from living donors, and the procedure has been made safer since the advent of laparoscopic living donor nephrectomy in 1995. Laparoscopic renal procurement is a challenging operation. Re-interventions for the same cause are rare but may occur.
Methods: Our centre has performed more than 280 cases of laparoscopic living kidney retrievals since October 2018, with low morbidity and mortality rates. We present a unique case, in which the laparoscopic donor procedure had to be temporarily stopped due to a complication during the recipient's surgery. The left kidney of the donor and its ureter were fully dissected and almost ready to be removed. However, the donor's kidney was successfully retrieved seven months later. Patient's demographics and operations data are presented in Table 1.
Results: Although this case is a one-of-a-kind occurrence, we present it for its management and findings from the second attempt. The chronic gap between the two surgeries was seven months. New Computed Tomography was performed prior to the second operation. Intraoperatively, the second surgery required again mobilization of the kidney due to adhesions in the retroperitoneum, but the renal vessels and ureter ligation was performed without any issue. The renal graft has been successfully transplanted. Hospitalization length was three days. No blood loss was occurred, while less analgesic consumption and uneventful postoperative course has been noticed.
Conclusions: Laparoscopic donor nephrectomy is a challenging operation, but remains the safest procedure with low morbidity and mortality rates, offering early hospital discharge and improved post-operative quality of life to donors. Re-interventions for the same cause to the donors are rare, but may occur.

Table1. Patient Demographics	
Age	71
Gender	Male
BMI	29.7
Laterality	Left
Renal Anatomy	Single Vein/Artery
Prior surgeries	No

P710 TIMING OF PERITONEAL DIALYSIS CATHETER REMOVAL IN KIDNEY TRANSPLANT RECIPIENTS: A MULTICENTER PROPENSITY SCORE MATCHED COHORT STUDY

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Background: An ongoing discussion challenges potential benefits of removing peritoneal dialysis (PD) catheters after kidney transplantation. Such an approach might help patients quickly restart PD in case of early graft dysfunction while also exposing them to the risk associated with the need of additional hospitalization, the occurrence of potential catheter-related infections, and complications after the removal procedure. We aimed to establish the optimal timing for PD catheter removal in renal graft recipients.
Methods: We conducted a 1:1 nearest neighbourhood propensity score matched cohort study in kidney transplant recipients with PD catheters removed either at the time (the experimental) or after their renal transplant (the control group). We compared the incidence of (1) needing dialysis within two post-transplant months, (2) catheter-related infection, peritonitis and/or surgical site infection (a composite endpoint), and (3) length of hospitalization.
Results: The experimental and control groups consisted of fifty-five patients each (mean age [interquartile range, IQR], 40 [31 – 56] vs. 40 [32 – 55] years; 51% vs. 48% of males; 5% vs. 4% of living-donor transplants). Eighteen per cent of patients needed dialysis within two posttransplant months with no statistically significant differences between the experimental and control group (20% vs. 15%; χ_1^2 = 0.45; P = .504). Hemodialysis was utilized in all cases. The median time for PD catheter removal in the control group was 71 days (IQR, 39 - 107). No differences were found between the groups regarding the incidence of infectious complications when adjusted for donor's age and donor's BMI (odds ratio, 0.51; 95% confidence interval, 0.11 - 2.36; P = .393). Patients in the experimental group had significantly shorter time of hospital stay (median [IQR], 9 [7 - 12] vs. 13 [9 - 18] days, U = 921.0, P < .001).
Conclusions: Haemodialysis was the preferred dialysis modality in all patients, even with PD catheter in place . PD catheter removal after kidney transplant does not increase the incidence of infections but is associated with longer hospital stay. Our study does not support the routine of postponing the removal of PD catheter in patients undergoing kidney transplants.

P712 IMMUNOADSORPTION-BASED HLA DESENSITIZATION IN PATIENTS AWAITING DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: Whether immunoadsorption (IADS) as part of desensitization protocols could facilitate deceased donor kidney transplantation (KT) in highly sensitized (HS) patients remains to be proven.
Methods: We retrospectively analyzed our IADS based desensitization protocol for deceased donor KTs between 2013 and 2018.
Results: Fifteen HS patients (age 52 years [40-56]) were included. Waiting time before IADS was 6 years [5-10] and the interval between IADS initiation and KT was 5 months [1–12] for the 14 transplanted patients. Nine patients had prior KT. Calculated panel reactive antibody decreased significantly during the protocol (99.3%[92.5-99.9] vs. 79.4%[56.7-81.9]; p=0.004). Death-censored graft survival was 85.7% at 1 year and 2 years post-transplantation. One-year median plasma creatinine level was 135 µmol/L [111-202]. Six developed active antibody mediated rejection (ABMR) at 1 year, with a median delay of 13 days [11-26]. Eight patients developed severe infections, including 2 fatal outcomes. Finally, compared to 93% of patients who received desensitization receiving a KT, only 43% of a control with similar characteristics underwent transplantation.
Conclusions: These results suggest that IADS-based desensitization may allow for deceased donor KT in patients with otherwise very restricted access, but at the cost of a high rate of ABMR and severe infectious complications.

P713 NO ASSOCIATION BETWEEN ARTERIAL REPERFUSION TIME AND CLINICAL OUTCOMES FOR LIVER TRANSPLANTATION USING DONATION AFTER CIRCULATORY DEATH GRAFTS

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Background: Biliary complications, especially ischemic cholangiopathy as a result of ischemic bile duct injury, remain a major source of morbidity after liver transplantation (LT) using donation after circulatory death (DCD) grafts. Little is known about the effect of timing of arterial reperfusion during DCD LT on the incidence of biliary complications. The objective of this study is to assess the association between the arterial reperfusion time and clinical outcomes after DCD LT.
Methods: Data for patients undergoing LT with DCD grafts between 2001-2018 were retrospectively collected by three centres, including donor and recipient characteristics, reperfusion sequence, ischemic and arterialization times and post-operative complications. Parameter of interest was arterialization time (time between portal and arterial reperfusion). Primary endpoint was the occurrence of biliary complications, secondary endpoints were graft and patient survival, as well as re-transplantation rates.
Results: Data were available for 292 patients with a median follow-up of 4.5 years. Median arterialisation time was 34 (13-134) minutes. Overall, biliary complications occurred in 46% of patients (28% anastomotic strictures, 26% non-anastomotic strictures, 12% bile leaks), and re-transplantation in 20%. 1-, 3- and 5-year patient and graft survival were 89%, 79%, 74% and 75%, 64%, 58%, respectively. There was no association between arterialization time and occurrence of biliary complications, graft and patient survival or re-transplantation rates.
Conclusions: Variation in timing of arterial reperfusion during DCD liver transplantation does not seem to affect clinical outcomes of LT using DCD grafts.

P714 ADDED-VALUE OF RITUXIMAB AND PE ON TOP OF STANDARD INDUCTION THERAPY IN KIDNEY TRANSPLANT RECIPIENTS WITH PREFORMED HIGH-TITER DSA

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Background: Optimal induction strategy in highly sensitized kidney transplant recipients (KTRs) is still a matter of debate. The place of therapies, such as plasma exchange and rituximab, with potential side effects and high cost, is not clearly established.
Methods: We compared two induction strategies with (intensive) or without (standard) rituximab and plasma exchange in KTRs with high levels of preformed DSA transplanted between 2012 and 2019.
Results: Sixty KTRs with a mean age of 52.2±12.2 years were included, 36 receiving standard and 24 intensive induction. Mean fluorescence intensity of immunodominant DSA in the cohort was 8903±5469 pre-transplantation and similar in both groups. DSA level decrease was similar at 3 and 12 months after transplantation in the two groups. An intensive induction strategy was not associated with better graft or patient survival, nor more infectious complications. The proportion of patients with rejection during the first year was similar (33% in each group), but rejection occurred later in the intensive group (211±188 days, vs. 79±158 days in the standard group, p<0.01).
Conclusions: Our study suggests that an intensive induction therapy including rituximab and plasma exchanges in highly sensitized kidney recipients is not associated with better graft survival but may delay biopsy-proven rejection.

P715 DECEASED DONOR LIVER TRANSPLANT (DDLT) WITH DUCT-TO-DUCT ANASTOMOSIS USING CONTINUOUS OR INTERRUPTED SUTURING, AND 5-0 OR 6-0 SUTURE SIZE

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Background: Bile duct complications in deceased donor liver transplant (DDLT) are common. This study reviews a large number of transplants with duct-to-duct reconstruction at a single center, and compares continuous and interrupted suturing, and use of 5-0 or 6-0 polydioxanone (PDS) suture.
Methods: Single center data were extracted from the electronic medical record using a retrospective review of all DDLTs between 2013 and 2022, including original operative notes and any duct imaging procedures, including endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous cholangiogram (PTC). Anastomoses in all cases included the donor and recipient bile ducts anastomosed in an end-to-end fashion with PDS suture. Choice of technique and suture size was at the discretion of the surgeon with the technique otherwise being essentially equivalent. Indication for imaging included any unexplained elevation in the liver function laboratory values, not explained with standard liver ultrasound. In general, biliary imaging was obtained primary to biopsy for evaluation of elevated enzymes, resulting in a large number of studies. Study outcomes included 1-year post transplant need for any duct imaging, presence of anastomotic strict or leak, and 90-day and 1-year graft survival.
Results: There were 1177 DDLTs included in the analysis. Overall, 37% of patients had any bile duct imaging in the first year, 44% continuous versus 36% interrupted (p=0.11), and 39% 5-0 PDS versus 31% 6-0 PDS (p=0.03). Any anastomotic stricture was seen in 28% of patients, 35% continuous versus 28% interrupted (p=0.13), and 31% 5-0 PDS versus 22% 6-0 PDS (p<0.01). Any bile duct leak was seen in 7% of patients, 8% continuous versus 7% interrupted (p=0.78), and 7% 5-0 PDS versus 6% 6-0 PDS (p=0.85). Ninety-day and 1-year graft survival were statistically equivalent for the different groups.
Conclusions: In this cohort, duct-to-duct reconstruction with interrupted suturing using 6-0 PDS suture appeared to have the lowest rate of biliary complications, including a lower need for imaging, a lower rate of anastomotic stricture, and with similar risk of bile duct leak. Early and late graft survival were not affected by suture technique nor by suture material.

P716 TACROLIMUS CONCENTRATION-TO-DOSE RATIO AND ITS ASSOCIATIONS WITH TACROLIMUS METABOLITES: PRELIMINARY ANALYSIS OF THE TIPS TRIAL

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Background: Tacrolimus remains a cornerstone of immunosuppression in kidney transplantation (KT). The common use of pharmacokinetic tools for tacrolimus prescription suggests new tools to improve graft survival and patients' quality of life. Interindividual differences of tacrolimus metabolization pathways (TMP) suggest individualization targets. Tacrolimus concentration-to-dose ratio (Tac C/D) has been suggested as a tool for such individualization.
Methods: This is a preliminary pharmacokinetic analysis of the TIPS trial (NCT04526431). We prospectively monitored tacrolimus blood levels in incident KT recipients (KTR), including 3 tacrolimus metabolites as a reflection of TMP, and evaluated the associations of these levels with Tac C/D. These metabolites were measured simultaneously by liquid-chromatography – tandem mass-spectrometry (LC-MSMS), on whole blood.
Results: As of 2022, we could analyze data in 51 KTR, corresponding to 247 tacrolimus and metabolites measures over the first year post-KT. Tacrolimus metabolites (M-I, M-II and M-III) could all be detected in patients' blood, with concentrations in the range of 1/100 of the mother tacrolimus molecule. There were 10 fast metabolizers (Tac C/D < 1.05) and 41 with a standard metabolization (Tac C/D > 1.05). Trough concentrations between fast metabolizers and standard metabolizers were significantly different (5.98 VS 7.77 µg/l, Wilcoxon p=0.013). On the other hand, in this small sample, there were no significant differences in trough metabolites concentrations between fast and standard metabolizers (p=ns for all comparisons).
Conclusions: Tacrolimus metabolites can be efficiently measured in whole blood using an adapted LC-MSMS assay. In this early, small sample analysis, Tac C/D was associated with traditional tacrolimus levels. Further data is pending analysis to decipher the potential use of metabolites concentrations in drug prescription individualization.

P717 PREDICTIVE OUTCOMES OF ACCEPTED AND DECLINED KIDNEY OFFERS: ARE WE DECLINING GOOD KIDNEYS !

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Background: Although the national shortage of deceased donor kidneys, around 55% standard criteria (SCD) DBD and 63% SCD DCD are declined at least once before being utilised elsewhere. Based on the data from National Health System, Blood and Transplant (NHSBT), The Winton Centre for Risk and Evidence Communication has developed a Kidney Transplant Tool (KTT) that provides a predictive graft and patient survival. We wanted to see if the predictive scores of the declined kidneys in terms of graft and patient survival were significantly worse leading to offer rejection.
Methods: In this single centre, retrospective pilot study, we used KTT to compare the predicted outcomes for the accepted and declined kidneys in our centre during 2022. Recipient's age, ethnicity, primary kidney disease, waiting time, previous transplant and HLA mismatch, with donor's age, history of hypertension and body mass index were collected to be used on the online KTT to calculate the allograft and patient survival figures of 1, 3 and 5 years. We included all accepted kidneys and kidneys declined by our centre but used elsewhere.
Results: The predicted outcomes of 112 accepted offers showed expected kidney survival of 89.32%±4.05, 84.76%±5.65 and 80.77%±6.94, while the expected patient survival was 94.47%±4.02, 90.88%±6.47 and 88.69%±7.73 at 1, 3 and 5 years respectively. Of the 101 declined deceased kidney offers that were transplanted elsewhere, the expected kidney survival was 88.21%±4.42, 83.19%±6.14 and 78.76%±7.43, and patient survival was 93.14%±4.03, 88.72%±6.22 and 86.26%±7.41 at 1, 3 and 5 years respectively. Comparing the means of both groups showed no significant difference with p-value >0.05.
Conclusions: This analysis does not look into the reasons of decline (patient decline, unwell recipient, positive crossmatch or low risk apatite), hence it is not possible to draw direct conclusions, but it highlights the subjective nature of decision making when accepting organs. With no significant difference between accepted and declined offers predicted survival estimates in this study, we wonder if a more granular look at the causes of organ refusal will identify areas of focus to improve organ utilisation. This analysis also highlights the benefits of prompt re-offering of organs after first decline to improve utilisation.

P718 HEPATITIS B VIRUS REACTIVATION IN KIDNEY TRANSPLANT RECIPIENTS TREATED WITH BELATACEPT

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Background: Hepatitis B virus (HBV) reactivation in kidney transplant recipients may be associated with liver failure and graft loss, especially in anti-HBc antibody (HBcAb)-positive HBs antigen (HBsAg)-negative patients. Belatacept, a selective costimulation blocker, has been used in kidney transplantation for some time and has been associated with reactivation of other viruses as BK or CMV. However, there are few data on HBV reactivation among kidney recipients treated with belatacept.
Methods: We performed a retrospective study in two French kidney transplantation centres including all transplant recipients receiving belatacept. Among HBcAb-positive patients, we analyzed HBV reactivation rate, outcomes and risks factors.
Results: 135 patients treated with belatacept were included, and 32 were HBcAb-positive. Seven patients reactivated HBV (21.9% of HBcAb-positive patients), including 5 HBsAg-negative patients (16.7%); reactivation occurred 54.8 (± 70.9) months after transplantation. There was no significant difference in survival between patients that reactivated HBV and patients that did not: 5-year patient survival of 100% (28.6; 100) and 83.4% (67.6; 100), respectively (p=0.363) and 5-year graft survival of 100% (28.6; 100) and 79.8% (61.7; 100), respectively (p=0.335). No factor, including HBsAb positivity and antiviral prophylaxis, was statistically associated with the risk of HBV reactivation.
Conclusions: Compared to the few studies that exist in this area, the HBV reactivation rate was high in patients treated with belatacept in our study. Our findings suggest that systematic antiviral prophylaxis for anti-HBc antibody (HBcAb)-positive HBs antigen (HBsAg)-negative patients should be considered and that there should be close monitoring of HBV serology and viral load in these patients to detect early HBV reactivation.

P721 COMPARISON OF SYSTEMIC VENOUS ANASTOMOSIS TECHNIQUES IN PANCREAS TRANSPLANTATION

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Background: Pancreas transplantation is an established method of treatment of diabetes mellitus patients. Advances in as well as surgical techniques as immunosuppressive treatment have led to improving results in pancreas transplantation recipients.
Methods: We reviewed 254 consecutive pancreas transplants performed in our Centre since 2004 until February 2023. Among these patients we performed 218 SPK, 28 PTA and 8 PAK. In years 2004-Februray 2018 we performed systemic venous anastomosis with the donor's iliac vein (n=196). Since February 2018 until February 2023 we performed 57 venous anastomosis with the donor's inferior vena cava (IVC).
Results: We statistically analysed the two groups pf patients – one with the systemic venous anastomosis with iliac vein and one with the anastomosis with the IVC. There were no significant differences in patient, kidney, or pancreas allograft survival rates. The statistical significance was found in pancreas graft thrombosis incidence.
Conclusions: Systemic venous drainage is the most common type of the venous anastomosis. The results show that pancreas graft thrombosis was less common in the IVC group. Systemic anastomosis with IVC seems to be more beneficial for the pancreas graft recipients.

P722 OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS CLASSIFIED AS HIGH RISK

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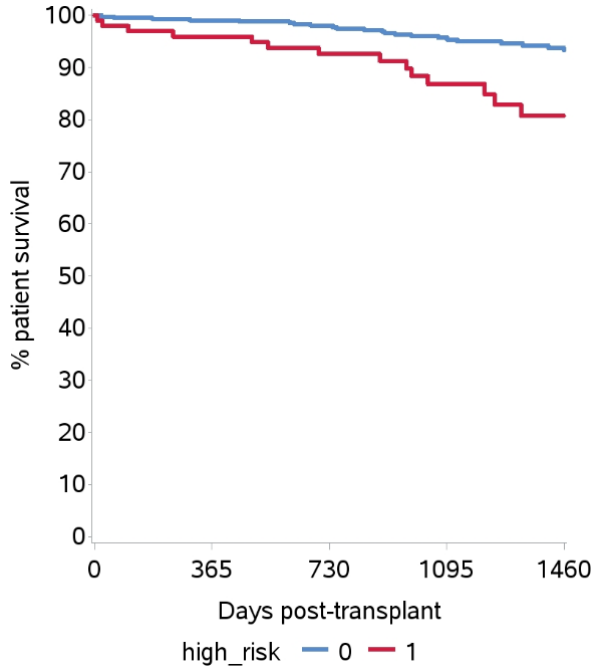
Background: Kidney transplantation (KT) is increasingly offered to older more comorbid patients: 'high risk recipients' (HRR). The UK kidney allocation scheme preferentially allocates kidneys from expanded criteria donors to these patients, with associated increased risk of graft failure and poor graft function. The aim of this study is to understand outcomes of HRRs and their predictors in a contemporary dataset to quantify the potential risks and benefits of KT for this cohort.
Methods: This single-centre cohort study of patients receiving deceased donor KT between 01/10/2014-31/12/2019. Data about previous co-morbidity, biochemical and haematological markers of frailty were used in multivariate models of graft and patient outcome.
Results: 645 patients were included of which 111 were HRR. HRR were older (60 yrs vs 51.5 yrs ,p<0.001), predominantly male (69.4% vs 61.6%, p=0.12) with a higher incidence of diabetes (32.4% vs 6.3%,p<0.001), ischaemic heart disease (27.9% vs 3.9%,p=0.0001) and peripheral vascular disease (8.1% vs 0.5%,p<0.001). There were no significant differences in donor demographics, cold ischaemia time, or brain/circulatory death donors. HRR had higher rate of abnormal red-cell distribution width (RDW) pre-operatively (57.7% vs 39.7% ,p=0.0005). Post-operative complication rate did not differ between groups, however, HRR had higher incidence of post-operative myocardial infarction or stroke (6.4% vs 1.5%,p=0.002). EGFR at 3 (47.5 vs 49,p=0.36) and 12 months (46 vs 51,p=0.13) was no different between groups. Death-censored graft survival was no different at 1 year (94.5% vs 95.2%) and 3 years (93.2% vs 88.8%; p=0.16). However, HRR patient survival was significantly lower at 1 (95.9% vs 99.6%) and 3 years (86.8% vs 95.7%; p=0.007;figure 1). Cox proportional hazards survival analysis showed recipient age (1.74, 95% CI 1.4-2.3,p=0.0001), RDW (1.8, 95% CI 1.06-3.07,p=0.03) and previous stroke (6.7, 95% CI 1.6-29.9,p=0.01) to be independent predictors of survival post-transplant.
Conclusions: HRR are older and more co-morbid than standard risk recipients. Whilst there is no difference in eGFR or graft survival in this cohort, they suffer a survival disadvantage post-transplant. It is likely that KT offers significant advantages over dialysis for HRR, but careful consent is critical.



P726 IS THERE VALUE IN PROPHYLACTIC TREATMENT OF POST-TRANSPLANT RECURRENCE OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS? A MULTI-CENTER RETROSPECTIVE STUDY

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Background: Recurrence of focal segmental glomerulosclerosis (rFSGS) is common after kidney transplantation (KT), particularly in patients who have already had a recurrence in a previous graft. Many transplant centres try to prevent this recurrence by using prophylactic treatments without their benefit having been clearly demonstrated.
Methods: We identified 66 adults patients who presented rFSGS on a previous graft and received KT in 01/2005-12/2020 at 25 French centres: 40 received a prophylactic treatment (PT) including intravenous cyclosporine and/or Rituximab and/or plasma exchange and 26 have not received any prophylactic treatment (WPT).
Results: Age at diagnosis of FSGS and time to progression to end-stage renal disease was similar between the 2 groups. Patients in the PT were younger at the time of the KT of interest (36.2 ± 10.5 years vs. 46.5 ± 13.2 years in the WPT, p=0.002) and lost their previous graft faster (37 months [17; 73] vs. 72 [21; 158] in the WPT, p=0.08). The overall recurrence rate was 72.7%, 76.9% in the PT and 70.0% in the WPT (p=0.54) with a more rapid onset in the PT (4 days [1; 120] vs 32.5 [4; 150], p=0.059). At least partial remission was achieved in 87.5% of patients (95.0% in the WPT and 82.1% in the PT, p=0.21). The 5-year renal survival was 74.2% in the PT and 72.1% in the WPT.
Conclusions: Our study suggests that prophylactic treatment of rFSGS should not be used routinely. However, it cannot be excluded that it is of interest in the most at-risk patients (young patients with rapid loss of the previous graft). The 5-year graft survival was over 70% even if a recurrence occurred.

P727 PORTAL VEIN THROMBOSIS AND LIVER TRANSPLANTATION: OUR EXPERIENCE

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Backround: Portal vein thrombosis is a common problem in candidates for liver transplantation, affecting not only waitlist enrolment, but surgical procedure as well. Aim of the present study is to record the incidence of portal vein thrombosis in liver transplant recipients. Furthermore, a comparison between pre- and intraoperative findings, in refer to presence and extend of thrombus in portal vein will be performed.
Methods: We recorded the incidence of portal vein thrombosis in 45 liver recipients transplanted in our institution, during the period from February 2018 to February 2023. Preoperative imaging findings had been documented, while every diagnosed thrombosis had been accurately classified.
Results: Portal vein thrombosis was present in 16 out of 45 recipients. All patients were successfully transplanted, after thrombus removal via thrombectomy and concomitant enhanced postoperative anticoagulation. Thrombectomy technique consisted in simple or even eversion's thromboendovenectomy and additional passage of a fogarty catheter. In 9 of these 16 cases, the thrombosis had not been preoperatively identified; even though an actual complete radiological imaging was conducted. A single incident of early postoperative re-thrombosis was successfully treated with anastomosis reconstruction.
Conclusion: Presence of portal vein thrombosis may negatively affect the outcome of transplantation. The complexity of this entity is simply suggested by the difficulty in establishing a widely accepted classification system. Furthermore, mismatch between preoperative and intraoperative finding, raises questions regarding the timing and the type of required imaging study for enlisted candidates.

P728 PRE-TRANSPLANT MITOCHONDRIAL RESPIRATION IN HUMAN KIDNEY ALLOGRAFTS PREDICTS CLINICAL OUTCOME UPON TRANSPLANTATION

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Background: With the increasing use of extended criteria donors for kidney transplantation biomarkers with robust predictive capacity are necessary. The renal cortex has low ischemia tolerance as proximal tubuli have the second highest mitochondrial density in the human body and oxidative phosphorylation (OXPHOS) is essential for ATP synthesis. Furthermore, post-reperfusion mitochondrial respiration is associated with delayed graft function (DGF). Therefore, we evaluated the predictive value of pre-transplant mitochondrial respiration towards graft function after transplantation.
Methods: In a prospective study, cortex biopsies were taken in 45 human kidneys at the end of static cold storage (SCS) and/or hypothermic machine perfusion (HMP). Mitochondrial respiration was assessed by high-resolution respirometry. OXPHOS capacity, maximal mitochondrial respiration and ATP production efficiency with the respiratory substrate succinate were evaluated. Additionally, conventional histology was graded after Remuzzi et al.
Results: We found significantly lower OXPHOS capacity (53.4 ± 17.6 *vs.* 74.2 ± 23.0 $pmol^{-1} \cdot s^{-1} \cdot mg$ wet $mass^{-1}$ [mean ± SD], p = 0.0083), maximal respiration (60.9 ± 22.9 *vs.* 91.1 ± 29.0 $pmol^{-1} \cdot s^{-1} \cdot mg$ wet $mass^{-1}$, p = 0.0029), and ATP production efficiency (0.73 ± 0.12 *vs.* 0.82 ± 0.06, p = 0.0023) in biopsies of kidneys developing delayed graft function as compared to those with normal post-transplant function. These values also correlated significantly with the 7-day creatinine and glomerular filtration rate (GFR) values. The OXPHOS capacity in the biopsy after HMP inversely correlated with the 3-month creatinine values (Pearson r = -0.41, p = 0.039). In contrast, the Remuzzi score did not correlate with DGF, 7-day or 3-month creatinine and GFR values.
Conclusions: In kidney grafts eventually developing DGF, mitochondrial respiration and ATP production efficiency are heavily impaired at the end of SCS and HMP. Pre-transplant mitochondrial respiration also correlates with the 3-month creatinine values. Thus, mitochondrial respiratory function is a highly promising biomarker with predictive capacity towards kidney function in transplantation, integrating both chronic alterations and acute subcellular damage.

P729 EX-SITU SPLIT LIVER TRANSPLANTATION: A SAFE PARACHUTE PROCEDURE WHEN IN-SITU SPLITTING IS NOT POSSIBLE

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Background: Split liver (SL) transplantation is an established technique which enables to procure two liver grafts from the same deceased donor: the left-lateral section (LLS) for a pediatric recipient and the extended right lobe (ERL) for an adult. Despite the splitting is generally performed in-situ during multi-organ retrieval, sometimes either for donor hemodynamic instability or for logistic reasons it may be necessary to perform ex-situ SL. Thanks to this technique, surgeons can expand the number of grafts suitable for pediatric liver transplant recipients. Hereby, we present results from our centre's experience.
Methods: From January 2016 to December 2022, we performed 195 liver transplants: 56 whole-livers, 131 in-situ SL and 8 ex-situ SL. 1 out of 8 was a retransplantation.
Results: According to UNOS criteria, 6 (75 %) patients were Status 1 and 2 (25 %) were Status 3, thus confirming the high waitlist priority of these recipients. The recipients' median age and body weight were 4 months and 6.5 Kg, respectively. The median waitlist time was 4 days. Three grafts were obtained from ex-situ SL during Dual Hypothermic Oxygenated Perfusion (D-HOPE). Two of them were from the same donor, one standard LLS and one ERL. Mean total ischemia time was 633 min. As for the practise at our centre, we applied we applied a synthetic biodegradable glue on the resection site for further haemostasis. Mean Intensive Care Unit (ICU) stay was 29.5 days while mean length of stay was 123 days. One (12.5 %) patient underwent retransplantation because of Primary Non-Function (PNF). However, also the second transplant was an ex-situ SL but unfortunately the patient died because of Multi-Organ Failure (MOF). On the other hand, only one out of four adult recipients who got the extended right lobe after ex-situ SL transplantation died because of PNF. Overall, no significant differences in outcomes were observed between in-situ and ex-situ SLs.
Conclusions: Ex-situ SL is a safe procedure that may contribute to rescuing pediatric grafts even in hemodynamically instable donors. However, considering the high proportion of severally ill recipients, it is burdened with a relatively high risk of immediate post-transplant death and complication rate. D-HOPE should be systematically introduced in order to improve post liver transplant results.

P730 THE RING OF POWER -DIFFUSE SUB-EPICARDIAL LGE AS A NEW MARKER OF CARDIAC REJECTION IN HEART TRANSPLANT RECIPIENTS

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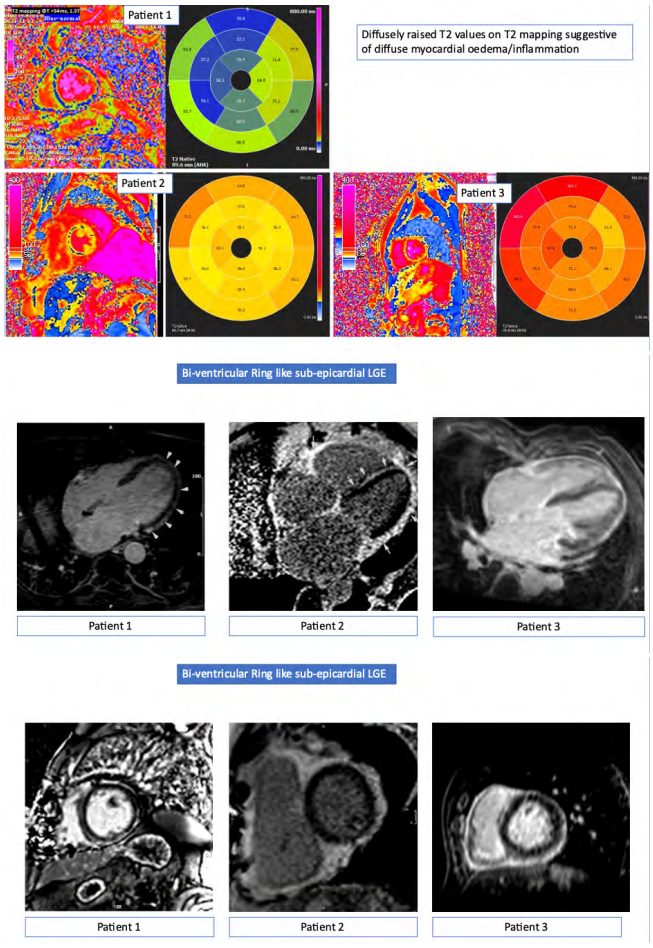
Background: We report an identical unusual pattern of late gadolinium enhancement (LGE) involving both ventricles,in 3 heart transplant recipients who displayed either rapid clinical deterioration or/and rejection (cellular or antibody mediated rejection AMR) on subsequent myocardial biopsy.
Methods: Patient #1 was a 66 y.o male, 12 years post orthotopic heart transplantation (HT) for DCM with new onset heart failure (HF) and arrhythmias. Patient #2 was a 65 y.o female,4 years post HT who presented with new-onset HF and recurrent pleural effusions. Patient #3 was an asymptomatic 12 y.o boy, 7 years post HT , who presented for his surveillance evaluation.
Results: All cases underwent echocardiography and Cardiovascular Magnetic Resonance (CMR). The adult patients manifested low LVEF<35%, while the pediatric patient had new-onset mild mitral regurgitation, low normal LV systolic function with abnormal diastolic function and significantly echo-bright myocardium.CMR studies revealed diffuse rise of both T1 and T2 values on the respective mapping sequences.Furthermore,CMR illustrated an identical, unique pattern of diffuse subepicardial and pericardial, ring-like Late Gadolinium Enhancement (LGE) engaging both ventricles.Interestingly,patients #2 and #3 had myocardial biopsy proven acute cell and/or AMR whereas patient #1 had no evidence of rejection.Patient #1 had severe CAV3 .Rapid deterioration of his condition was noted with multiple admissions for HF decompensation and arrhythmias that led to ICD implantation.Patients #2 and #3 were treated for cellular and AMR with normalization of LVEF and stabilization of clinical status, respectively.
Conclusions: Such diversity in clinical presentation and diagnostic findings highlights the challenges in managing patients post orthotopic HT.Assessment of myocardial edema via mapping techniques and identification of such ring-like sub-epicardial/pericardial LGE distribution could potentially serve as red flags and assist in prompt recognition of patients who may warrant meticulous work-up to exclude acute myocardial rejection and/or vasculopathy. Further investigation is needed to elucidate the pathogenesis and clinical significance of this specific LGE pattern affecting the entire heart in this less understood population.



P731 ORAL SEMAGLUTIDE SAFETY IN KIDNEY TRANSPLANT RECIPIENTS WITH TYPE 2 DIABETES

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Background: Diabetic kidney transplant recipients (KTR) have a high cardiovascular mortality. GLP-1 agonists have proven to reduce CV morbidity and mortality in diabetics, and its subcutaneous presentation has at least proven to be safely administered in KTR. The aim of this study is to determine the safety of oral semaglutide in the KTR population.
Methods: This is a retrospective observational study of a KTR population who were prescribed oral semaglutide. Medical data were taken from electronic health records. Proper maintenance of tacrolimus levels was measured by calculating the coefficient of variation (CV). Oral semaglutide was taken at least 2 hours before lunch or dinner, as preferred by the patient.
Results: 12 patients were analysed. Their mean age was 63, 58% of them were men. 10 had type 2 diabetes before transplantation (Tx), while 2 presented new onset diabetes after transplant, 7 were on oral antidiabetics and became insulin dependent after Tx, 9 patients were started on oral semaglutide at discharge after Tx. 2 abandoned treatment, one due to nausea and the other due to lack of appetite. From the remaining 10, one patient's dose was not increased from 3mg daily due to unknown reasons, 2 reached the 14mg dose with good tolerance, and 7 were maintained on 7mg according to their physician's advice, though none reported drug intolerance. The mean BMI reduction with the 3mg dose was 1.6 kg/m2 during the 1st month, 3.65 kg/m2 with 7mg in the 2nd month and was maintained at 2.6 kg/m2 in the 3rd month. The 2 patients that took 14mg, had a BMI reduction of 3,5 kg/m2 by the 6th month. Their insulin dose was reduced by 3 UI at 3 months, and 12 UI at 6 months after initiating treatment. We did not find an HbA1C reduction. Total cholesterol reduced by 2.3 mg/dL, LDL by 19.4 mg/dL, and triglycerides by 28.8 mg/dL, while HDL increased by 21 mg/dL, 3 months after oral semaglutide introduction. The mean tacrolimus CV was 27.8%. There were no rejections since the beginning of the medication.
Conclusions: Although this study has some limitations, we can at least state that oral semaglutide can be safely administered in KTR, and that it seems to be associated with a reduction in BMI and an improvement in lipid panel parameters while not significantly affecting tacrolimus absorption. More studies are needed to study further impact of this medication.

P732 EPIDEMIOLOGICAL AND CLINICAL CORRELATIONS BETWEEN ERECTILE DYSFUNCTION AND KIDNEY TRANSPLANT STATUS

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Background: Chronic kidney disease(CKD) is a major burden in terms of life quality.Renal transplantation generally associates with an improvement in life quality,the data regarding patients' sexual activity after the kidney transplant generated controversial results.Therefore, new data is necessary to establish the relationship between kidney transplant status and erectile dysfunction in terms of prevalence,risk factors and severity.
Methods: We conducted a single-center,retrospective observational study on adult male patients with chronic kidney disease who underwent renal transplants.Demographic and clinical data such as primary kidney disease,type of impairment,history of dialysis,presence of comorbidities,surgery and early post-transplantation period were collected.Patients were asked to fill out a standard validated survey for sexual function,namely the International Index for Erectile Function(IIEF).
Results: 179 adult male patients met the inclusion criteria and were enrolled in the study.At the time of inclusion,all patients had normal renal function and were receiving immunosuppressive therapy.The total mean IIEF score was 16.32±6.93.Mild-moderate erectile dysfunction was found in 33.5% of patients,-moderate and severe ED was noted in 20.6% and 20.6 of cases.Among the chronic medication only alpha-blockers and non-steroidal-anti-inflammatory drugs were found to be significantly associated with the presence of erectile dysfunction (p=0.026andp=0.013, respectively) not only with the general IIEF score but also with each of the five domains.Other patient characteristics such as obesity,the type of immunotherapy,time since the renal transplant,surgical complications,transitory rejection episodes,causes of renal failure,presence of common risk factors did not seem to influence the presence or the severity of erectile dysfunction.The prevalence of ED increased with age (42.6% of patients<40,47.4% of patients aged 40-60 and 78.9% of patients>60).
Conclusions: Sexual impairment represents an important issue in kidney transplant recipients due to its prevalence and associated risk factors.Age along with alcohol intake,type and time on dialysis and the type of donor are potential risk factors for developing erectile dysfunction after renal transplantation.

P734 INFLUENCE OF RENAL GRAFT FUNCTION IN PREGNANT WOMEN WHO UNDERWENT WITH KIDNEY TRANSPLANT

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Background: Concern regarding the next generation and how to maintain graft renal function are two subjects which must be faced when discussing post-kidney transplantation (KTx) in pregnant women. The aim of this study is to compare renal graft function and outcomes between female KTx recipients who are either pregnant or not.
Methods: From the period May 1983 to March 2022, a total of 788 patients received KTx at our center (Age: 15-74 years, Female/Male: 351/437). Overall, there were 22 female KTx recipients who were pregnant, and of a similar age, with a similar duration of KTx, as well as 22 non-pregnant female KTx recipients who served as the control group. We compared their renal graft function during gestation trimesters, and the periods of 1-, 2- and 5-year after delivery, as well as graft and patient survival.
Results: The median age at pregnancy was 33.8 (range: 22.1-39.9) years, and the median time of transplant-to-conception interval was 4.8 (range: 1.0-14.6) years. Renal graft function was not found to be significantly different between the case and control groups at long-term follow-up. Serum creatinine (sCr) in the graft failure recipients was higher at initial (1.5 ± 0.6 *vs.* 1.1 ± 0.4 mg/dL; P = 0.050) and third trimester (1.6 ± 0.6 *vs.*1.1 ± 0.4; P = 0.042) than those without, respectively. The fetal outcomes demonstrated a low birth weight and gestation age in the graft failure group, but it did not reach any analytic significance. A Kaplan–Meier survival curve to compare graft and patient survival did not reveal any significantdifferences between the case and control groups.
Conclusions: Childbearing is a developmental task for KTx recipients, as pregnancy in female KTx recipients is high-risk, with an acceptable risk of complications having successful outcomes. However, its detrimental effect on graft kidney and fetal outcome should provide any medical consultant with strong preconceived ideas regarding, gestational care and follow-up after delivery. Consequently, because most female recipients of KTx wish to bring to term their pregnancy, transplant physicians have the responsibility to provide them with all necessary information regarding both the maternal and fetal outcomes.

P735 ASSESSMENT OF EXTENDED CRITERIA DONOR LIVERS WITH INDOCYANINE GREEN DURING EX-VIVO MACHINE PERFUSION

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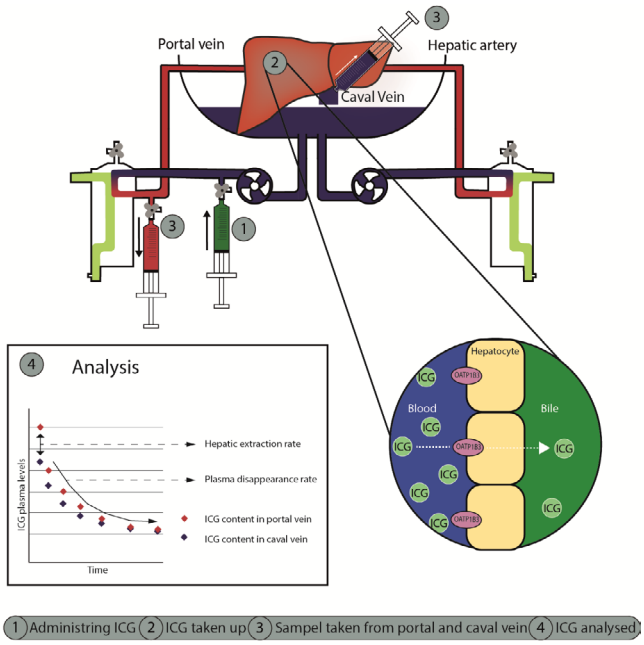
Background: Normothermic machine perfusion (NMP) enables assessment of donor liver viability pre-transplantation. However, objective tests for measuring integrated liver function during NMP are lacking. We assessed the clinically validated indocyanine green (ICG) elimination test to objectively evaluate liver function during ex-vivo machine perfusion

Methods: A combination of dual-hypothermic machine perfusion (DHOPE) and NMP was performed on extended criteria donor livers in an optimization phase (n=10) and clinical phase (n=22). In the optimization phase, the ICG test was performed during DHOPE and NMP (Figure), with optimization for use during NMP. In the clinical phase, the ICG clearance was correlated to clinical perfusions parameters and post-transplantation outcomes.

Results: During DHOPE no ICG perfusate elimination was seen. During NMP, significant ICG plasma elimination was demonstrated. The ICG plasma disappearance rate (PDR) was dependent on perfusion blood flow and plasma volume. After correcting the PDR for these factors, this corrected NMP-PDR was closely correlated to the hepatic extraction rate (R=0.923; P>0.001) and also to ATP content in liver biopsies (R=0.692; P=0.027). The NMP-PDR was however not correlated to liver damage (ALT, AST, LDH, and TUNEL). In the clinical phase, 22 liver grafts were evaluated for transplantation, being blind for outcome of ICG testing. Eleven livers were transplanted. The NMP-PDR was higher in the transplanted cohort than in the non-transplanted cohort (16.7 (12.9-23.3) vs 10.3 (8.5-12.1) %/L·Kg; P>0.0001). Both the overall hepatocellular and cholangiocellular acceptance criteria were correlated to the NMP-PDR. One transplanted liver developed early allograft dysfunction (12.3 %/L·Kg) and one non-anastomotic biliary stenosis (13.3 %/L·Kg).

Conclusions: We demonstrated that ICG elimination is not present during DHOPE, but the test is feasible during NMP. A NMP-PDR ≥13.3 %/L·Kg is indicative for absence of post-transplant hepatocellular or biliary failure in extended criteria donor livers. The ICG plasma elimination test has the potential to increase the donor liver utilization rate, while at the same time preventing complications after transplantation.



1 Administring ICG 2 ICG taken up 3 Sampel taken from portal and caval vein 4 ICG analysed

P736 SHORT-TERM OUTCOME AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION WITH ALEMTUZUMAB VS. BASILIXIMAB INDUCTION; A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Both T-cell depletion by alemtuzumab (ALEM) as well as IL-2 receptor blocking by basiliximab (IL2R) are used as induction for simultaneous pancreas-kidney (SPK) transplantations. Multiple studies have reported higher rates of infections with ALEM versus IL2R. Due to the COVID-19 pandemic we adapted our standard induction from ALEM to IL2R for low immunological risk SPK transplantations. We compared 180 days transplantation outcomes between ALEM and IL2R induction.

Methods: Patients with low immunological risk who underwent SPK between September 2015 and June 2022 at our center were analyzed. Induction was either ALEM (30 mg, until February 2020) or IL2R (2x 20 mg, from February 2020 onwards) and triple maintenance therapy (prednisolone, tacrolimus, mycophenolate acid). All pancreas allograft transplants were performed using enteric drainage. Standard prophylaxis included antibacterial, antifungal and antiviral therapies. Valganciclovir prophylaxis for cytomegalovirus (CMV) infection was risk stratified. All patients routinely went to the intensive care unit postoperatively.

Results: Thirty-five SPK transplant recipients were included (67% males, mean age 42±10 yr). Fifty-four percent of patients were transplanted pre-emptively, 37% received organs from a DBD donor and mean donor age was 31±11 yr. Twenty-one recipients received ALEM and 14 recipients IL2R induction therapy, see Table. Two pancreas grafts were lost in the ALEM group and one kidney graft was lost in the ILR2 group. No patient deaths occurred. No differences between ALEM and IL2R groups in kidney and pancreas graft function or rejection incidence were observed. More recipients in the ALEM group suffered from bacterial (81% vs. 50%, p=0.05) and viral infections (57% vs. 38%, p=0.21) compared to the IL2R group. The duration of initial hospitalization was longer for the ALEM group compared to the IL2R group (28 [20-39] vs. 12 [10-16] days, p<0.001). The percentage of recipients with hospital readmission was equal (57%) for both groups.

Conclusions: Our experience, although limited, with IL2R induction for SPK transplants with low immunological risk has shown encouraging results with equivalent short-term graft function and decreased post-operative infection rates and hospital admission duration compared to ALEM induction.

Induction	ALEM N=21	IL2R N=14	P-value
Demographics at baseline			
Sex (male), N (%)	14 (67)	9 (64)	0.88
Age recipient, years	42.2 ± 8.0	42.6 ± 12.4	0.90
Pre-emptive, N (%)	11 (52)	8 (57)	0.78
DBD, N (%)	N=8 (38)	N=5 (36)	0.89
Age donor, years	31.8 ± 10.3	29.2 ± 13.0	0.52
Pancreas 180 days post transplantation			
Rejection, N (%)	N=1 (5)	N=0	0.41
Delayed Graft Function	N=0	N=0	N/A
Graft Thrombosis, N (%)	N=2 (10)	N=2 (14)	0.66
Pancreatitis (all cause), N (%)	N=6 (29)	N=2 (14)	0.32
Graft Loss, N (%)	N= 2 (10)	N=0	0.23
HbA1c, mmol/mol	37 [33-40]	33 [32-39]	0.27
Kidney 180 days post transplantation			
Rejection, N (%)	N=2 (10)	N=0	0.23
Delayed Graft Function, N (%)	N=9 (43)	N=2 (14)	0.07
Graft Loss, N (%)	N=0	N=1	0.21
Creatinine, µmol/l	126 [105-168]	117 [103-136]	0.36
Complications 180 days post transplantation			
Bacterial infection (≥1), N (%)	N=17 (81)	N=7 (50)	0.05
Viral infection (≥1), N (%)	N=12 (57)	N=5 (36)	0.21
Leucopenia, N (%)	N=11 (52)	N= 5 (36)	0.33
Surgical reintervention (≥1), N (%)	N=8 (38)	N=4 (29)	0.56
Duration initial hospitalization, days	28 [20-39]	12 [10-16]	<0.001
Rehospitalization (≥1), N (%)	N=12 (57)	N=8 (57)	1.00

P737 STABLE RECOVERY AFTER A MYOCARDITIS TREATED WITH CENTRAL ECMO AND IMPELLA: SHOULD WE DESIGN DIFFERENT ALLOCATION RULES FOR MYOCARDITIS?

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Background: Cardiogenic shock (CS) carries a high mortality risk; ECMO is becoming the standard treatment for CS as a bridge to recovery (BTR) or decision. The impella system (IS) is easy and effective for left ventricular (LV) support. It has been shown that IS can unload LV while ECMO provides good perfusion in overt cardiogenic shock due to biventricular failure.
Methods: In November 2012, a 20-year-old girl experiencing sudden dyspnea was referred to a local hospital for pericardial effusion. After a successful pericardiocentesis, LV contractility rapidly worsened despite increased inotropic support. A 2.5 L IS was implanted to maintain circulation but precipitated toward right ventricular failure; the patient was referred to our hospital with an indication for ECMO implantation and transplantation. Due to technical issues with the femoral vessels, ECMO was implanted via median sternotomy to ensure optimal perfusion.
Results: The IS was maintained to ensure myocardial unloading and fair chances of myocardial recovery. A fine-needle biopsy of the LV showed minimal necrosis with a high probability of myocarditis and encouraged the feasibility of BTR. ECMO implantation was complicated by severe coagulopathy that required massive administration of blood products and re-exploration by tamponade. BNP dosage decreased rapidly during the first postoperative week, a suboptimal donor was discarded, and ECMO was removed on day 6. On day 7, IS was removed percutaneously.
Conclusions: This report further supports the synergistic effect of IS and ECMO when dealing with potentially reversible diseases. Imaging and functional tests performed after ten years showed complete recovery. Etiologic diagnosis through biopsy should be performed whenever possible to avoid wasting organs for patients whose recovery may be full and whose postoperative outcome is suboptimal.

P738 KIDNEYS FROM UDCD WITH NRP SUPPORT VS KIDNEYS FROM BRAIN DEAD DONORS: A COMPARATIVE ANALYSIS OF TRANSPLANTATION OUTCOMES

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Background: Normothermic regional perfusion (nRP) is a preservation strategy that re-establishes the flow of oxygenated blood following cardiac arrest and can reverse warm ischemic injury in donation after uncontrolled circulatory death (DCD) especially.
Methods: In this study, we compared the transplantation outcomes of kidneys from uDCD with nRP support, with the results attained using kidneys from brain-dead donors. The analysis entailed a single-Centre, prospective cohort of 294 consecutive kidney transplantations performed from January 2016 to December 2020. 117 transplants were from brain-dead donors defined as standard criteria (SD) (39.8%), 93 from expanded criteria (ECD) (31.6%) and 84 from cardiocirculatory arrest (DCD) donors (28.6%).
Results: For uDCD, warm time ischemia (WIT) pre-ECMO correlated with PNF along the years (2017, PNF 0% median WIT 60min (45-100); 2018 PNF 15.4%, median WIT 90min (86.3-62.5); 2019 PNF 23.48%, median WIT 100min (90-120); 2020 PNF 0%, median WIT 45min (45-45); After adjusted analysis, uDCD is associated with a 2.84 risk higher for PNF and 6.44 for DGF. Independently of donor type, we have an increase of 9,2% risk to DGF for each hour. Allograft survival (both uncensored and censored by death) at 5 years post-transplantation was higher in SCD (89.3% and 80.8%) than in ECD (74.8% and 69.5%; p=0.003 and p=0.001), but no difference to uDCD (83.2% and 83.2%; p=0.09 and p=0.06). Donor age (HR=1.036) was the most significant predictor of censored allograft loss to death. DGF was higher in uDCD versus ECD but after 5 years, the eGFR of uDCD and SCD recipients is similar (65.48 vs 62.27 ml/min/1.73m2, p=1.0). Since the 18 months, eGFR is higher for uDCD than ECD (difference mean 9,623ml/min/1.73m2; p=0.043). At 5 years the mean difference of uDCD-eGFR is higher at 26,87ml/min/1.73m2 than ECD (p<0.001). In recipients from SCD and uDCD, eGFR increased in 1.31ml/min/1.72m2 (p=0.039) and 2.62 1.31ml/min/1.72m2 (p=0.007) per annum respectively, independently of age and sex. Although, the eGFR of those from ECD declined to -2.21ml/min/1.73m2 per annum (p=0.026).
Conclusions: At 5 years, uDCD kidney transplantation outcomes are similar to brain-dead donors in all major transplantation criteria supporting the use of uDCD kidneys as a successful mean to address organ scarcity

Table 4. Risk factors for PNF and DGF (logistic regression).

	Univariate logistic analysis			Multivariate logistic analysis*		
	Odds Ratio	95% CI	*p* value	Odds Ratio	95% CI	*p* value
PNF						
uDCD donor	3.056	1.097, 8.508	**0.033**	2.84	1.01 - 7.97	
ECD donor	3.526	1.310, 9.490	**0.013**	2.13	0.60 - 7.56	**0.047**
Age of donor (years)	1.03	1.003, 1.065	**0.030**	1.03	0.984 - 1.070	0.235
Polytraumatism cause of death of donor	0.732	0.305, 1.758	0.485			
Preoperative serum creatinine, mg/dL, of donor	1.146	0.348, 3.770	0.823			
Age>60 years of recipient	1.575	0.757, 3.275	0.224			
Original nephropathy	—	—	0.465			
Dialysis vintage (years)	0.996	0.983, 1.009	0.528			
Cold ischemia time (hours)	1.03	0.952, 1.114	0.466			
PRA (%)	—	—	0.518			
Induction therapy antitimoglobulin	1.282	0.608, 2.702	0.513			
DGF						
uDCD donor	8.143	4.060,	**<0.001**	6.436	2.840, 14.586	**<0.001**
ECD donor	3.08	1.684, 5.634	**<0.001**	1.641	0.727, 3.700	0.233
Age of donor (years)	1.011	0.994, 1.029	0.199			
Polytraumatism cause of death of donor	0.373	0.210, 0.663	**0.001**			
Preoperative serum creatinine, mg/dL, of donor	4.255	1.802,	**0.001**			
Age>60 years of recipient	1.294 (0.761-2.201)	1.294 (0.761-2.201)	0.341			
Original nephropathy	—	—	0.057			
Dialysis vintage (years)	0.995	0.987, 1.003	0.119			
Cold ischemia time (hours)	1.077	1.018,	**0.010**	1.092	1.019, 1.171	0.013
Panel Reactive Antibody (%)	—	—	0.599			
Induction therapy antitimoglobulin	2.281	1.378, 3.777	**0.001**			

*Forward Stepwise (LR).

Table 5. Factors associated with death-censored graft survival.

	Univariate Cox analysis			Multivariate Cox analysis*		
	Hazard Ratio	95% CI	*p* value	Hazard Ratio	95% CI	*p* value
uDCD donor	1.995	0.886, 4.492	0.443			
ECD donor	2.846	1.345, 6.021	**0.006**			
Age of donor (years)	1.036	1.011, 1.062	**0.003**	1.036	1.011, 1.062	**0.003**
Polytraumatism cause of death of donor	0.590	0.275, 1.265	0.152			
Preoperative serum creatinine, mg/dL, of donor	1.036	0.391, 2.741	0.944			
Age>60 years of recipient	2.030	1.137, 3.618	**0.017**			
Original nephropathy	—	—	0.653			
Dialysis vintage (years)	1.008	0.916, 1.110	0.864			
Cold ischemia time (hours)	1.026	0.963, 1.092	0.428			
Panel Reactive Antibody (%)	—	—	0.190			
Induction therapy antitimoglobulin	1.056	0.584, 1.912	0.856			
DGF	1.766	0.529, 5.888	0.355			

*Forward Stepwise (LR) Cox regression.

Table 6. Clinical factors associated to graft function over 5-years follow-up

	Estimated value*	95% CI	*p* value
Mean eGFR differences at baseline			
SCD	66.15	64.17, 68.08	**<0.001**
In uDCD *vs* SCD	-14.58	-17.66, -11.42	**<0.001**
In ECD vs SCD	-15,05	-18,21, -11.84	**<0.001**
Adjusted mean eGFR differences at baseline**			
SCD	88.37		**<0.001**
In uDCD *vs* SCD	- 14.22	-20.37, -8.26	**<0.001**
In ECD vs SCD	- 11.64	-17.77, -5.50	**<0.001**
Mean eGFR slope per year			
In SCD	0.109	0.005, 0.213	**0.038**
In uDCD	0.218	0.056, 0.38	**0.007**
In ECD	-0.184	-0.348, -0.02	**0.025**

eGFR (in mL/min/1.73 m2), estimated Glomerular Filtration Rate.
*Parameters were estimated from a linear mixed model with a symmetric covariance matrix.
**Adjusted for age and gender of recipient.
Mean eGFR between 1 month post-transplant (baseline) and 5-year follow-up (slope).

P739 A RETROSPECTIVE OBSERVATIONAL STUDY ON THE DECLINING LIVER TRANSPLANT ASSESSMENT RATES AT EDINBURGH TRANSPLANT CENTRE

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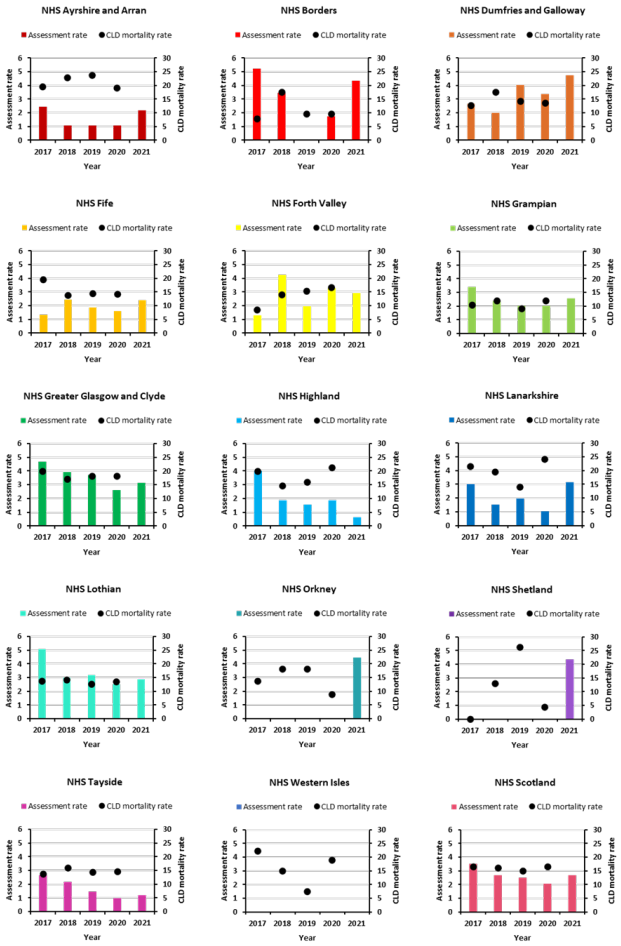
Background: Despite the increasing prevalence of liver disease, there has been a significant reduction in the number of liver transplant assessments as well as a corresponding decrease in liver transplants at Edinburgh Transplant Centre (ETC) since 2018. Given that this predates the COVID-19 pandemic, we sought to explore the other potential reasons for this decline through a retrospective analysis of the ETC database.
Methods: Data were collected for all adult patients assessed for primary elective liver-only transplantation at ETC between 2017-2021. Patients assessed for multi-organ transplants, for Variant or Super-Urgent indications, <18 years old and repeated assessments were excluded. Variables including patient demographics, transplant indication, referring healthboard and Scottish Index of Multiple Deprivation (SIMD) were examined by year. Kruskal-Wallis and Chi-square tests were used to assess for significant differences in variables over time.
Results: A total of 733 patients fit the study criteria. There was no statistically significant change in sex, age, bilirubin, creatinine, INR, sodium, UKELD, height, BMI, indication, or SIMD over the study time period (p>0.05). Patient weight significantly increased over time (median 78kg in 2017, 85kg in 2021, p=0.014). Geographical variation was also noted, with NHS Healthboards referring for assessments at varying rates not necessarily accounted for by differences in disease prevalence (CLD mortality rates were taken as a surrogate for disease prevalence) (Figure 1).
Conclusions: Geography may be contributing to changes in assessment rates at ETC with implications on resource allocation and transplantation. As such, more research into geographical variations must be taken forward to find solutions, which may include local leads to standardise decision making and regular external auditors, as well as the continuation of ongoing weekly invitations to external referring physicians to transplant assessment meetings and outreach clinics.

Figure 1. NHS Healthboard Assessment rates (2017-2021) and Chronic Liver Disease Mortality rates (2017-2020) per 100,000 population



P740 LIVER STIFFNESS MEASUREMENT IS ASSOCIATED WITH THE DEVELOPMENT OF PERSISTENT ASCITES AND POSTOPERATIVE COMPLICATIONS AT 90 DAYS AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is associated with high morbidity and mortality. Persistent ascites (PA) develops in 5-7% of the cases and its management is still very challenging. The diagnostic and prognostic role of transient elastography (TE) in cirrhotic patients has already been established, however its impact in patients undergoing LT remain unclear.
Methods: Prospective observational study in patients undergoing liver stiffness measurement (SSM) at 30 days after LT between August 2020 and December 2022 at Bologna Transplantation Unit, IRCCS. Spleen stiffness measurement (SSM) was also collected when available. Postoperative complications were categorized according to the Clavien-Dindo Classification (CDC) and Comprehensive Complications Index (CCI).
Results: A total of 109 patients were included in this study. Median LSM and SSM were 8.8 kPa (IQR 6.6 – 13.1) and 30.0 kPa (22.1 – 44.7) respectively. The development of persistent ascites was observed in 16 patients (14.7%). Medical therapy was the main treatment for PA, while splenic artery embolization was performed in two cases. Thirteen patients with PA underwent hepatic vein pressure gradient (HVPG) measurement (median 13 mmHg, IQR 9 – 15). LSM and SSM were both associated with the development of PA (OR 1.159, 95% CI 1.069 – 1.255, p=0.000) and (OR 1.018, 95% CI 1.011 – 1.086, p=0.010). LSM also correlated strongly with HVPG (Pearson coefficient 0.632, p=0.015). Severe complications (grade 3 or higher) occurred in 37 patients (36%). LSM was significantly associated with CCI at 90 days (Pearson coefficient 0.195, p=0.046).
Conclusions: LSM is associated with the development of medical and surgical complications at 90 days after LT. Transient elastography can play an important role in the diagnosis and management of persistent ascites after transplantation.

Table 1 Predictive role of LSM for complications at 90 days after LT

	OR (95% CI)	p value
Early Allograft Dysfunction	1.02 (0.99 – 1.05)	0.2
Persistent ascites	1.16 (1.07 – 1.26=	0.000
Biliary Complication	1.03 (0.99 – 1.07)	0.1
Vascular Complications	1.05 (1.01 – 1.08)	0.008
Severe complication	1.02 (0.99 – 1.05)	0.2

P741 SHORT- AND LONGTERM OUTCOME IN LIVER TRANSPLANT RECIPIENTS WITH EARLY ALLOGRAFT DYSFUNCTION

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Background: Liver transplantation is the established standard procedure for the treatment of chronic and acute end-stage liver disease. However, limitations remain, such as the limited number of donor organs and the high incidence of early allograft dysfunction (EAD) due to the compensatory increase in the number of expanded criteria donors (ECD). The aim of this work was to investigate the short- and longterm outcome in liver transplant recipients with and without EAD.
Methods: A retrospective analysis of adult patients who underwent deceased donor liver transplantation between January 2007 and December 2017 was performed. EAD was defined by one or more of the following criteria: (i) bilirubin ≥10 mg/dL on postoperative day 7; (ii) international normalized ratio ≥1.6 on postoperative day 7, and (iii) alanine aminotransferase or aspartate aminotransferase >2000 IU/L within the first seven days after transplantation.
Results: A total of 631 patients were studied and 53.6% of recipients developed EAD. Recipient criteria such as age (49.19 vs. 49.64 years; p=0.652), dialysis requirement (18.9% vs. 16.6%; p=0.451), invasive ventilation before transplantation (5.9% vs. 5.3%; p=0.740) as well as cold ischemia time (595.53 vs. 578.44 minutes; p=0.081) showed no significant differences between the EAD and non-EAD groups. However, donor ventilation time (5.2 vs. 4.5 days; p=0.013), graft weight (1834.39 vs. 1589.73g; p<0.001), donor BMI (27.38 vs. 25.83; p<0.001) and number of donors with ECD criteria (59.2% vs. 49.5%, p=0.018) differed significantly between the two groups. Compared to the non-EAD group, patients with EAD had a higher likelihood of needing dialysis post-transplant (38.2% vs. 23.0%; p<0.001) or re-transplant (16.0% vs. 4.6%; p<0.001). They also had higher mortality during ICU stay (16.8% vs. 5.7%; p<0.001) and significantly lower graft survival (98.0 vs. 116.0 months; p=0.005), but without a significant difference in patient survival (111.0 vs. 120.0 months; p=0.177).
Conclusions: EAD and non-EAD recipients differ primarily in donor rather than recipient criteria. EAD has a significant impact on graft survival and postoperative mortality on the ICU.

P742 TIXAGEVIMAB/CILGAVIMAB FOR PREVENTING SARS-COV-2 IN HEART TRANSPLANTED PATIENTS POOR VACCINE RESPONDERS: A HOPE OR YET ANOTHER GUY IN THE FIELD?

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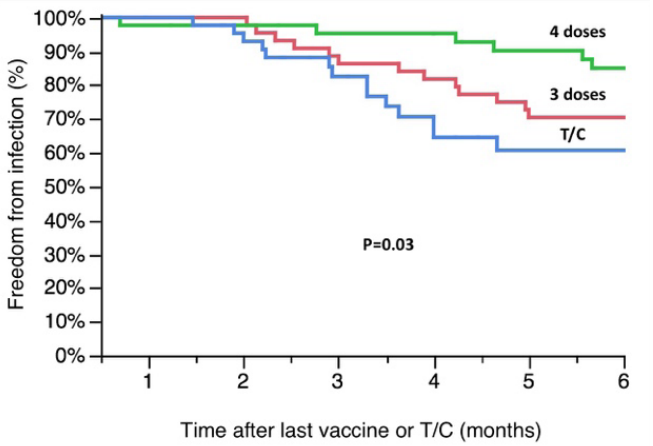
Background: Tixagevimab/cilgavimab (T /C) has been recently suggested for the prophylaxis of SARS-CoV-2 infection in solid organ transplant recipients with low levels of antibodies after repeated vaccine's doses. There are no published data in heart transplanted (HT) patients (pts). The aim of our study is to investigate its safety and efficacy in HT pts with low antibodies after at least three doses of m RNA vaccine.
Methods: We included a subgroup of pts enrolled in the CONTRAST study (ORCHESTRA Project) with known antibodies after last dose of vaccine (third or fourth dose). Patients with low anti-RBD antibodies (<100 U/ml), regardless of a previous infection, received T/C 150/150 mg; in a subgroup, Elispot assay was performed before its administration. The endpoint was survival free from SARS-CoV-2 infection at 6 months. For descriptive purposes, we performed a comparison with pts with antibody response after three or four doses of vaccine, excluding from this cohort those with prior infection, to avoid any potential influence of infection- derived immunity on the analysis. In pts with positive antibody response, the follow up was started after last dose of vaccine.
Results: 45 pts [71% males, median 4.5 yrs (2.2-11.7 yrs) from HT] received T/C; 33 with previous 3 doses, 12 with 4 doses. We did not observe any adverse reactions or cardiovascular events. The incidence of the endpoint was 60.7±8.4% at 6 months. Two patients (14%) required hospitalization. Among 23 pts with available Elispot data, 21 were negative, one borderline, one positive. In the cohort of pts with positive antibodies after vaccine, 45 had received three doses, 44 four doses. The observed survival free from infection at 6 months was higher in the 4 doses group, intermediate in the 3 doses, lowest in the T/C group (85.0±5.6% vs 70.4±6.8% vs 60.7±8.4%, p=0.03). The 2 pts without a negative Elispot did not get the infection. Lymphocytes and clinical variables were not associated to an increased risk of infection in the T/C group.
Conclusions: HT patients without antibody response after repeated doses of m RNA SARS-CoV-2 vaccine receiving T/C for prophylaxis still have a high risk of SARS-CoV-2 infection. These results could be related to the lack of T-mediated immunity in these patients. Other strategies to protect this fragile cohort need to be found.



P743 CONTEMPORARY MANAGEMENT OF RENAL TRANSPLANT RECIPIENTS WITH DE NOVO URINARY STONES. A SINGLE INSTITUTION EXPERIENCE

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Background: Urolithiasis is an infrequent complication in kidney transplanted patients, although its diagnosis and management is challenging and its consequences potentially serious. Our aim is to analyze the management of renal transplant recipients with de novo urinary lithiasis in a series of more than 1500 transplanted patients.
Methods: A total of 1543 transplant patients were included in a and single-center study from 2013 to present. The inclusion criteria were patients who developed de novo allograft lithiasis. Demographic data, graft survival, diagnoses, treatment, stone free rate (SFR) and complications were described.
Results: Nineteen patients developed urinary stones in the study period. The prevalence observed in our sample was 1.22 cases per 100 transplanted patients. The median time to the appearance of lithiasis was 85 months (IQR = 222 months). In nine patients (47,36%) were multiple stones and the most frequent location was the renal pelvis (12 patients (62%). The median of the largest diameter of lithiasis was 10mm (IQR = 11mm). In nine cases (47,36%) were obstructive stones (being the main indication for surgical treatment). Three patients (15,7%) were treated by URS, three patients (15,7%) by standard percutaneous surgery, one patient (5,2%) by laparoscopy surgery and in a one patient a nephrectomy was performed due to graft failure. One patient (5,2%) had a spontaneous expulsion. In the remaining 10 cases medical treatment or observation was performed, observing the stability of the lithiasis or its resolution in 80% of the cases. Only 2 of the patients (10,5%) required auxiliary treatment. One patient died in the early postoperative period by urinary sepsis and one patient lost the graft function.
Conclusions: The prevalence of lithiasis in the kidney graft is low but can be potentially severe. Its diagnosis, due to the graft denervation, is usually incidental and delayed. Surgery in cases of obstruction is the main indication, but it requires a multimodal treatment tailored according to stone and graft characteristics. In non-obstructive lithiasis cases, active surveillance and medical treatment is a good option.

P744 COVID-19 AND ACUTE PANCREATITIS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Acute pancreatitis is a rare extrapulmonary manifestation of COVID-19, with a prevalence of 0.27%. Pancreatic islet cells express ACE surface receptors being a target for the SARS-CoV-2 virus, with consequent damage to the gland either by the generalized inflammatory response or by the direct cytopathic effects of the virus. Acute pancreatitis is a rare complication after kidney transplantation, which may be associated with the use of immunosuppressive drugs in the absence of traditional risk factors (gallstones, alcohol). Remdesivir may induce acute pancreatitis through elevation of serum tryglicerides.
Methods: We examined the occurrence, clinical presentation and outcomes of acute pancreatitis in our cohort of kidney transplant recipients with acute COVID-19.
Results: Between October 2020 and August 2022, 408 adult kidney transplant recipients were diagnosed with SARS-CoV-2 at our center. Pancreatitis was diagnosed in three patients (0.7%). All of three patients had: abdominal pain, a serum amylase and lipase three or more times the upper limit of normal, and CT and utrasound imaging findings consistent with pancreatitis, without morphological and laboratory signs of obstruction of the pancreatobiliary system. First patient, female, age 69, had diabetes prior to COVID-19 infection, rapidly progressive GN as the underlying disease. Second, male, age 61, with Fabry disease, on regular therapy with agalsidase beta. Third, female patients, 65, with membranoproliferative GN before kidney transplantation, with cholecystectomy before transplantation. Two of them had tacrolimus and one cyclosporine with MMF and steroid in immunosuppressive regimen. All of them were treated with remdesivir and one also got casirivimab and imdevimab monoclonal antibodies in COVID-19 treatment. They were treated with broad-spectrum antibiotics, fluids, analgesics and supportive treatment, with laboratory and clinical resolution. Graft functions were stable during and after treatment in 2 patients, while function deteriorated in one.
Conclusions: The mechanism of injury to the pancreas and its correlation with the severity of the COVID-19 infection in kidney transplant recipients remains warrants further research.

P745 CLINICAL MANIFESTATIONS AND OUTCOMES OF CORONAVIRUS DISEASE-19 IN HEART TRANSPLANT RECIPIENTS

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Background: Coronavirus disease 2019 (COVID-2019) is already considered the most important pandemic of the 21st century. Heart transplant (HT) recipients represent a unique population that often presents advanced age and comorbidities.In addition,HT recipients are chronically immunosuppressed and its impact on COVID-19 infection is still a subject of debate.Although immunosuppression could facilitate viral replication at the early infection phase, at this point we acknowledge the benefits of steroids in COVID-19 patients with hypoxemia or requiring ventilatory support.The aim of our study is to describe characteristics and outcomes of HT recipients infected by the SARS-CoV-2, in Greece.
Methods: In this case series,we prospectively included all adult HT recipients (>18 y old), who received the diagnosis of COVID-19. The enrollment was carried out from April 5, 2020 to January 5, 2023. Inclusion criteria for this case series were adult HT recipients with 1 or more clinical symptoms of SARS-CoV-2 infection in the last 7 d (fever, dry cough, malaise, and/or dyspnea) and positive SARS-CoV-2 RT-PCR in nasopharyngeal samples.HT recipients with suspected symptoms of COVID-19 whose diagnostic test was not performed, were not included in this analysis.
Results: Seventy-one patients were included.The majority of patients were men; the median age was 543 (30–60) years old; median HT time was 34 mo; and median follow-up time 162 d. No one needed hospitalization. Immunosuppressive therapy was reduced in the majority of patients, except from steroids, which were maintained.Four patients had recurrent infection .The remarkable was that only 1 patient died due to complications after acute renal failure 60 days after the initial diagnosis .The majority of the patients were vaccinated Three months after the initial infection all patients underwent surveillance control with PCR for CMV and EBV viral load .Surprisingly ,the majority of the infected patients presented with increased viral load both for CMV and EBV.They received treatment with valganciclovir with decrease in viral load after 4 months.
Conclusions: Our report shows that a significant rate of later events such as CMV and EBV infections may happen suggesting that a strict midterm surveillance is advisable to HT recipients with coronavirus disease 2019.

P747 FIRST EXPERIENCE WITH COVID-19 VACCINATION IN HEART TRANSPLANT PATIENTS

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Background: Infectious complications are one of the leading causes of morbidity and mortality in heart transplant recipients. On April 2021 the ISHLT has published guidelines for COVID-19 vaccination that included the use of Sputnik V.
Objective: to evaluate the first experience of vaccination against COVID-19 in patients after heart transplantation (HTx).
Methods: After HTx all recipients were included in the dispensary follow-up group, and as of 31 January 2023, it contained 159 patients. Prior to vaccination, 75 (47%) recipients had COVID-19, of which 57% had mild severity. We analyzed retrospectively the results of vaccination against COVID-19 in heart recipients.
Results: From April 2021 to January 2023 Sputnik V vaccination was performed in 125 recipients (52±14 year-old; 78 - males) and a booster – in 32 of them. Patients were vaccinated more than 6 months after HTx. Tolerability of vaccination was satisfactory: 12 hours after vaccination temperature rise to subfebrile figures (37.0-37.2 C) was in 5 patients (4%) aged 18 to 27 years. A year after the vaccination, 28 (22%) patients were infected with COVID-19: 14 were males, from 19 to 73 year-old. In 26 (93%) sick recipients who were vaccinated before, there were no changes in the levels of WBC or C-reactive protein and they did not develop post-covid complications (i.e. no pneumonia, no rejection). Only 1 patient, who had a history of twice COVID-19 before vaccination, had a moderate course of COVID-19, complicated by pneumonia: up to 40% lung damage with the appearance of consolidation foci 16 days after the onset of the disease. He was successfully treated. One recipient (71 year-old), who had been vaccinated 5 months prior to COVID-19, died in the hospital at the place of residence from gastric bleeding 14 days after the onset of the disease. The patient was self-medicating and did not follow the recommendations of his transplant cardiologist: treatment against COVID-19 and reduction of immunosuppression were initiated 10 days after the onset of the disease.

Conclusions: Sputnik V vaccination is well tolerated in most heart transplant recipients. Vaccinated patients have reduced the incidence and severity of COVID-19, as well as the incidence of post-COVID complications. There was no allograft complications associated with vaccination against COVID-19.

P748 THE SERIOUS CONSEQUENCE OF DECREASE INMUNOSSUPRESSION AFTER COVID-19 IN A COHORT OF KIDNEY TRASPLANTATION

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Background: In February of 2020, a novel virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cause the coronavirus disease 2019 (COVID-19) pandemic. The physician ignored the disease course and different treatments have been proven. Kidney transplantation recipients (KTRs) had increased risk of development serious complications or deaths, and the withdrawn or decrease immunosuppression treatments was widespread. Nowadays, we find the consequences of these decisions.
Objetives: We aim to assess long term effects of decrease o withdrawing immunosuppression treatments in kidney function, develop a rejection or novo donor specific antibodies (nDSA), allograft's survival and patient's survival.
Methods: Retrospective observational study that included all KTRs who were infected by SARS-CoV-2 during first and second pandemic waves from January 2020 to December 2020. KTR were followed since the COVID-19 to February 2023 or death or graft lost. We included demographic variables, renal function measure as estimate glomerular filtration rate (eGFR), renal biopsy performed after COVID-19, nDSA, renal and patient survial and their causes of lost.
Results: Our study included 73 KTR. The table shown the demographics and the outcomes of the patients. After two years of COVID-19 pandemia, the global graft survival was 62,9%, graft survival death censored 82,6% and patient survival 82,6%. The majority of patient death in the first year, but the graft lost occurred after two year of SARS-CoV-2 infection.
Conclusion: COVID-19 had and has a high impact in KTR both in patient's survival in the first year after infection and nowadays in the renal function and graft survival. We need more time to understand the graves complication derivate of the pandemia.

Variable	Patients (73)	
Gender (male), n (%)	44 (60,3%)	
Etiology ESRD, n (%)		
Diabetic nephropathy	11 (15,1%)	
Nephroangiosclerosis	8 (11%)	
Glomerulonephritis	14 (19,2%)	
Interstitial nephropathy	9 (12,3%)	
Polycystic renal disease	13 (17,8%)	
Systemic vasculitis	1 (1,4%)	
Others	17 (23,3%)	
Baseline inmunological risk, n (%)		
No sensitized	58 (79,5%)	
Sensitized	15 (20,5%)	
Induction therapy, n (%)		
Basiliximab	26 (35,6%)	
Antithymocyte globulin	47 (64,4%)	
Immunosuppressive regimen COVID diagnosis, n (%)		
Steroids + Tacrolimus	15 (20,5%)	
Steroids + Tacrolimus + Mycophenolate	49 (67,1%)	
Steroids + Tacrolimus + mTOR inhibitors	5 (6,8%)	
Others	4 (5,6%)	
Hospitalization, n (%)	17 (23,3%)	
Intensive care unit, n (%)	10 (13,7%)	
Discontinue Immunosuppressive regimen at COVID-19 diagnosis, n (%)		
STOP tacrolimus	5 (6,8%)	
STOP mycophenolate	7 (9,6%)	
STOP both	40 (54,8%)	
No	20 (27,4%)	
COVID-19 treatment, n (%)		
Remdesivir	3 (4,1%)	
Lopinavir/Ritonavir	5 (6,8%)	
Hydroxychloroquine	14 (19,2%)	
Azitromicine	15 (20,5%)	
Steroid pulse	36 (49,3%)	
Acute Kidney Injury during admission, n (%)	38 (52,1%)	
Renal replacement therapy, n (%)	6 (8,2%)	
Biopsy	14 (19,2%)	
Biopsy proven rejection, n (%)	6 (8,2%)	
Acute tubular necrosis	5 (6,8%)	
Chronic damage	1 (1,4)	
Return to Hemodialysis, n (%)	11 (15,1%)	
Death, n (%)	19 (26%)	
COVID	14 (19,2%)	
Non COVID infection	3 (4,1%)	
Cardiovascular	2 (2,7%)	
Control of nDSA	12 (16,4%)	
None	6 (8,2%)	
Positive, but nDSA	4 (5,5%)	
nDSA	2 (2,7%)	
Graft function		
PreCOVID eGER, (IQR)	43 (29-54)	
At COVID diagnosis eGFR, (IQR)	35 (22-52)	0,007*
7 days after COVID eGFR (IQR)	40,5 (26,5-55,25)	0,375*
15 days after COVID median eGFR (IQR)	45 (29-59)	0,147*
2 months after COVID median eGFR (IQR)	48 (34-66)	0,143*
6 months after COVID median eGFR (IQR)	41 (29-55,75)	0,008*
12 months after COVID median eGFR (IQR)	39 (31-56)	0,009*
24 months after COVID median Cr (IQR)	41 (30-58)	0,001*
Tacrolimus levels		
PreCOVID, (IQR)	7,1 (5,6-8,9)	
At COVID diagnosis (IQR)	5,5 (4,6-8,8)	0,150*
2 months after COVID (IQR)	7,1 (5,25-8,45)	0,506*
6 months after COVID (IQR)	7,3 (5-8,7)	0,862*
12 months after COVID (IQR)	7,3 (5,8-8,9)	0,391*
24 months after COVID (IQR)	7 (5,7-9)	0,413*

*Compared with preCOVID levels

P749 ROLE OF CORONARY CALCIUM SCORE IN RULING OUT CORONARY ARTERY DISEASE AND IN WAITLIST PATIENTS SELECTION FOR LIVER TRANSPLANT CANDIDATES

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Background: Cardiovascular (CV) events are a major cause of morbidity and mortality after liver transplantation (LT). Consensus is lacking about the optimal CV screening in LT candidates. In addition, incidence and predictors of CV events in the early postoperative phase are unclear. Coronary artery calcium (CAC) score is a widely available and reproducible test based on chest CT scan without contrast media, to assess risk of coronary artery disease (CAD) and CV events in general population. Herein we evaluate if in LT candidates CAC may help to rule out significant CAD and early CV events reducing the need for invasive or more expensive tests.
Methods: We included all LT candidates who received CV risk assessment in our center between 2019 and 2021. CAC score was required in case of at least 1 CV risk factor or pathological ECG/echocardiogram. Coronary CT was performed when technically feasible and in patients with high CV risk, per choice of consultant cardiologist. Study endpoint was occurrence of in-hospital post-LT CV events (acute myocardial infarction, stroke, acute heart failure, atrial fibrillation, CV death).
Results: 314 pts received CV risk evaluation, and 184 (59%) were listed. CV risk factors were highly prevalent, with 65% of patients bearing at least 2 CV risk factors. CAC score was assessed in 190 patients. CT coronary angiography was performed in 89 (28,3%) patients, with evidence of critical stenosis in 18 (20%), of whom 17 had CAC score >35 (negative predictive value of 97%; P<0.01). CV risk profile including CAC score was significantly lower in listed patients than those not listed (Table). Of note only 7 patients with coronary lesions at CT scan were listed, two of them after coronary stenting. 182 patients underwent LT of whom 12 (7%) died, 1 for CV cause. Additional 16 patients experienced non-fatal CV events, only one of them had coronary lesions. Low numbers prevented any factor to be significantly associated to CV events. However, CAC score was higher those with CV events than those without (43 (2,4 - 117) vs. 8,7 (0-155)).
Conclusions: CAC score showed very high negative predictive value for significant CAD and may help to reduce the need for additional testing in LT candidates. CAC score guided screening allowed to list patients with lower CV risk profile resulting in a very low occurrence of posttransplant CV events.

Tab.1 Population characteristics

Population characteristics	Overall population (N=314)	Listed (N=184)	Not listed (130)	p
Age, yrs	56 ± 9	55 ± 10	57 ± 9	0,28
Hypertension, n (%)	129 (41)	67 (36)	62 (48)	0,046
Dyslipidemia, n (%)	71 (22,6)	35 (19)	36 (28)	0,07
Diabetes, n (%)	88 (28,0)	48 (26)	40 (31)	0,36
Smoke, n (%)	186 (59,1)	108 (59)	78 (60)	0,81
Family history, n (%)	32 (10,2)	13 (7)	19 (14)	0,031
≥2 CV Risk factors, n (%)	204 (64,9)	105 (57)	99 (76)	0,0004
Calcium score performed N=190				
Calcium score, m [IQR]	35 [0-291]	11 [0-144]	93 [0-570]	0,032
CS>50° percentile, n (%)	95 (50)	46 (43)	49 (58)	0,05

P752 A SINGLE CENTRE FIRST EXPERIENCE OF PAEDIATRIC HEART TRANSPLANTATION FROM ADULT DONORS

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Purpose: To estimate early and long-term outcomes in recipients under 18 year-old who have been heart transplanted from adult donors.
Methods: From April 2011 to January 2023 we performed 12 heart transplantations (HTx) in paediatric recipients (7 – female) from adult donors (37 [27; 41] years old). The median of age was 15 (range 10-17) year-old, LVEF prior HTx - 22% (10-65 %). Causes of heart failure (HF) were dilated cardiomyopathy (n=7), non-compacted myocardium (n=1), arrhythmogenic ventricular dysplasia (n=2) restrictive cardiomyopathy (n=1) and Ebstein's anomaly (n=1). They spent in HT waiting list 155 (12-684) days. Two patients were bridged to transplant by ECMO followed with Berlin Heart EXCOR implantation (n=1; days on support - 250) and LVAD implantation (n=1; days on support – 355). Due to coronary angiography (CAG) results 1 patient underwent HTx and CABG simultaneously. All recipients managed with triple-drug therapy (steroids, calcineurin inhibitors, mycophenolate mofetil), induction (thymoglobulin - n=4, basiliximab - n=8). We analyzed retrospectively outcomes of paediatric HTx.
Results: Eleven recipients are alive, 7 of them (currently from 18 to 26 year-old) already became adults and were transitioned to the adultcare transplant follow-up. In a year 1 died from early-term developed neurological complications without being discharged after HTx. Patients spent in ICU 10 (range 4-18) days: 1 of them spent 18 days due to posterior reversible encephalopathy syndrome (PRES), tacrolimus was switched to cyclosporine. They required inotrope support during 4 (3-8) days. In 1 year after HTx TTE results got to normal values, the same as VO_{2peak} quality of life estimated by SF-36 significantly improved. During 1st year episodes of rejection (R2, AMR2) were diagnosed in 16% cases: 1 case of AMR3 in 9 months due to non-compliance and discontinuation of immunosuppression for 3 weeks. In long-term follow-up there were no significant transplant complications and co-morbidities.
Conclusions: Paediatric HTx is an successful treatment of end-stage HF and there are successful. Adult donors are acceptable to transplant children if they are matched. All patients recovered and went back to normal life. Physical capacity improved in all recipients.

P754 A SINGLE-CENTRE EXPERIENCE OF COVID-19 MANAGEMENT IN HEART TRANSPLANT RECIPIENTS

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Background: to estimate the frequency and outcomes of COVID-19 in patients after heart transplantation (HTx).
Methods: Between January 2010 and January 2023 it was performed 207 HTx, 18 of them were infected with COVID-19 and recovered from it prior to surgery. All recipients were included in the dispensary follow-up group that is leaded by one transplant cardiologist. We analyzed retrospectively results of 165 patients excluding those who died before the COVID-19 era.
Results: From February 2020 to January 2023 68% (n=112; 46±13 year-old, n=73 - male) of heart transplant patients were diagnosed with COVID-19: 37 – were re-infected in more than 1 month after the first recovery, 10 – were infected 3 times. Pneumonia was developed in 69% (n=110) of cases; swabs were positive in 60% cases. From the 1st day of the onset of clinical symptoms, MMF / everolimus were temporarily discontinued (< 14 days). Outpatient treatment included the appointment of oseltamivir, bromhexine, levofloxacin, anticoagulants and vitamins C and D. In 52 cases steroids were prescribed or the initial dose was increased. And in 32 cases patients were admitted to the hospital and 13 of them had oxygen inhalation through nasal cannulas; none required invasive ventilation. In 2 weeks after the onset of fever 3 recipients with pneumonia (COVID-19 plus bacterial) developed heart transplant dysfunction that was successfully treated by pulse steroid therapy and resumption of MMF in high doses. Since the beginning of pandemia the mortality rate from COVID-19 is 3.7%. There were 3 patients who reported about their condition days after the onset of symptoms died from gastrointestinal bleed, thrombosis and acute kidney injury, respectively. In 6 months after the recovery from COVID-19 Epstein-Barr virus antibody tests were positive in 63% recipients and Cytomegalovirus – in 10%.
Conclusions: The remote consultations of heart recipients lead to the on-time diagnosis of COVID-19 and treatment initiation from the 1st day of the onset of clinical symptoms what allowed to decrease the number of hospital admissions and to increase the survival. Temporal reduction of immunosuppression is a key to manage COVID-19.

P755 PRE-EXPOSURE PROPHYLAXIS WITH TIXAGEVIMAB/CILGAVIMAB IN A SLOVENIAN NATIONAL COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: Tixagevimab/cilgavimab (TIXA/CILGA) is a promising new drug for the prophylaxis and treatment of COVID -19 disease in immunocompromised patients. The aim of our study was to evaluate the efficacy and safety profile of TIXA/CILGA in a Slovenian national cohort of kidney transplant recipients (KTRs) as pre-exposure prophylaxis in the Omicron era.
Methods: All KTRs who received TIXA/CILGA (150 mg TIXA and 150 mg CILGA - prophylaxis dose) from May 1 to October 31, 2022, were included in the historical cohort study. Demographic, clinical, laboratory, and therapeutic data were collected from electronic and paper medical records.
Results: 106 patients with a transplanted kidney received preexposure prophylaxis with TIXA/CILGA; 72 men, 34 women, mean age 60 years (range 20 to 82 years), mean time since transplantation 9 years (range 1 month to 25 years). 45% were not infected with Sars CoV-2 before treatment with TIXA/CILGA. 45% had recovered once from COVID -19, and 8% had been infected twice. Only one patient had COVID -19 three times before treatment with TIXA/CILGA. Almost all patients had been vaccinated against COVID -19; only one patient had not been vaccinated due to severe adverse reactions to influenza vaccination in the past. Six patients (5.7%) acquired Sars-CoV-2 infection after receiving TIXA/CILGA. The incidence of Sars-CoV-2 infection was only slightly lower than in patients who did not receive TIXA/CILGA (7.0%). All patients who received TIXA/CILGA had a mild disease course, whereas 20% of patients who did not receive TIXA/CILGA required hospitalization and two died. Adverse effects most likely related to TIXA/CILGA occurred in 12% of patients, one of whom experienced deep vein thrombosis. None of the patients suffered acute myocardial infarction or cerebrovascular insult.
Conclusions: In the Slovenian KTRs population the benefits of using TIXA/CILGA appear to outweigh the potential risk of adverse events and provide additional protection against severe COVID-19 progression.

P756 ACUTE KIDNEY INJURY AFTER ALIROCUMAB APPLICATION IN A KIDNEY TRANSPLANT RECIPIENT WITH LUPUS NEPHRITIS – A CASE REPORT

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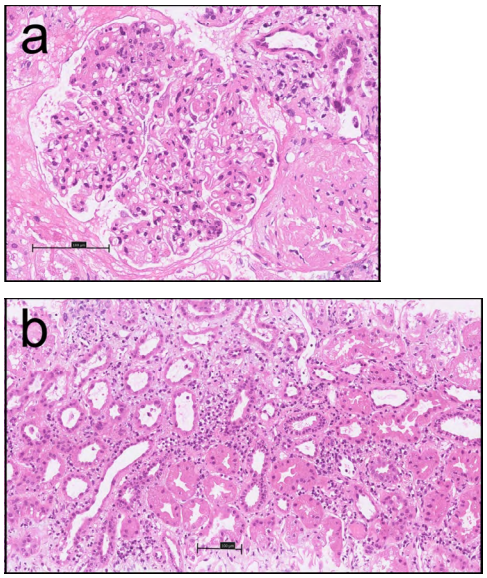
Background: Alirocumab is a human monoclonal antibody IgG1 to proprotein convertase subtilisin-kexin type 9. Some case reports describe alirocumab associated acute kidney injury (AKI) by an unknown mechanism.
Case Report: 54-year-old female, 25 years after kidney transplantation due to lupus nephritis on cyclosporin monotherapy (she self-discontinued mycophenolate) was clinically stable (serum creatinine 65 µmol/l, daily proteinuria 0,5-1 gram) when started on alirocumab for uncontrolled hyperlipidemia. Diarrhoea and malaise occurred after the first application, progressing to maculopapular rash, malaise, joint paint and hypertension after the second dose 14 days later. Her serum creatinine rose to 214 µmol/L, serum albumin decreased to 22 g/L with daily proteinuria of 9 grams. Immunoserology was positive with an elevated anti-dsDNA 0.74 (upper limit of normal 0.35), ANA titre 1:320, and low C3 and C4 levels. Donor-specific antibodies were borderline positive. Kidney biopsy revealed lupus glomerulonephritis with predominant membranous component (Figure 1a), with the addition of focal acute plasma cell rich interstitial nephritis (Figure 1b) and diffuse C4d positive staining, consistent with either drug-induced AKI, lupus nephritis or antibody-mediated rejection. Immunofluorescence showed abundant glomerular and extraglomerular (tubular, interstitial and along ptc) IgG deposits that were polyclonal, with IgG1 predominance. Molecular microscope diagnostic system testing was inconclusive and pointed to elements of both rejection-like inflammation and moderate AKI with minimal atrophy-fibrosis, but the test is not validated to assess primary renal disease. Based on these findings, acute rejection seemed less probable. We initiated methylprednisolone (5 mg/kg pulses on 5 consecutive days, followed by 0.4 mg/kg/d orally) and mycophenolate, and switched cyclosporine to tacrolimus. Alirocumab was discontinued. Immediate clinical improvement and partial remission were achieved (albumin rose to 30 g/L and proteinuria dropped to 1.9 grams daily), with persistent kidney dysfunction.
Conclusions: The presented case demonstrates a possible association between either alirocumab therapy and relapse of lupus nephritis or alirocumab induced interstitial nephritis in the renal graft.



P757 ROBOTIC VS LAPAROSCOPIC VS OPEN NEPHRECTOMY FOR LIVE KIDNEY DONATION: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROL TRIALS

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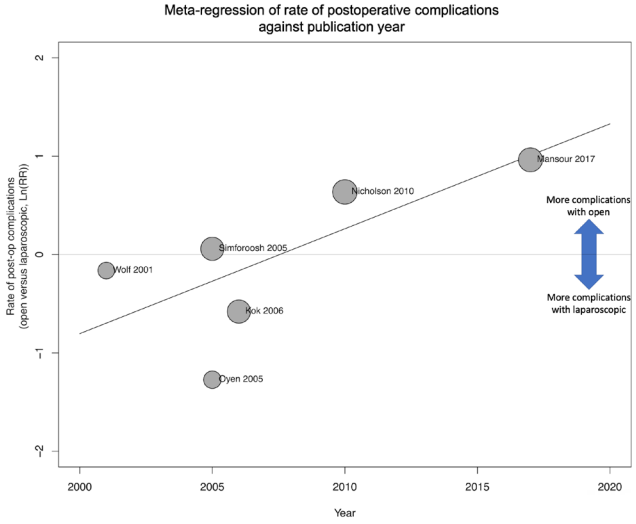
Background: Live kidney donation significantly reduces waiting times and offers recipients significant long-term benefits. Multiple minimally invasive nephrectomy techniques are now available. We aimed to define and compare the benefits and harms between these techniques for live kidney donors.
Methods: A systematic review and meta-analysis, using Cochrane methodology, of randomised control trials (RCTs) comparing outcomes between open donor nephrectomy (ODN), laparoscopic donor nephrectomy (LDN), hand-assisted laparoscopic donor nephrectomy (HALDN), or robotic donor nephrectomy (RDN) for live kidney donation. Mixed-effects meta-regression was also conducted to investigate trends of change in outcomes over time.
Results: Twelve RCTs were included, randomising 1230 live kidney donors. Seven RCTs randomised 815 donors between LDN and ODN. LDN was associated with reduced analgesia use, shorter hospital stays, longer procedure duration and longer warm ischaemia time (Mean difference 2.92 min, 95% CI 1.09 to 4.74 min). Three RCTs randomised 270 donors between LDN and HALDN. HALDN was associated with reduced warm ischaemia time (Mean difference 1.05 min, 95% CI 0.72 to 1.37 min). One RCT randomised 45 donors between LDN and RDN and found RDN to have a longer warm ischaemia time. Conversion rates to ODN were 6/587 (1.02%) in LDN, 1/135 (0.74%) in HALDN, and 0/15 in RDN. In meta-regression analysis between LDN and ODN, procedure duration changed in favour of LDN significantly over time (yearly reduction = 7.12 minutes, 95% CI 2.56 to 11.67; P = 0.0022). Differences in perioperative complications also changed in favour of LDN significantly over time (yearly change in LnRR = 0.107, 95% CI 0.022 to 0.192; P = 0.014).
Conclusions: LDN is associated with less pain compared to open surgery and has comparable pain to HALDN and RDN. HALDN is comparable to LDN in all outcomes, except in warm ischaemia time where it is associated with a significant reduction. As surgeons have become more experienced with laparoscopic techniques, laparoscopic nephrectomies are no longer associated with increased procedure duration or complications compared to ODN.

Table 1. Summary of findings comparing open vs laparoscopic vs robotic live donor nephrectomy

Outcomes	Comparison	Intervention favoured	No. of participants (RCTs)	Effect size (95% CI)	P value
Analgesia requirements	**ODN vs LDN**	**LDN**	**556 (5)**	**0.45 (0.10, 0.80)**	**0.01**
	HALDN vs LDN	LDN	270 (3)	0.08 (-0.40, 0.55)	0.76
Duration of procedure (min)	**ODN vs LDN**	**ODN**	**815 (7)**	**48.55 (10.86, 86.25)**	**0.01**
	HALDN vs LDN	HALDN	270 (3)	10.00 (-24.13, 44.13)	0.57
Warm ischaemia time (min)	**ODN vs LDN**	**ODN**	**815 (7)**	**2.92 (1.09, 4.74)**	**0.002**
	HALDN vs LDN	**HALDN**	**270 (3)**	**1.05 (0.72, 1.37)**	**<0.001**
Hospital stay (days)	**ODN vs LDN**	**LDN**	**775 (6)**	**0.88 (0.27, 1.49)**	**0.005**
	HALDN vs LDN	LDN	270 (3)	0.18 (0.05, 0.42)	0.13
Blood loss	ODN vs LDN	LDN	775 (6)	0.06 (-0.19, 0.31)	0.64
	HALDN vs LDN	LDN	270 (3)	-0.16 (-0.64, 0.31)	0.50
Perioperative complications	ODN vs LDN	LDN	775 (6)	1.06 (0.59, 1.90)	0.84
	HALDN vs LDN	HALDN	270 (3)	1.32 (0.79, 2.22)	0.29
Reoperations	ODN vs LDN	ODN	596 (6)	0.57 (0.09, 3.64)	0.55
	HALDN vs LDN	HALDN	270 (3)	1.61 (0.20, 12.81)	0.65

CI - confidence interval; **HALDN** - hand-assisted laparoscopic donor nephrectomy; **LDN** - laparoscopic donor nephrectomy; **ODN** – open donor nephrectomy; **RCT** - randomised control trial

Figure 1. Meta-regression of perioperative complications against publication year



P758 NON HEART-BEATING DONOR PROGRAM FOR KIDNEY TRANSPLANTATION : FIVE YEAR RESULTS FROM A PORTUGUESE UNIT

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Background: Kidney transplantation (KTx) is the best therapeutic option for ESRD patients (pt). Organ shortage is a significant limitation and several countries have implemented a variety of policies to overcome it. Donation after cardiac death (DCD) has been a highly successful strategy. In Portugal, DCD was permitted in 2014 but technical and logistical considerations postponed the implementation of our program until 2017.
Methods: All KTx performed with DCD from 2017 to 2022, donor(Dn) and recipient(Rp) characteristics, technical data, graft function (GF) and complications were analysed.
Results: 19 KTx were performed. Dn gender: male (84,2%), median age 48 (26-65) years. Mean BMI: 26.7 ± 2.8 Kg/m^2. Median warm ischemia time (WIT) before ECMO: 55 (14-72) min. Median serum creatinine (Scr):1,3 (1-1,6) mg/dl; CKD EPI 60.5 ml/m/1.73 m^2. All grafts were submitted to pre-implantation biopsies. Rp gender: male (57,9%), median age: 53 (39-63) years; median BMI: 24.7 ± 3.9 Kg/m^2. Median dialysis vintage: 76 (48-96) months (M). 94,7% had hypertension and one pt was diabetic. Mean PRA: 0% (CDC) and mean HLA mismatch (MM): 4. Seven pts had DSA identified at transplantation (MFI:1370 - ®LUMINEX). All but one pt had induction therapy with Thymoglobulin. All pts submitted to MPD, MMF and postponed introduction of Tacrolimus. Surgical median cold IT was 13 (12.7-15.5) hours and WIT: 30 (25-34) min. Most pts (89,5%) had delayed GF. Onley one graft was lost, due to early renal vein thrombosis. Two other pts suffered vascular complications (renal artery stenosis and hematoma). Seven patients developed post KTx diabetes. No rejections or deaths were recorded over the follow up period, median 33.5 (12-40)M. Infection was the most common complication in the first 6M (57,9%). GF had a positive evolution, mean Scr: 2,6 mg/dl-1M; 1,8 mg/dl -6M; 1,3 mg/dl- 36 M post Ktx. Although the small number of pts, univariate analysis showed donor/recipient gender MM; donor BMI; dialysis vintage and Scr value at 6M, as possible predictors of CKD EPI<45 ml/m/1,73 m^2 at 24 M.
Conclusions: Our results are reassuring and consistent with those presented by other units confirming that this is a valid option for kidney donation and encouraging other countries to overcome legal and technical issues, that are still a barrier to the development of these programs.

P759 POST-TRANSPLANT DIABETES MELLITUS IN PEDIATRIC PATIENTS AFTER KIDNEY TRANSPLANTATION: INCIDENCE AND OUTCOMES

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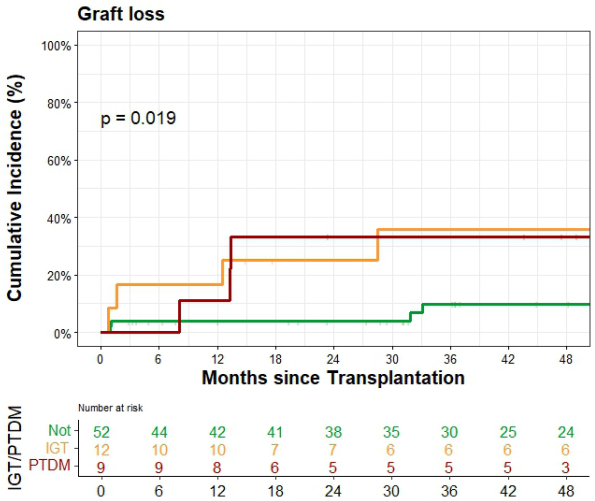
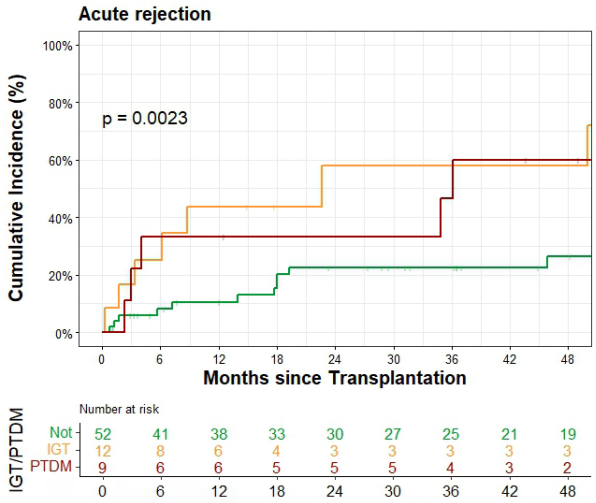
Background: Post-transplantation diabetes mellitus (PTDM) is a serious complication following solid organ transplantation, which significantly increases cardiovascular events and mortality. PTDM has also been associated with decreased graft survival. In contrast to PTDM the evidence linking impaired glucose tolerance (IGT) to those complications is scarce. The aim of this study was to evaluate the incidence of IGT and PTDM and the risk of acute rejection and graft loss in pediatric kidney transplant recipients.
Methods: The study cohort included patients aged <18 years who underwent a kidney transplant in a tertiary transplant center, from 2005 to 2020. Primary outcome was acute rejection and secondary outcome included graft loss and mortality. Survival analysis using Kaplan Meier curve was used to compare outcomes by PTDM/IGT group. Cumulative incidence of acute rejection and graft loss was estimated considering death as a competing risk. The proportional subdistribution hazard model of Fine and Gray was used to analyze the effect of PTDM/IGT status on the event. Follow up was defined as the period from transplantation until the occurrence of the outcome or otherwise censored at death, lost to follow up or end of the study.
Results: A total of 73 pediatric kidney transplant recipients were included. Average age was 13.4 years. IGT was presented in 12 (16.4%) patients and 9 (12.3%) PTDM. Acute graft rejection occurred in 5 (55.6%) of PTDM, 7 (58.3%) of IGT and 11 (21.2%) of non-PTDM/IGT patients. Comparing to non-PTDM/IGT patients, kidney graft recipients with PTDM and IGT had a higher risk of acute rejection (PTDM: HR = 1.12 95% CI 1.12-8.44, p-value 0.029, and IGT: HR = 1.35, 95% CI 1.54-9.57 p=0.004). Regarding graft loss, a total of 3 (33.3%) patients in PTDM group, 6 patients (50%) in IGT group and 7 patients (13.5%) in non-PTDM/IGT group had graft loss during the follow up. PTDM and IGT were found to have a higher risk of graft loss when compared with non-PTDM/IGT patients (IGT: HR 1.69 95% CI 1.47-19.9, p=0.011, and PTDM: HR 4.99, 95% CI 1.15-21.7, p=0.032).
Conclusions: PTDM and IGT patients had a higher risk of acute rejection and graft loss in pediatric kidney transplant recipients. Which justify a close follow up with these patients also in pediatric population.

Figure 1: Kaplan Meier curve stratified by IGT/PTDM status





P762 SAFETY AND EFFICACY OF GLP1-RAS AND ISGLT-2-COMPARED WITH THE STANDARD OF CARE IN A COHORT OF LIVER TRANSPLANTED PATIENTS: A RETROSPECTIVE STUDY

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Background: Few data on the use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium-glucose co-transporter-2 inhibitors (iSGLT2) are available after liver transplantation (LT). The aims of this study were to evaluate the safety and the efficacy of this treatment 6 months after LT compared to the standard of care.
Methods: we performed a retrospective monocentric comparative study on 36 liver recipients with pre/post-transplant-diabetes treated with GLP1-RAs and/or iSLGT2 after LT. A matched (1:2) control group of standards of care therapy was performed to compare the outcomes. The effectiveness was defined as: glycated hemoglobin (Hb1Ac) target <7% and fasting glycaemia ranged to 0.8-1.3g/l at 6 months. Side effects were collected.
Results: 36 LT adult patients were treated with GLP-1RAs and/or iSGLT2 after LT (mean age: 58.91,+/-8.4). The median MELD was 14 (IQR 10-21). 52,7% (n=19) of patients have alcoholic cirrhosis and 44.4% (n=16) NASH. Pre-transplant-diabetes was reported in 47.2% (n=17) of patients. After LT 63,9% (n=23) of patients have GLP1-RAs and 61.1% (n=22) iSLGT2 therapy. Patients were comparable for clinical and biological characteristics to the control group. Non-serious adverse event was reported in patients with GLP1-RAs and/or iSLGT2 treatment. The hypoglycemia rate was similar between the two groups (p=0.1). Fasting glycaemia target was achieved in 78,1% (n=25) and in 61,8%(n=34) of patients in the GLP1-RA and/or iSLGT2 group compared to the control group (p=0,1). Hb1Ac<7% was achieved for 81.2%(n=26) and 75.9% (n=41) of patients in GLP1-RAs and/or iSLGT2 group and in the control group (p= 0,5), respectively. Fast and slow acting insulin withdrawals were statistically significantly different between the 2 groups in the sub-group of patients with post-transplant diabetes with GLP1-RAs and/or iSLGT2 treatment(s) (p<0.001, p<0,001).
Conclusions: in our study performed on liver transplant recipients with a higher rate of NASH and alcoholic diseases, the GLP1-RAs and ISLGT2 treatments for diabetes was safe. The effectiveness was similar to the standard of care with a benefit of insulin withdrawal in a subgroup of patients with post-transplant diabetes. Futures prospective studies are needed to evaluate the benefit of the GLP1-RAs and SLGT2 on long-term outcomes.

Abstracts of the 21st Biennial European Society for Organ Transplantation (ESOT) Congress, Athens, Greece, 17 – 20 September 2023

LATE BREAKING ORALS

Late Breaking Full Orals

LOS1_1 THE MOLECULAR MICROSCOPE (MMDX) IN THE PROGNOSTIC STRATIFICATION OF HEART TRANSPLANTED PATIENTS: JUST A RESEARCH TOOL OR A USEFUL GUY?

Marco Masetti*[1], Gianmarco Spinozzi[2], Laura Borgese[1], Laura Giovannini[1], Letizia Marcantoni[1], Barbara Corti[3], Chiara Baldovini[3], Mario Sabatino[1], Alessio Aloisio[1], Sofia Martin-Suarez[4], Davide Pacini[5], Philip F. Halloran[6], Luciano Potena[1]

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Background: The microarray analysis of mRNA transcripts on endomyocardial biopsies (molecular microscope, MMDx), has been recently studied in heart transplantation (HT) as a potential tool to assess the probability of rejection. However, its use is actually limited to the research field and its prognostic ability has never been investigated in the clinical practice. We sought to study the prognostic role of MMDx when integrated with the information derived from histology (H), donor-specific antibodies (DSA), right heart catheterization (RHC) and echocardiography in heart transplanted patients.
Methods: In our monocentric retrospective study we included all patients undergoing to MMDx analysis between 2016-'19. We report the prevalence of cellular (ACR) and antibody mediated rejection (AMR) according to H and MMDx and their relationship with hemodynamic and echocardiographic data. The primary endpoint was the freedom from major cardiovascular events (MACE) at 7 years after the first MMDx analysis.
Results: 243 biopsies with MMDx analysis were performed in 110 patients (3.7±3.1 years from HT). 40.3% and 29.6% were ACR+ and AMR+ according to H, 5.8% e 14% for MMDx respectively; 25% of histologically detected ACR were labeled as AMR by MMDx. LVEF was not different according to the histological diagnosis, whereas it was lower in patients with a pathologic MMDx (MMDx+); diastolic dysfunction was more frequent in patients with AMR at H and in those with MMDX+ ($p<0.01$). Patients with AMR at either H or MMDX had an higher pulmonary capillary wedge pressure, those with ACR at MMDX had a lower cardiac index ($p<0.01$ all). At univariate analysis, the predictors of MACE were: H+, MMDX+ , an impaired RHC, DSA (OR: 6.7, 4.0, 5.3, 3.3 respectively, $p< 0.05$ all). Patients with H+/MMDX- or H-/MMDX+ were in an intermediate risk group between those H+/MMDX+ and H-/MMDX- (90.7±5.8% vs 85.7±13.2% vs 82.2±7.2% vs 56.6±12.9%, H-/MMDX- vs H-/MMDX+ vs H+/MMDX- vs H+/MMDX+, $p=0.04$).
Conclusions: Our study shows a good correlation between MMDx and hemodynamics and a prognostic role of this tool, thus suggesting its integreated use with histology hemodynamic in the every day clinical practice.

LOS1_2 CLINICAL IMPACT OF THE PREDIGRAFT/IBOX SYSTEM AS A CLINICAL DECISION SUPPORT FOR KIDNEY TRANSPLANT PATIENTS MANAGEMENT: RESULTS OF A PROSPECTIVE RCT

Alexandre Loupy[1], Olivier Aubert[1], Rozenn Cabioch[2], Florian Grahammer[3], Laurent Mesnard[1], Nassim Kamar[4], Johannes Stegbauer[5], Sapna Shah[6], Simon Knight[7], Caroline Dudreuilh[8], Adnan Sharif[9], Marta Crespo[10], Lluis Guirado[11], Isabel Beneyto[12], Ayelet Grupper[13], Hoang Tranminh[1], Arnaud Delbello[1;4], Dany Anglicheau[1], Gillian Divard[1], Sofia Naser[1], Jessie Aouizerate[13], Michelle Elias[1], Annemarie Weissenbacher[14], Sunil Daga[15], Carmen Lefaucheur*[1]

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Background: Computer based decision support systems are emerging tools for decision-making optimization, but their clinical benefit for patient care has not been demonstrated.
Methods: We designed a European multicenter RCT involving 16 centers from Europe (France, UK, Spain, Germany, Austria and Israel). Kidney recipients were randomly (1:1) assigned from 3 months up to 10 years after transplant to receive either SOC or management guided by a companion software Predigraft (CE mark FRMF 601) that provides automatic iBox patient risk assessment and prognostic trajectories. The primary endpoint was the number of allograft biopsies amenable to therapeutic changes. This study presents the interim period results at 9 months after randomization (NCT05112315)
Results: A total of 507 subjects were recruited, among which 252 in the Predigraft group and 254 in the SOC group. The mean time from transplant to inclusion was 4.4±5,7 yrs. Mean recipient and donor age were 52±14 and 52±15 yrs respectively. Other baseline characteristics were similar between groups. The mean follow-up time after randomization was 9.6± 3.6 months. In the Predigraft group, 398 iBox alerts were recorded among which 232 (58%) were deemed clinically relevant by physicians and 133 (33%) were followed by a change in clinical management and/or therapeutics. A total of 61 biopies were performed overall, 32 in the Predigraft and 29 in the SOC groups respectively (incidence of 12.6 vs 11.4%, p=NS). Biopsies revealed rejection (TCMR or ABMR) in 28% Predigraft *vs* 10% SOC patients respectively (p=0.08), CNI toxicity (28% *vs* 17%, p=0.2), and others including BKVN, AKI, IFTA, recurrent GN and Borderline lesions (50% *vs* 27%, p=0.07). Finally, the rate of biopsies leading to therapeutic changes (primary endpoint) was 25/32 (78.1%) in the Predigraft group compared with 3/29 (10.3%) in the SOC group ($p<0.0001$). Treatment modifications mostly included change in IS regimen type, dose, target in 20/32 (62.5%) in the Predigraft *vs* 3/29 (10.3%) in the SOC groups respectively, $p<0.001$).
Conclusions: These results show the ability of an automatized computer based decision support system to screen for allograft instability and help physicians to improve the rate of clinically relevant biopsies enabling therapeutic changes, including the detection of allograft rejection.

LOS1_3 LONGITUDINAL DD-CFDNA MONITORING REDUCES TIME TO ABMR DIAGNOSIS IN DNDSA POSITIVE KIDNEY TRANSPLANT RECIPIENTS: A DIAGNOSTIC RANDOMIZED CLINICAL TRIAL

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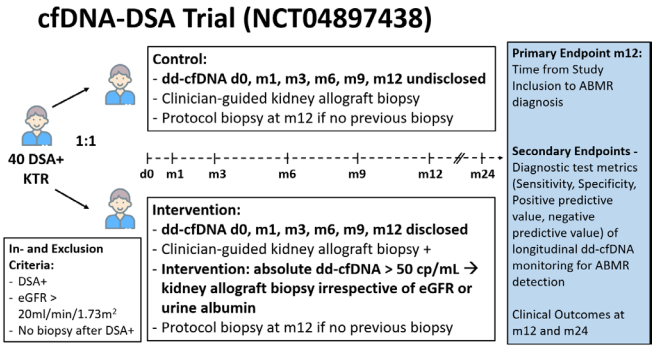
Background: Donor-derived cell-free DNA (dd-cfDNA) is a valid biomarker for the detection of antibody-mediated rejection (ABMR) in kidney transplant recipients (KTR) with de novo donor-specific anti-HLA antibodies (DSA+). However, the clinical benefits of dd-cfDNA monitoring still need to be established.
Methods: In this diagnostic, single-center, open label, randomized clinical trial, we randomly assigned 40 DSA+ KTR with eGFR > 20 mL/min/1.73m², but without biopsy after DSA occurrence into dd-cfDNA-guided biopsy (intervention group) or clinician-guided biopsy (standard of care) over a period of 12 months. Dd-cfDNA monitoring was performed at study inclusion and after 1, 3, 6, 9, and 12 months, and values above 50 cp/mL indicated a biopsy in the intervention group. Additionally, treating physicians could indicate a biopsy at any point during the study period, and 12 months after study inclusion, a biopsy was scheduled per protocol for patients without previous biopsy. The primary endpoint was time from study inclusion to diagnosis of active or chronic active ABMR. Secondary endpoints included diagnostic test metrics among others.
Results: From 40 patients, one patient died in the control group unrelated to the study investigation. From the remaining 39 patients, all had a functioning graft at the end of the observation period. In total, 26 patients underwent biopsy, 13 in each group. In the intervention group, 7/13 (54%) had ABMR and in the control group 5/13 (38%) patients had ABMR. Time from study inclusion to ABMR diagnosis was significantly shorter in the intervention group than in the control group (3.6 +/- 3.0 vs. 14.1 +/- 1.9 months, p<0.001) among patients with ABMR. Longitudinal dd-cfDNA monitoring in this cohort of KTR with dnDSA had a positive predictive value (PPV) of 0.77 and negative predictive value (NPV) of 0.85 for the diagnosis of ABMR.
Conclusions: Dd-cfDNA-guided kidney allograft biopsy in DSA+ KTR can reduce time to ABMR diagnosis and hereby expedite therapy initiation.

Table 1. Diagnostic test metrics of longitudinal dd-cfDNA monitoring for ABMR in DSA+ KTR. Prev – Prevalence of ABMR, Acc – accuracy, Sens – sensitivity, Spec – specificity,

	ABMR	No ABMR	Total	Prev 0.46
> 50 cp/mL	10	3	13	PPV 0.77
≤ 50 cp/mL	2	11	13	NPV 0.85
Total	12	14	26	
Acc 0.81	Sens 0.83	Spec 0.79		

Figure 1. Study Outline.



LOS1_4 AN EXOME-WIDE STUDY OF RENAL OPERATIONAL TOLERANCE

Annick Massart*[1;2], Richard Danger[3], Catharina Olsen[4], Mary Emond[5], Ondrej Viklicky[6], Valérie Jacquemin[7], Julie Soblet[8], Sarah Duerinckx[8], Didier Croes[8], Camille Perazzolo[7], Petra Hruba[6], Dorien Daneels[4], Ben Caljon[4], Mehmet Sever[9], Julio Pascual[10], Marius Miglinas[11], Isabelle Pirson[8], Lidia Ghisdal[12], Guillaume Smits[13], Magali Giral[3], Daniel Abramowicz[2], Marc Abramowicz[7;14], Sophie Brouard[3]

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Background: Renal operational tolerance is a rare and attractive state of prolonged renal allograft function in the absence of immunosuppression. The underlying mechanisms are unknown. We hypothesized that tolerance might be driven by inherited protein coding genetic variants with large effect, at least in some patients.
Methods: We set up a European survey of over 218,000 renal transplant recipients and collected DNAs from 40 recipients of an allogeneic kidney transplant who maintained good graft function (serum creatinine <1.7 mg/dL and proteinuria ≤1g/day or /g creatinine) in the absence of immunosuppression for at least one year. We performed an exome-wide association study comparing the distribution of moderate to high impact variants in 36 tolerant patients and 192 controls, selected for genetic homogeneity using principal component analysis, using an optimal sequence-kernel association test adjusted for small samples.
Results: We identified rare variants (allele frequency < 1%) of HOMER2 (3/36, False discovery rate (FDR) 0.0387), IQCH (5/36, FDR 0.0362), and LCN2 (3/36, FDR 0.102) in 10 tolerant patients vs 0 controls. One patient carried a variant in both HOMER2 and LCN2. Furthermore, the three genes showed an identical variant in two patients each. The three genes are expressed at the primary cilium (p_0=0.01), a key structure in immune responses. Both LCN2 variants were located 9 base pairs apart, in the 20 amino-acid long signal peptide of the encoded NGAL protein, suggesting the possibility of a shared functional effect.
Conclusions: We show for the first time that rare protein coding variants in a small set of genes are associated with operational tolerance in a sizable portion of patients (n=10/36). Our findings may have important implications for a better understanding of immune tolerance in transplantation. ClinicalTrials.gov Identifier NCT05124444.

LOS1_5 IDENTIFICATION OF PROTEIN SIGNATURES THAT PREDICT KIDNEY TRANSPLANT OUTCOME

Ivan Hartling*[1], Sarah Fawaz[2], Rebecca Vaughan[2;3], Ioannis Michelakis[2;4], Rutger Ploeg[2;3], Philip Charles[1], Cecilia Lindgren[1], Maria Kaisar[2;3]

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Background: Kidney transplantation is a life-saving treatment for end stage kidney disease, but every year hundreds of patients with kidney failure die while waiting for a transplant. Donor organ acceptance criteria have been expanded in an effort to decrease organ shortage; however, current acceptance criteria depend heavily on immune matching and donor age and lack granularity. This study aimed to identify donor circulating protein signatures to improve granularity of assessing donor kidneys, predicting kidney transplant outcomes.
Methods: We analysed deceased donor plasma samples that were linked to complete donor and recipient metadata obtained from the QUOD biobank. A selection of 49 analytes were measured at three timepoints in the plasma of 132 brain death donors (DBD) and at two timepoints in the plasma of 119 circulatory death (DCD) donors. These measurements, along with donor age, height, and sex, were used to construct separate DBD and DCD 10-fold cross-validated lasso regression models using 12-m recipient averaged eGFR as outcome end point. Models were compared using root mean squared error (RMSE) which is a measure of prediction accuracy.
Results: Lasso regression identified unique protein signatures in both DBD and DCD donors consisting of 20 and 22 proteins respectively with 8 proteins common to both models. The DBD model achieved a RMSE of 18.7 mL/min/1.73 m2 while the DCD model RMSE was 19.0 mL/min/1.73 m2. Both models performed considerably better than models containing clinical variables alone which had RMSEs of 21.7 mL/min/1.73 m2 and 22.7 mL/min/1.73 m2 for DBD and DCD respectively.
Conclusions: This study identified protein signatures in DBD and DCD kidney donor plasma that could improve prediction of posttransplant outcome compared to using clinical variables alone. Identified protein signatures will be validated in a follow-up study on 1000 donors to develop a predictive score which could be used to improve transplant outcome prediction.

LOS1_6 URINARY CELL-CYCLE ARREST BIOMARKERS FOR PREDICTION OF ACUTE KIDNEY INJURY FOLLOWING LUNG TRANSPLANT

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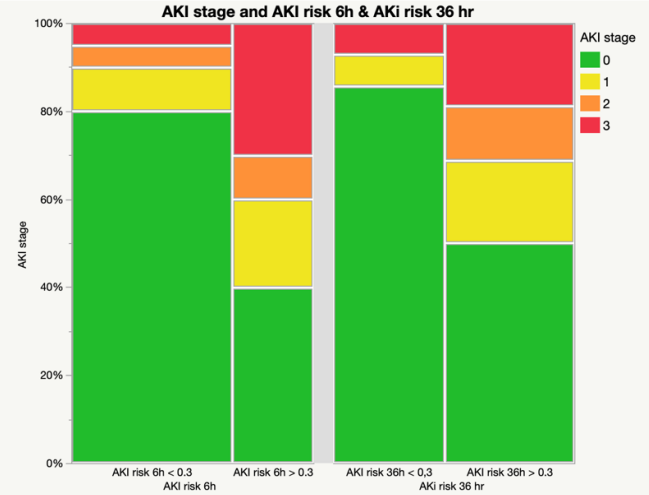
Background: Lung transplant (LUTX) is a feasible option for end-stage respiratory failure. Acute kidney injury (AKI) is a common and impactful complication of LUTX. Urinary cell cycle arrest proteins as early indicators of AKI have never been tested in LUTX recipients.
Methods: In a single-center prospective observational study, we assessed the capabilities of early urinary Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) and Insulin-Like Growth Factor Binding Protein 7 (IGFBP7) (i.e., [IGFBP7]x[TIMP-2], Astute Medical, Paris, FRA) in predicting AKI and acute kidney disease (AKD) following KIDGO criteria, in adult patients undergone primary double LUTX. Exclusion criteria were preoperative chronic kidney disease (stage > 3) and emergent enlistment. AKI score was measured at 6 and 36 hours from graft reperfusion.
Results: Thirty consecutive adult LUTX patients were included (12 (40%) females, 51.5 (43.8-60.0) years old, Lung Allocation Score 40.5 (36.6-46.6)). Restrictive (14 (46%)) and suppurative (7 (23%)) diseases were the most frequent indications. Enlistment creatinine and estimated glomerular filtration rate were 0.78 (0.68-0.9) mg/dL and 91.0 (74.5-106.0) mL/min/1.73 m^2 (see Table 1), respectively. Creatinine peaked 2 [1-5] days after LUTX, at a median 0.98 (0.82-1.17) mg/dL, with 4 (13%), 2 (7%), and 4 (13%) patients having postoperative AKI stages 1, 2, and 3, and 3 (10%) needing renal replacement therapy during ICU stay. 6 (21%), 3 (10%), and 9 (31%) developed AKD stage 1, stage 2, and 3, respectively. AKI score was > 0.3 at 6 and 36 hours detected in 10 (33%) patients and 16 (53%) patients, respectively. 6-hours AKI score > 0.3 was associated with increased risk of AKI > 0 (p=0.036, OR 6.0 (1.2-31)) with AUC 0.66 (0.49-0.8 95% CI), with sensitivity of 0.6 (0.31-0.83 CI 95%) and specificity 0.8 (0.58-0.91 CI 95%). 36-hours AKI score > 0.3 was associated with increased risk of AKI > 0 (p=0.049, OR 5.9 (1.0-35)) with AUC 0.65 (0.47-0.81 95%CI), with sensitivity of 0.8 (0.49-0.94 CI 95%) and specificity 0.6 (0.38-0.78 CI 95%) (see Fig 1). AKI score > 0.3 was not associated with increased risk of AKD.
Conclusions: Patients undergone LUTX have high risk of AKI and AKD. Measurement of urinary cell cycle arrest proteins was predictive of AKI and may be used to guide AKI preventive measures in LUTX recipients.



	Clinical Characteristic	
Enlistment	Age (years)	51 [43 – 60]
	Sex (male)	18 (60%)
	BMI (kg/m2)	23,2 [19,3 – 25,3]
	Diagnosis group (restrictive)	17 (56,7%)
	Creatinine (mg/dL)	0,78 [0,68 – 0,90]
	eGFR (mL/min/1.73 m^2)	91,0 [74,5 – 106,0]
	Waiting List (days)	119 [34 – 277]
	Bridge to LUTX (%)	1 (3,3%)
	LAS	40,58 [36,65 – 46,66]
Perioperative	Intraoperative ECMO (%)	15 (50%)
	Postoperative ECMO (%)	4 (13,3%)
	Blood components (units)	2 [0 – 4,5]
	Red Blood Cells (units)	3 [1,75 – 6,5]
Donor	DBD donor (%)	27 (90%)
	Oto SCORE	4 [2 – 5]
	Total warm ischemia time (min)	77,3 [54,2 – 100,4]
	Total cold ischemia time (min)	769,5 [618 – 913,8]
	EVLP (%)	5 (17%)

LOS1_7 TNF-A PATHWAY ACTIVATION ON DECEASED KIDNEY DONORS: A CRITICAL MEDIATOR OF UNFAVORABLE POST-TRANSPLANT OUTCOMES

Ioannis Michelakis*[1;2], Sarah Fawaz[1], Ivan Hartling[3], Rebecca Vaughan[1], Smaragdi Marinaki[2], Philip Charles[3], John Boletis[2], Rutger Ploeg[1], Maria Kaisar[1]

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Background: Elevated levels of TNF-α pathway related proteins have been linked with kidney function decline and injury; yet the mechanisms have not been fully elucidated neither evaluated on deceased donors. The aim of this study was to evaluate the circulating levels of TNF-α, TNFRSF1A, TNFRSF1B and TNFRSF17 in donors after brain (DBD) and circulatory death (DCD) and investigate whether high levels of these mediators may impact graft function posttransplant.
Methods: Plasma samples from 284 deceased donors (158 DBD, 126 DCD) were obtained from the Quality in Organ Donor (QUOD) biobank. Using Luminex assays, longitudinal levels of the analytes were quantified in plasma samples collected during donor management (prior to cross clamp in DBDs and withdrawal of support in DCDs). Statistical associations were performed of donor analyte levels and posttransplant events of primary non-function (PNF), delayed graft function (DGF), acute rejection (AR), 12-month posttransplant graft function (eGFR<30, 30-59, >60 ml/min) and graft loss (GL), within 60 months of follow up.
Results: Among 568 paired recipients of 284 donors, 11 (2%) recipients developed PNF, and 128 (22%) recipients developed DGF (24 pairs, 80 non-pairs). Fifty recipients (9%) experienced at least one AR episode (9 pairs, 32 non-pairs) and 74 (13%) donors had a GL during follow-up. High donor levels of TNFRSF17 were associated with DGF (p=0.04). Donor TNF-α, TNFRSF1A, TNFRSF17 levels were significantly elevated (p<0.05) in donors who offered concordant grafts with suboptimal 12-month post-transplant function (eGFR<30 ml/min, Fig 1). GL associated with significantly higher levels of TNFRSF1A and TNFRSF17 pre-transplant (p<0.05, Fig 2). Grafts developed PNF were obtained from donors with higher levels of TNFRSF1A, TNFRSF2A, TNFRSF17 compared to donors who offered kidneys with immediate function (TNFRSF17, p=0.04). Finally, in AR, higher levels of the markers were observed, but were not of significance.
Conclusions: We demonstrated that increased circulating inflammatory levels are associated with poorer prognosis. In an era of donor shortage crisis, our study sheds light on a critical pathway of donor kidney injury in “high-risk” and of uncertain quality donors and offer the opportunity for more granular assessment of transplants.

Fig 1.

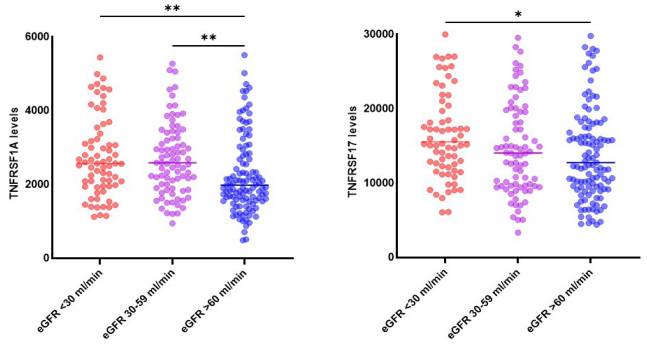
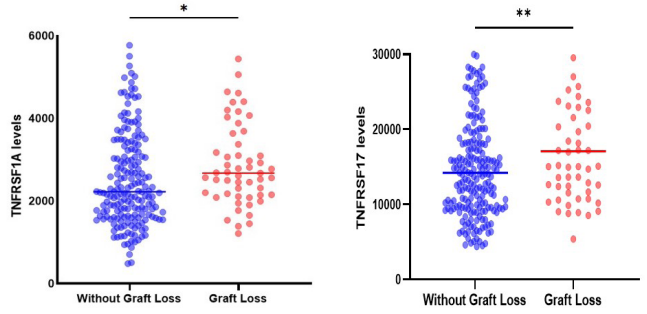


Fig 2



LOS1_8 SINGLE-CELL RNA SEQUENCING REVEALS ACTIVATION OF IMMUNE CELLS IN STABLE HUMAN KIDNEY AFTER TRANSPLANTATION

Gang Huang*[1], Hui Zhang[1], Xutao Chen[1], Guodong Zhao[1], Jinquan Luo[1], Shicong Yang[1], Jiang Qiu[1]

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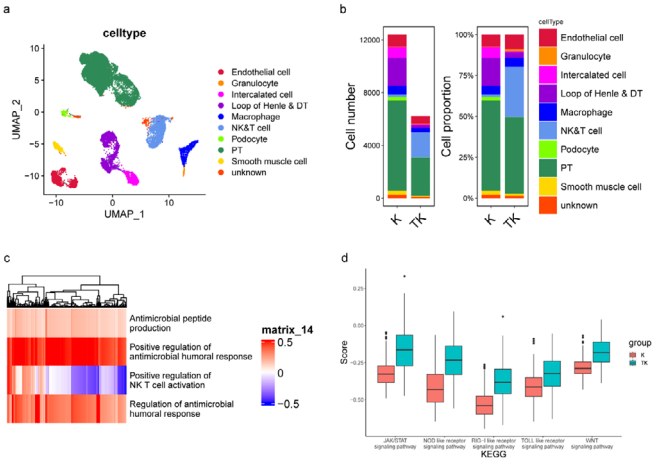
Background: Our objective was to determine differences between native kidney and stable transplanted kidney (STK) using single cell RNA sequencing (scRNA-seq).
Methods: Single cell transcriptome profiles were generated from two STK samples and merged with data of six native kidneys from the Gene Expression Omnibus (GEO) database. The cell types were determined according to reported marker genes by scRNA-seq analysis. Cell cell communication analysis, trajectory analysis, and gene-set variation analysis (GSVA) were used to explore differences of natural killer T (NKT) cells, macrophages, and proximal tubule cells (PTcs) between native kidney and STK.
Results: Nine main cell types were identified: endothelial cells (ECs), granulocytes, intercalated cells, PTcs, loop of Henle and distal tubule (DT) cells, NKT cells, mononuclear cells and macrophages, smooth muscle cells, and podocytes. Intercellular and molecular interactions were elevated in STK. The number of NKT cells was increased in STK, and NK cells accounted for the largest proportion, with the expression of some rejection-related genes. The WNT signaling pathway, Jak-STAT signaling pathway, and pattern-recognition receptor (PRR) signals were activated in macrophages of STK. PTcs in STK exhibited elevated metabolism.
Conclusions: There are differences in cell communication and gene enrichment between STK and native kidney. These differences may be helpful in the research of kidney transplant complications.

Table Information of two patients with stable transplanted kidneys.

Patient	Case 1	Case 2
Age	28	36
Sex	Male	Female
Time after surgery	two months	two months
Immunosuppressive regimen	Tac + MMF + Prednisone	Tac + MMF + Prednisone
eGFR (ml/min/1.73m^2)	69.98	88.75
Creatinine (umol/L)	135	69
Proteinuria	No	No
PRA	Negative	Negative
Global glomerulosclerosis	0/28	1/12
g	0	0
cg	0	0
t	0	0
i	0	0
v	0	0
ptc	0	0
ct	1	1
ci	1	1
i-IFTA	0	0
t-IFTA	0	0
C4d	-	-
SV40-T	-	-



(a) UMAP plot showing the identified cell types. (b) The number and proportion of the assigned cell types in the different groups. (c) Heat map showing the enhanced Gene Ontology biological process terms in NK&T cells by GSVA analysis. (d)Box plot showing the GSVA score of KEGG pathway in macrophage of different group.

LOS2_1 KNOCK-OUT OF THE ACTIVATING LIGAND REPERTOIRE OF HUMAN STEM CELL-DERIVED BETA CELLS AVOIDS CHRONIC ALLOGRAFT REJECTION MEDIATED BY NK CELLS

Raniero Chimienti[*1;2], **Gabriel Siracusano[1;2], Federica Deambrogio[1], Cuozzo Federica[1], Valeria Sordi[1], Mauro Malnati[3], Lorenzo Piemonti[1;2]**

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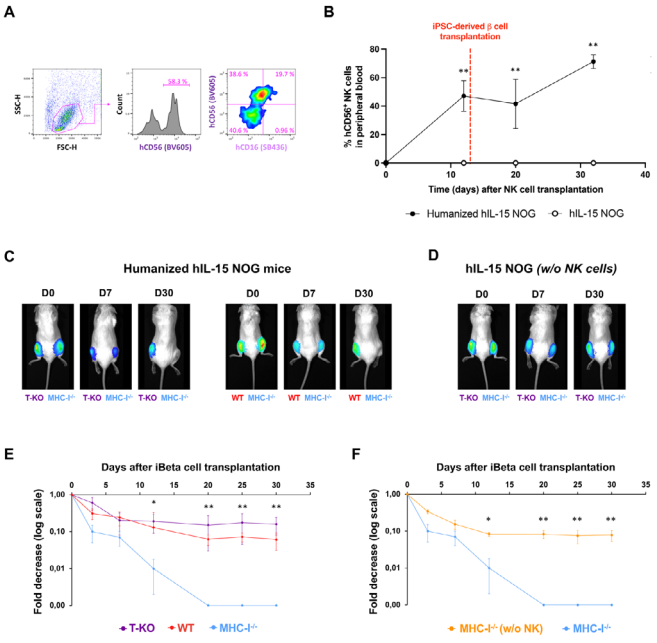
Background: Natural Killer (NK) cells are an heterogeneous population of lymphocytes that, in addition to anti-viral and anti-tumoral activities, regulates several aspects of the alloimmune response in solid organ transplantation. The early activation of NK cells upon transplantation depends on the repertoire of ligands exposed by the allogeneic target cells. In the last years, MHC-I-null stem cell-derived β cells have been proposed as alternative source for treatment of Type 1 Diabetes (T1D). However, despite their use prevents T cell response, it could trigger NK cells via missing-self recognition leading to graft loss. As we described that stem cell-derived β cells express high levels of the NK activating ligands CD276 and CD155, we focused on their engineering to escape NK recognition after transplantation.
Methods: We generated luciferase-expressing wild type (WT) (negative control of rejection), MHC-I$^{-/-}$ (positive control of missing-self recognition) and MHC-I$^{-/-}$/CD276$^{-/-}$/CD155$^{-/-}$ (TKO) human induced pluripotent stem cells (iPSCs). Gene-edited iPSCs were differentiated into β cells (iBeta) following 35-days *in vitro* protocol. We transplanted 200 islet equivalent in the lower limb muscles of hIL-15 NOG mice humanized with donor-derived NK cells, then assessed iBeta engraftment up to 30 days through *in vivo* imaging system.
Results: Gene-edited iPSCs differentiated into iBeta with high efficiency (> 50% of NKX6.1^{+} and > 40% of INS^{+} cells) and viability (> 80%). Strikingly, once transplanted into mice reconstituted with human NK cells, T-KO iBeta successfully escaped NK recognition and killing. Indeed, we observed only a slight reduction of graft area and bioluminescence signal of T-KO iBeta, comparable to WT counterpart. Conversely, MHC-I$^{-/-}$ iBeta was quickly recognized and totally rejected by circulating NK cells within two weeks ($p < 0.001$, n = 9). Finally, T-KO iBeta long-term persisted *in vivo* (30 days for TKO vs 10±6 days for MHC-I$^{-/-}$) and properly maintained their functionality as confirmed by measuring of plasma human c-peptide levels.
Conclusions: We proposed genetic manipulation of the NK activating ligands as next-generation strategy to make grafts invisible to NK cells, offering new perspectives for using clinical-grade stem cell pancreatic derivatives as cell therapy for T1D treatment.



(A) Representative FACS plots of peripheral blood cells from hIL-15 NOG mice after 12 days from NK injection. Cells were stained with anti-hCD56 and anti-hCD16. **(B)** Relative frequencies of hCD56^{+} NK cells into humanized hIL-15 NOG mice (n=5) compared with mice that did not receive human NK cells (n=3). Data are expressed as mean ± SD. **(C)** Representative images taken at different timepoints by IVIS of transplanted mice humanized with donor-derived NK cells, and **(D)** of the control group mice that did not receive NK cells. **(E)** Fold decrease of total emission expressed as photons per second from WT, MHC-I$^{-/-}$ and T-KO iBeta and **(F)** from MHC-I$^{-/-}$ graft in mice injected or not with human NK cells. Data are expressed as mean ± SD. N = 9. * $p < 0.01$, ** $p < 0.001$.

LOS2_3 ARE THERE ANY BENEFITS OF PROLONGED HYPOTHERMIC OXYGENATED PERFUSION (HOPE)? – RESULTS FROM A NATIONAL RETROSPECTIVE STUDY

Riccardo De Carlis[*1], **Raffaele Cerchione[1], Andrea Lauterio[1], Andrea Schlegel[2], Enrico Gringeri[3], Damiano Patrono[4], Stefania Camagni[5], Daniele Dondossola[6], Davide Ghinolfi[7], Davide Bernasconi[8], Maria Grazia Valsecchi[8], Leonardo Centonze[1], Umberto Baccarani[9], Matteo Cescon[10], Enzo Andorno[11], Vincenzo Mazzaferro[12], Salvatore Gruttadauria[13], Fabrizio Di Benedetto[14], Paolo De Simone[7], Lucio Caccamo[6], Michele Colledan[5], Renato Romagnoli[4], Umberto Cillo[3], Luciano De Carlis[1]**

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Background: In recent studies, hypothermic oxygenated perfusion (HOPE) was found beneficial in extending liver preservation. However, it remains uncertain whether prolonged preservation with HOPE is equally beneficial for all liver types. We, therefore, carried out a retrospective national study to investigate the advantages of this practice and whether livers with different risk profiles are equally eligible for prolonged HOPE.
Methods: We sent out a preliminary survey to all the Italian centres to access their eligibility. Then, we collected all consecutive liver transplants between 2015 and 2023 preserved with HOPE for ≥ 4h. The impact of risk profiles and preservation times on the transplant outcomes was assessed with both univariate and multivariate regression models.
Results: Twelve of 21 (57%) transplant centres were included and contributed 181 cases with a median preservation time of 6h (static cold storage, SCS: 4.4h, HOPE: 5h). Fifty-four cases (29.8%) were from donation after circulatory death, and the median donor risk index (DRI) was 2.6 (IQR: 2.23–3.09). One-year patient and graft survivals were 89.6% and 89.1%, respectively. The incidence of early allograft dysfunction was 53%, acute kidney injury (AKI) was 32%, and biliary complications were 23.2% (10.5% anastomotic and 3.9% non-anastomotic strictures, 4.4% leaks, 4.4% mixed cases). No significant differences in transplant outcomes were observed according to different risk profiles (DRI, Eurotransplant definition for marginal grafts, balance of risk score). SCS was longer due to the distance between donor and recipient hospital ($p<0.001$). HOPE duration was independent of SCS (Spearman correlation: -0.069). HOPE duration was associated with a lower risk of AKI in both univariate and multivariate models (OR: 0.714 [95%IC: 0.532-0.958], p=0.025). The best cut-off, calculated with the receiver-operating curve analysis for HOPE duration in association with AKI, was 5.25h.
Conclusions: Prolonged HOPE is widely used in Italy to improve transplant logistics and provides good results also with marginal grafts. Prolonging HOPE over 5.25h is associated with a lower risk of posttransplant AKI. These results provide further evidence of the metabolic role of this technology and promote the use of HOPE in preventing posttransplant complications.

LOS2_4 OXYGENATED HYPOTHERMIC MACHINE PERFUSION OF OLDER DCD KIDNEYS REDUCES MITOCHONDRIAL DAMAGE-ASSOCIATED MOLECULAR PATTERNS RELEASE IN PERFUSATE

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Background: Oxygenation during hypothermic machine perfusion ($HMPO_2$) of the kidney can reduce mitochondrial damage during organ preservation and consequently limit ischaemia reperfusion injury at time of transplant. The COPE COMPARE trial showed that $HMPO_2$ of older (>50) kidneys donated after circulatory death (DCD) is safe, reduces severe post-transplant complications and improves graft survival compared to non-oxygenated hypothermic machine perfusion (HMP) (Jochmans et al, 2020). Using perfusate samples collected in the COMPARE trial, the present study aims to assess whether $HMPO_2$ reduces the release of mitochondrial damage-associated molecular patterns (mitoDAMPS) into the perfusate compared to standard HMP.
Methods: Perfusate samples from the COMPARE trial collected at the beginning (P1) and end (P3) of the cold perfusion were selected from paired kidneys (i.e., one kidney of a pair received HMP and the other $HMPO_2$) (n=20 donors). Perfusate levels of typical mitoDAMPs including cardiolipin, succinate and TFAM (mitochondrial transcription factor A) were measured by fluorimetric, colorimetric and untargeted proteomics analysis, respectively. Perfusate levels of cell-free DNA and cell-free mitochondrial DNA are currently analysed by PCR.
Results: Perfusate cardiolipin levels were significantly lower in the $HMPO_2$ group (p=0.0426, linear regression analysis, Figure 1) and tended to increase in both groups of MP with longer preservation times. Similarly, succinate levels were lower in the $HMPO_2$ group compared to the end of HMP (p=0.005, Kruskal-Wallis with Dunn's multiple comparisons test). No TFAM could be detected in the perfusate samples.
Conclusions: Our results suggest that the release of mitoDAMPS is reduced in $HMPO_2$, confirming findings from previous animal studies that the addition of oxygen during HMP may protect mitochondria, which is essential for tissue recovery from IRI. Accumulating clinical evidence suggest that increased DAMPs levels in perfusate associate with poorer outcomes post-transplant. The reduced levels of mitoDAMPs observed in this study underpin the clinical benefit observed of $HMPO_2$ preserved kidneys in clinical transplantation and make markers of mitochondrial health a useful tool in assessing organ injury and recovery.

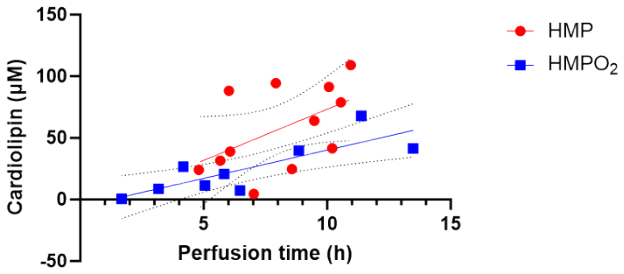

Figure 1. Linear regression analysis of perfusate cardiolipin levels (µM) vs perfusion time (h).

LOS2_5 COST-EFFECTIVENESS OF DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION VERSUS STATIC COLD STORAGE IN DCD LIVER TRANSPLANTATION

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Background: End-ischemic dual hypothermic oxygenated machine perfusion (DHOPE) of donor livers protects against ischemia-reperfusion related complications, such as post-transplant cholangiopathy, post-reperfusion syndrome, and early allograft dysfunction. Data on cost-effectivity, however, are lacking. We performed an economic evaluation of DHOPE versus static cold storage (SCS) alone, based on a multicenter randomized controlled trial in donation after circulatory death (DCD) liver transplantation (DHOPE-DCD trial).
Methods: Data of patients enrolled in the Netherlands were included in this study. Direct medical costs of the transplant procedure, hospital stay, diagnostics, and interventions, including all out-patients treatments up to one year post-transplant, were included in the analysis. Deceased patients and patients requiring re-transplantation were included in the mean cost per year of graft survival. The total cost for machine perfusion was calculated for three different scenarios: 1) costs for machine perfusion, including machine, disposables, and fluids; 2) costs for machine perfusion plus costs for personnel; 3) scenario 2 plus depreciation expenses for a dedicated organ perfusion room.
Results: A total of 118 patients were included; 58 received a liver after SCS and 60 received a liver after DHOPE. Mean total cost per patient up to one year post-transplant was €121.930 for the SCS group and €110.794 in the DHOPE group (including costs for DHOPE). When costs were separated in domains, a cost reduction was noted in each domain, but was most pronounced for intensive care treatment (-26.4%), non-surgical interventions (-22.2%), hospital stay (-17,1%), and out-patient treatments (-16.7%). In cost scenario 1, DHOPE was cost-effective after only one procedure. In cost scenarios 2 and 3, DHOPE was cost-effective after 38 and 45 procedures/year, respectively.
Conclusions: DHOPE in DCD liver transplantation is cost-effective and reduces total medical costs up to one year post-transplant, compared to SCS.

LOS2_6 SINGLE LOBE LUNG TRANSPLANTATION AFTER STEM CELL TRANSPLANTATION FROM THE SAME LIVING DONOR: A RISK WORTH TAKING

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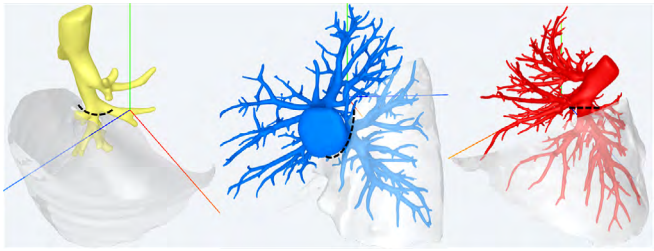
Background: Currently, living donor (LD) lung transplantation (LT) represents an extraordinary procedure in Western countries, where the access to deceased donor LT is safely improving. Irreversible pulmonary complications of hematopoietic stem cell transplantation (HSTC) may be an indication for LT. The availability of a lung graft from the same LD as for HSCT may provide immunological advantages, which may justify the risks of living donation.
Methods: We report a successful single lobe LT from the same LD as for HSCT. This is the first LD LT in our country and, to our knowledge, an almost unique case in Europe.
Results: A 4.2-year-old boy underwent haploidentical HSCT from his father due to thalassemia major, and consequently developed end-stage bronchiolitis obliterans syndrome, requiring LT. For the purpose of transplant tolerance, as a possible effect of full donor chimerism, single lobe LT from the patient's father appeared an appropriate and acceptable option. In January 2023, at age 5.8, the child underwent right LT with his father's right lower lobe. The estimated forced vital capacity (FVC) of the graft (1.17 l) was 192% of the predicted FVC of the recipient's right lung (0.61 l). Graft volume (622 cm^3) was 74% of the recipient's hemithorax (845 cm^3). Intraoperative veno-arterial-venous extracorporeal membrane oxygenation support was used. The graft pedicles were the result of a donor-friendly cutting line (figure): 8-shaped bronchial and venous stumps were anastomosed to the recipient's main bronchus and upper vein, respectively; the arterial stump was anastomosed to the recipient's right artery. The patient was extubated on postoperative day (POD) 9, and discharged on POD 35. Immunosuppression with low-dose tacrolimus and steroids was tapered till suspension. The child's lung function progressively improved, his FVC (0.99 l, 83% of predicted) now approaching the estimated graft FVC. No complications were observed in the donor.

Conclusions: The postulated immunological benefit, conferred by full donor chimerism, was deemed to exceed the risks for the LD, the high complexity of graft implantation, and the possible disadvantage of single compared to bilateral LT. Optimal size matching, meticulous surgical planning, and a multidisciplinary approach contributed to the success of this demanding strategy.



LOS2_7 REPEATED DOSE OF MESENCHYMAL STROMAL CELLS MITIGATED ASPIRATION-INDUCED LUNG INJURY AND PRIMARY GRAFT DYSFUNCTION IN A PORCINE TRANSPLANTATION MODEL

Franziska Olm[*1;2;3], Dag Edström[1;3;4], Margareta Mittendorfer[1;2;3], Haider Ghaidan[1;2;3], Anna Niroomand[1;3;5], Gabriel Hirdman[1;3], Embla Bodén[1;3], Martin Stenlo[1;3;4], Leif Pierre[1;2;3], Snejana Hyllen[3;4], Sandra Lindstedt[1;2;6]

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Background: Lung transplantation (LTx) is the primary treatment for end-stage pulmonary disease but faces challenges due to donor lung scarcity and low survival rates Lung injury from aspiration often leads to primary graft dysfunction (PGD), contributing to early mortality. This prompts an urgent need to restore donor lungs and reduce post-LTx mortality. We hypothesized that early passage mesenchymal stromal cells (MSCs) administered during ex vivo lung perfusion (EVLP) and after LTx could regenerate damaged lungs and reduce PGD incidence.
Methods: Pigs (mean weight 45 kg) were randomized into three treatment groups (n=6): Single EVLP dose, repeated dose (during EVLP and after LTx), and placebo (no MSC treatment). Acidic gastric contents were instilled in donor animals to induce lung injury over 6 hours. Lungs were harvested and subjected to 4-hour EVLP with respective treatments. The left lung was then transplanted into a recipient pig which was followed and closely monitored over 3 days. A right pneumonectomy was performed to evaluate the transplanted lung in isolation for the last four hours and PGD grades were determined in all recipients based on chest x-rays together with blood gases at 72 hours.
Results: Donor lung injury met the Berlin definition of ARDS with significantly decreased lung function. Histopathological assessment confirmed alveolar wall thickening, immune infiltration, and edema. The individuals treated with repeated doses of MSCs showed improved lung function together with improved histopathology assessed through lung injury scoring, which was also reflected in the incidence of PGD. At the 72-hour mark after LTx, most animals in the single dose and placebo groups exhibited PGD grade 2-3, whereas the repeated dose animals showed no signs of PGD.
Conclusions: A repeated dosage of early passage MSCs offers a promising therapeutic option to restore lung function in rejected aspiration-injured donor lungs and reduce PGD incidence post-transplantation.

LOS2_8 COMPLEMENT REGULATORY PROTEIN EXPRESSION DURING HYPOXIA-REOXYGENATION IN KIDNEY TISSUES

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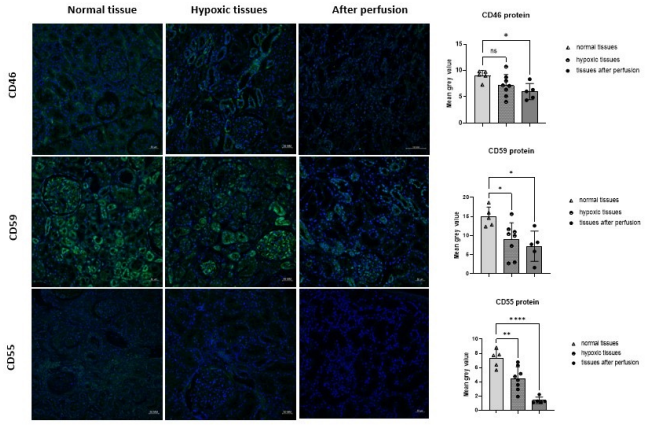
Background and aims: Ischemia in combination with reperfusion leads to complement activation during kidney transplantation resulting in tissue damage. The kidney has a capacity to protect itself from complement activation through cellular expression of complement regulatory proteins. We aimed to investigate whether hypoxia and reoxygenation alter complement regulatory protein expression (CD46, CD59 and CD55) in kidney tissues.
Methods: 5 formalin-fixed, paraffin embedded samples from unaffected poles of tumour nephrectomy were cut into 5-µm sections, then processed for immunofluorescence (IF) staining were used as a control group. 8 specimens after cold ischemic time (11-27h) and 5 post-perfusion samples (4-7h) were examined to determine CD46, CD59 and CD55 proteins in tubules. The signal intensity was quantified by ImageJ.
Results: Decreased IF staining of CD46 was observed in tubules of post-perfusion samples (p=0.0249). There was basal and cytoplasmic staining for CD46 in normal kidney samples, whereas there was weaker staining of CD46 protein on basolateral membrane during hypoxia and reoxygenation. A significant reduction of the IF signal of CD59 was seen in hypoxic and post-perfusion tissues (p=0.033, p=0.0134 respectively). A decrease of CD55 protein staining was observed in tubules in both conditions (p=0.0035, p=0.0001 respectively).
Conclusion: This finding suggests that hypoxia and reoxygenation significantly decrease expression of CD59 and CD55, and reoxygenation causes a significant decrease of IF signals of CD46 in tubules. This data may explain the high susceptibility of proximal tubular cells to ischemia-reperfusion injury during kidney transplantation. Altered expression of complement regulators within tubular epithelium may be a crucial factor permitting complement activation.



LBOS1_1 RESULTS OF THE NEW ALLOCATION RULES IN ITALY: THE ROAD TOWARD A MORE EQUITABLE ALLOCATION

Cristiano Amarelli[*1], **Luciano Potena[2], Andrea Lechiancole[3], Francesca Puoti[4], Lucia Masiero[4], Silvia Testa[4], Stefania Graziella Magrì[4], Alessandra Oliveti[4], Massimo Cardillo[4]**

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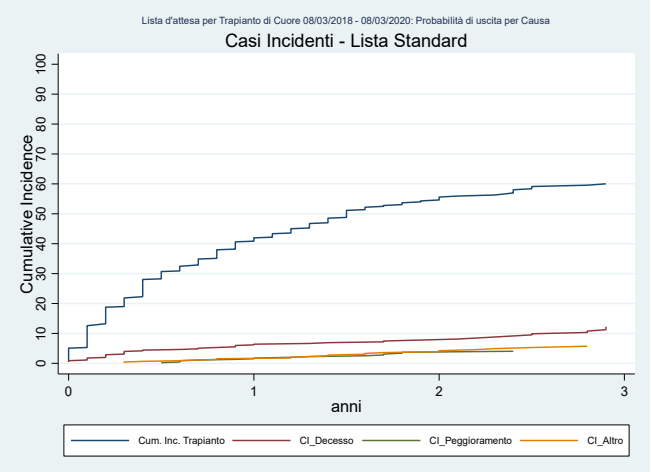
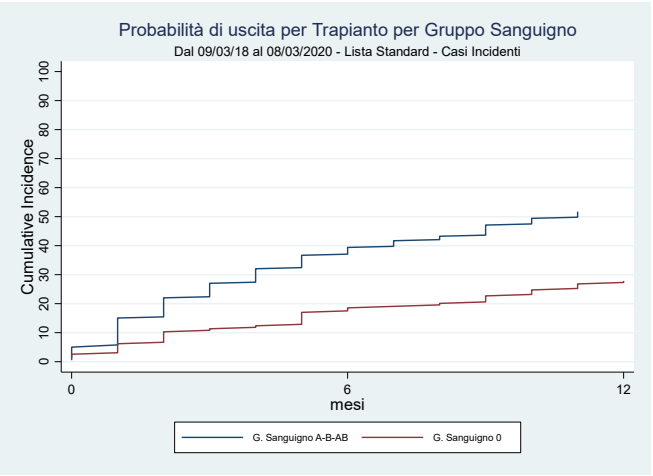
Background: Following a progressive increase in the requests for exemption in the access to the High Urgency (HU) Program for heart transplantation (HT), National Transplant Center found necessary to revise the criteria to apply for HU. Based on the new rules, active since 9 March 2020, two tiers of urgency are defined: national (1) and macro-area (2). Herein we compare the competing outcomes in patients listed before and after adopting the new criteria.
Methods: This analysis includes patients listed during the two years preceding the adoption of the new protocol (9 March 2018- 8 March 2020) and the two years after (9 March 2020 to 8 March 2022). The probability of transplant, death, improvement, and delisting were assessed on the newly listed patients. Pathophysiologic phenotypes and blood group impact on the waiting time were also analyzed.
Results: During the second period, the number of patients listed in High Urgency decreased from 26.6% to 15.2%, with a growing number of Urgent listings (19.1%). The probability of transplants at 180d and d365 at competing outcome analysis differed significantly during the second period (29.6% vs 35,4% p<0,001 and 41.3 vs 46% p=0,002). The number of listings with an elective urgency remained similar (65,7 vs 67:3%). Despite the COVID pandemic, the number of transplants during the second period was higher without a significant increase in waitlist mortality (8.5% vs 6%), with fewer patients remaining listed and fewer delisting due to worsening. As secondary endpoints, the protocol achieved a rise of transplants in Group 0 recipients and traditionally underserved populations like congenital adult recipients.
Conclusions: The new allocation system achieved an increased number of timely transplantations, reducing some of the inequalities of the allocation (i.e., Group 0). Despite the improvements achieved, the allocation system must be further trimmed to proactively capture patients with projected negative trajectories, address inequalities and warranting an equitable timely transplant.

09/03/18 – 08/03/2020

Outcome	Num	Percent
TRANSPLANT	187	41,3%
DEATH	27	6,0%
WORSENING	6	1,3%
DELISTING	7	1,5%
IN LIST	226	49,9%
Total	453	100,0%

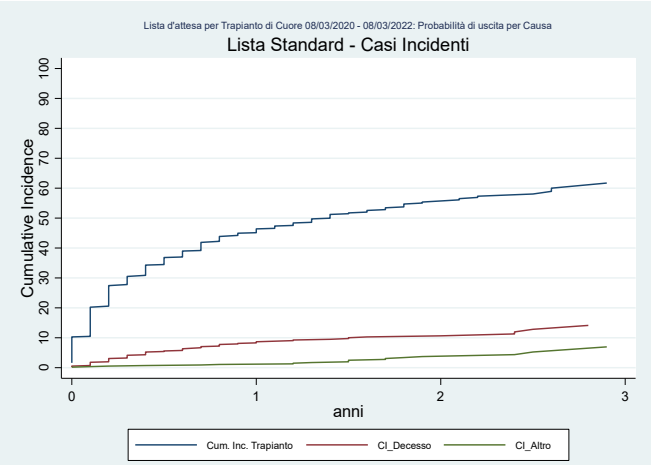


09/03/2018 - 08/03/2020	Probabilità di uscita di lista per:								
	TRAPIANTO			DECESSO			PEGGIORAMENTO		
Eventi Competitivi:	Decesso, Peggioramento e Cancellazione			Trapianto, Peggioramento e Cancellazione			Trapianto, Decesso e Cancellazione		
	%CIF	% [95% Conf. Int.]		%CIF	% [95% Conf. Int.]		%CIF	% [95% Conf. Int.]	
6 mesi	29,6%	25,4%	33,8%	4,4%	2,8%	6,6%	.	.	.
1 anno	41,3%	36,7%	45,8%	6,0%	4,0%	8,4%	1,3%	0,6%	2,7%

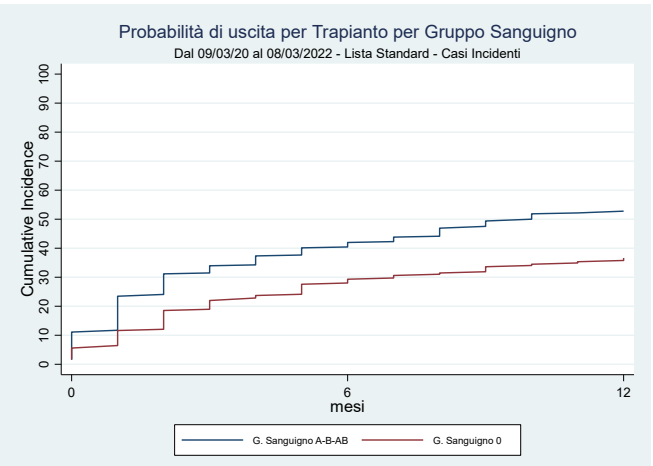


09/03/20 – 08/03/2022

Outcome	Num	Percent
TRANSPLANT	256	46,0%
DEATH	47	8,5%
WORSENING	4	0,7%
DELISTING	6	1,1%
IN LIST	243	43,7%
Total	556	100,0%



09/03/2020 - 08/03/2022	Probabilità di uscita di lista per:								
	TRAPIANTO			DECESSO			PEGGIORAMENTO		
Eventi Competitivi:	Decesso, Peggioramento e Cancellazione			Trapianto, Peggioramento e Cancellazione			Trapianto, Decesso e Cancellazione		
	%CIF	% [95% Conf. Int.]		%CIF	% [95% Conf. Int.]		%CIF	% [95% Conf. Int.]	
6 mesi	35,4%	31,4%	39,4%	5,4%	3,7%	7,5%	0,5%	0,2%	1,5%
1 anno	46,0%	41,8%	50,1%	8,5%	6,4%	11,0%	0,7%	0,3%	1,8%



LBOS1_2 GLOBAL DATA FROM THE RETROSPECTIVE/ PROSEPCTIVE IMPROVEMENT LIVER TRANSPLANT STUDY: DIFFERENCES AMONG WORLD AREAS

Alfonso Avolio*[1;2], Marco Pascale[1], Patrizia Burra[3], Liu Wei[2], Martin de Santibanes[4], Perfecto Valero Arkaitz[5], Mikel Gastaca[6], Zyiong Guo[7], Quirino Lai[8], Paulo Martins[9], Gabriel Oniscu[10], Cristiano Quintini[11], Wojciech Polak[12], Gonzalo Sapisochin[13], Julio Wiederkehr[14], Pia Clara Pafundi[15], Tina Pasciuto[15], Tommaso Partipilo[2], Roberta Angelico[16], Giammauro Berardi[17], Riccardo De Carlis[18], Jacopo Lanari[19], Monica Rizzo[20], Fabio Melandro[21], Daniele Ferraro[22], Paola Violi[23], Marco Bongini[24], Stefano Di Sandro[25], Roberta Rossi[26], Stefania Camagni[27], Riccardo Pravisani[28], Angela Licciardo[29], Andrea Della Penna[30], Jan Paul Gundlach[31], Marta García-Guix[32], Emilia Kruk[33], Jai Prasadh[34], Andres Murcia[35], Jimmy Walker Uno[4], Maíra Godoy[36], Ilka Boin[37], Takashi Ito[38], Songming Li[39], Ashwin Rammohan[40], Jagadeesh Krishnamurthy[41], Athaya Vorasittha[42], Louise Barbier[43], Carlo Pulitano[44], Marcos Perini[45], Vatche Agopian[46]

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Background: The IMPROVEMENT project (ClinicalTrial.gov NCT05289609) was designed to develop predictive models of 90-day/1-yr allograft failure after liver transplant (LT). The study was draw up by a steering committee from the 5 continents. Yet, the study collects 3,882 adult LTs. There are a retrospective cohort (at least 40 centers) and a prospective one (40 centers).
Methods: The study design includes 3 LT categories (living donors; DCDs and high-risk DBDs; standard DBDs). Since the prospective collection is ongoing, we focused on the retrospective data (3,051 LT; 2017-2020). Each Center was committed to enroll a fixed number of LT to minimize Center-volume bias.
We stratified the cases in 5 geographical areas: Italy (N=1,387, main study group); Europe except-Italy (N=735); Asia-Oceania (N=390); North America (N=296); South America (N=243); Fig. A. Cases belonging to the retrospective cohort were transplanted in 44 LT centers. Twenty-two centers had a high-volume (>65 LTs/yr); 22 centers, intermediate-volume (≤65 LTs/yr).
Results: Results were summarized (Fig. B, panels 1-20). Italy and Asia presented the larger adoption of perfusion machines (MP), while in Europe and in the North America there were fewer. DCDs were prevalent in Asia and in Europe. Living donors were mainly performed in Asia, while were less in the Western areas and even lower in Italy. Italy showed the highest prevalence of hepatocellular carcinoma (HCC); in the rest of the world, there was a dichotomic distribution (higher percentages in Asia and in Europe and reduced prevalence in the Americas). Further stratifications were performed (severity of primary disease, age of donor and recipients, comorbidities and donor-2-recipient match).
Conclusions: The epidemiological analysis of IMPROVEMENT data depicts a screenshot of global liver transplant activity, never done before. Differences are due to cultural and logistic issues. The prospective data (ongoing) will provide more accurate information.

Fig. A **The IMPROVEMENT study – RETROSPECTIVE COHORT - Map of 44 Centers** (updated July 26th, 2023)

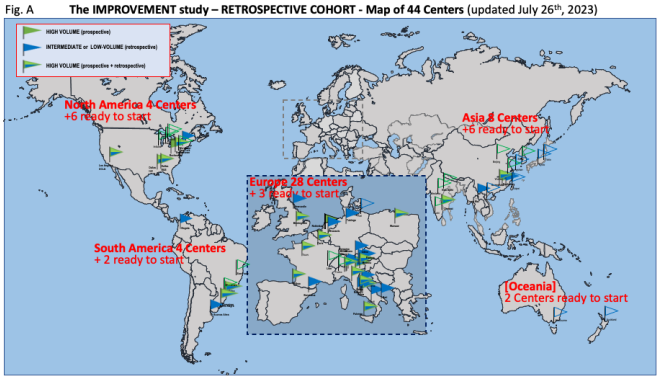
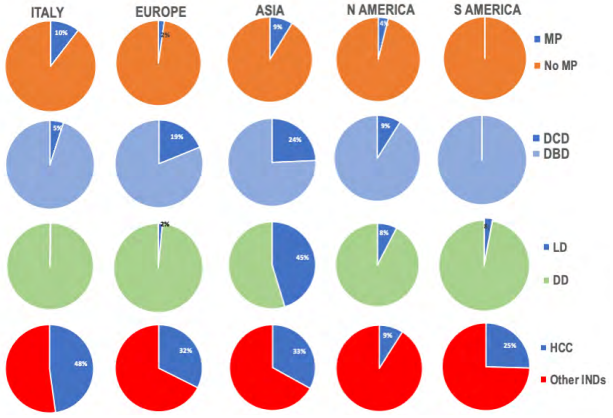


Fig. B



LBOS1_3 EXPLAINABLE MACHINE LEARNING MODELS FOR MULTIPLE OUTCOME PREDICTION AFTER RENAL TRANSPLANTATION

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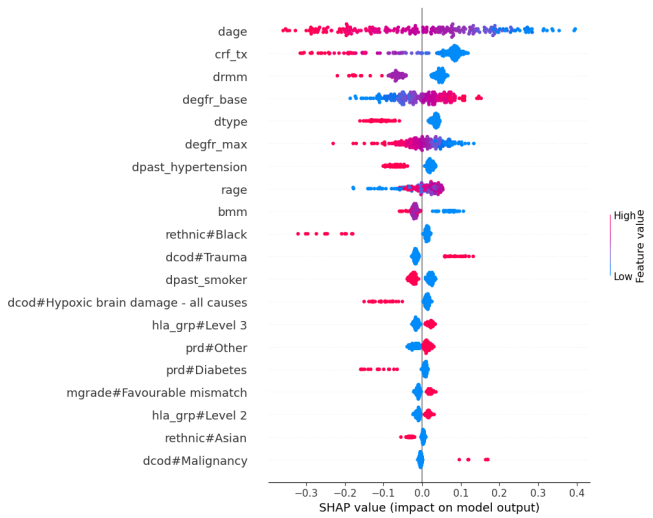
Background: The decision to accept an organ offer for transplant, or wait for something potentially better in the future, can be challenging. Clinical decision support tools predicting transplant outcomes from the time of offer are not readily available but might help in clinical decision making.
Methods: Using 20 years of recipient, donor, and transplant data available at the time of organ offer, along with associated outcomes from the UK Transplant Registry, we trained and validated single- and multiple-risk machine learning models to predict graft and patient survival following renal transplantation. Feature selection identified factors more important than random noise. We used *post-hoc* interpretability techniques to add clinical explainability to these models.
Results: In a single risk setting, neural networks provide comparable performance to the Cox proportional hazards model, with AUCROC of 0.71 and 0.81 for prediction of 10-year graft and patient survival respectively. Predictive performance improves with the time post-transplant, with the most accurate predictions seen at 10 years (*table 1*). Using SHAP as a *post-hoc* interpretability method, we found that recipient and donor age, calculated reaction frequency (CRF), cause of primary renal disease, donor eGFR, donor type and the number of HLA DR mismatches were the most important predictors for transplant outcome prediction, in keeping with the published literature (*figure 1*). We also extended the neural network approach to multiple competing outcome predictions, maintaining consistent performance and interpretability.
Conclusions: Neural networks perform well for the prediction of long-term outcomes following renal transplantation, and the use of SHAP values allows assessment of the most prominent predictive features for the model as a whole and for individual predictions. Use of interpretable models will improve clinician's trust over more traditional "black-box" methods, meaning that such predictions may be useful in offer decision-making and informed consent.

Table 1 – Performance of single-risk models for graft and patient survival at years 1, 5 and 10 post-transplant.

	Random forest		Cox PH model		Neural network	
	AUCROC	F1-Score	AUCROC	F1-Score	AUCROC	F1-Score
Graft survival						
Year 1	0.61	0.14	0.61	0.15	**0.62**	**0.18**
Year 5	0.60	0.35	**0.63**	**0.36**	**0.63**	**0.36**
Year 10	0.68	0.62	0.70	**0.63**	**0.71**	0.61
Patient Survival						
Year 1	**0.74**	**0.15**	0.73	0.14	**0.74**	0.12
Year 5	0.76	0.39	**0.77**	**0.41**	0.76	0.39
Year 10	0.80	**0.66**	**0.81**	**0.66**	**0.81**	**0.66**

Figure 1 – SHAP-based feature importance for 10-year graft survival using a neural network model.



LBOS1_5 POSOLEUCEL ASSOCIATED WITH REDUCTION OF BK VIREMIA AND INCREASES IN BK-REACTIVE T CELLS IN A PHASE 2 TRIAL

Anil Chandraker*[1], Anil Regmi[2], Reginald Gohh[3], Akhil Sharma[4], E. Steve Woodle[5], Mohammed Ansari[6], Vinay Nair[7], Ling-Xin Chen[8], Tarek Alhamad[9], Silas Norman[10], Francesca Cardarelli[11], Julie MA[11], Sarah Gilmore[11], Spyridoula Vasileiou[12], David Wojciechowski[13]

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Background: Kidney transplant (KT) recipients with BK virus infection are at risk of nephropathy and graft loss and are without treatment options. Posoleucel (PSL) is an off-the-shelf multivirus-specific T cell therapy targeting BKV.
Methods: In this phase 2 double-blind study (NCT04605484), KT patients with BK viremia were randomized 1:1:1 to receive PSL cells wkly for 3 wks then every 14 (PSL1) or 28 days (PSL2), or placebo (PBO) for 12 wks. Primary objective was safety; secondary was plasma BK viral load (VL) reduction. Functional BKV immune responses (infused and endogenous) were evaluated by IFNγ ELISpot analyses and the contribution of PSL to antiviral immunity was evaluated by T cell receptor (TCR) β immunosequencing. TCR sequences unique to PSL were identified computationally and used to track persistence.
Results: Baseline (BL) characteristics among 61 patients were similar across groups. No deaths, GVHD, or cytokine release syndrome were observed. Three PSL patients had graft rejection, but none related to treatment: 1 patient had a prior history of rejection, 1 had renal TB, and 1 had rejection 68 days after last PSL dose. Median eGFR was stable in all groups. The table shows VL changes in 52 patients with stable immunosuppression (IS) in the 30 days before randomization who completed the study demonstrating superior antiviral effects in both PSL groups vs PBO. At BL the majority of patients with high BK VL did not have pre-existing BK-specific T cell immunity. Recipients of PSL vs PBO had increases in BKV IFNγ+ T cells against PSL-target antigens at wks 14 and 24. Upregulation of endogenous BK-directed T cell activity against non PSL-target antigens was seen following PSL infusion. In PSL1 patients, the frequency of functional cells was greater and their overall BKV IFNγ+ T cell responses increased over 6-month study period, coincident with VL reduction. The presence and persistence of PSL was confirmed by TCRvβ deep sequencing out to 12 wks post dosing, with higher frequencies of PSL clones in patients with high VLs.
Conclusions: PSL was generally safe and well tolerated. Clinically meaningful BK VL reductions and increases in BK-reactive T cells occurred in PSL patients. PSL was detected during dosing and for up to 12 wks after infusion period, which is the first demonstration of PSL persistence in KT patients.

Results at week 24 in patients with stable IS* before randomization

Endpoint	PSL1 N=20	PSL2 N=18†	PBO N=14‡
Pts w/ BK VL decreased by ≥1 $\log_{10}$ BKV DNA copies/mL vs baseline, n (%)	10 (50)	5 (28)	2 (14)
BK VL reduction from baseline, median $\log_{10}$ BKV DNA copies/mL (min, max)	-0.9 (-2.1, 0.1)	-0.45 (-1.8, 0.5)	-0.15 (-2.1, 0.3)
BK VL ≥50% reduction, n (%)	17 (85)#	10 (56)	6 (43)
Change in eGFR, median mL/min/1.73 m^2 (min, max)	-2.5 (-11, 7)	0 (-16, 20)	0 (-21, 9)

*<50% reduction in CNI, mTOR, MMF/MPA, or azathioprine within 30 (+/-2) days of randomization.
†2 patients were lost to follow-up and 2 had pre-randomization IS reduction.
‡1 patient was lost to follow-up and 4 had pre-randomization IS reduction.
#p<0.05 vs PBO.

LBOS1_6 BUILDING AN EXPERT VALIDATED SCORECARD TO MEASURE TRANSPLANT SYSTEM PERFORMANCE

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Background: Measuring health system performance across countries may help to identify areas for improvement and guide national reform efforts. Here we present a set of expert validated indicators intended to form the basis of a scorecard for measuring the performance of national organ donation and transplant systems.
Methods: The indicators were collected and validated in five steps: (1) We extracted a total of 104 possible quality indicators from the websites and reports of national transplant organizations and other key documents (such as the Global Observatory on Donation and Transplantation). (2) We divided these according to the categories of prevention, donation, transplantation, follow-up, responsiveness, equity, and efficiency; based on a recently published framework for evaluating national organ donation and transplantation programs (Johnston-Webber et al; Transpl Int; 2023). (3) We convened a multinational, multiprofessional expert group consisting of a total of 10 experts including a patient representative. This group were initially asked to rank each indicator on a scale from 0 (not important) to 10 (very important). (4) We held a series of virtual meetings with the group of experts to discuss the outcomes of the ranking exercise in more detail and to further inform the final choice of indicators. (5) The findings from the ranking exercise and the virtual meetings were synthesized into a.) general lessons for building a national transplant system scorecard and b.) a shortlist of indicators that can be used to build a national transplant system scorecard.
Results: A transplant system scorecard needs to reflect different organ systems, be multidimensional, clear in its definitions and appropriately adjusted for demographic differences to make fair comparisons. We present a total of 11 possible indicators with strengths, limitations, and alternatives (Table 1).
Conclusions: This study presents a set of validated indicators that will be used to build a scorecard assessing national organ donation and transplant system performance in Europe.

Table 1: Indicators and Alternatives to build a National Scorecard for Transplant System Performance

Category	Indicator	Ranking	Strengths	Limitations	Alternative
Prevention	Percentage of patients screened for high blood pressure by a health professional within the last year	8.9	- Relevance for prevention of organ failure - Data availability via Eurostat	- Does not cover actions taken after screening - Limited attributability to transplant institutions	% of patients detected with high blood pressure that received an intervention within three months
Prevention	Total No. of patients on waiting lists for organ transplantation per year	8.8	- Data availability via Newsletter Transplant - Quick insight into capability of transplant system to put patients on waiting lists	- Limited comparability across systems - Prone to 'gaming' - Potential perverse incentive	- Time to first transplant - No. patients that died while listed - Ever active no. of patients on waiting list
Donation	Percentage of living kidney donors who develop end-stage kidney disease	8.9	Proxy indicator for quality of management	- Limited applicability in systems without living donation - Depends on duration of donor follow up	/
Donation	Donation rates (DBD/DCD/LD) pmp	8.6	- Data availability via GODT - Broad relevant indicator	- Does not cover quality of donation - Limited comparability across different systems	Donation rates per no. of (hospital) deaths
Transplantation	Total transplantation rate (pmp)	8.7	Data availability via GODT	Does not cover quality of care	Graft survival
Follow-Up	Total 5-year graft survival	8.4	Captures transplant quality	Short intervals have limited meaning for patients and incentivize overimmunosuppression	Total 10-year graft survival
Follow-Up	Number of transplant patients undergoing re-operation in the first 1.5 days/No. of transplants	8.9	Captures transplant quality	Does not cover quality of life	- PREMs - No. of organ recipients reporting chronic pain - No. of organ recipients returning to work
Efficiency	Average Number of organs donated and transplanted per deceased donor	8.9	Captures ressource efficiency	Dependant on demographics	Adjustment for donor age and comorbidities
Efficiency	No. of transplants / expenditure on transplant system	8.9	Captures cost efficiency	Data availability	No. of transplants/Total healthcare expenditure
Responsiveness	Rate of consent to organ donation	9.0	Data availability via Newsletter Transplant	- Does not cover efforts to approach families - Limited comparability across systems	Consent to organ donation pmp
Equity	Number of organs exported to other countries	8.0	Data availability	- Contrary to goal of self-sufficience - Limited reflection of equity	- No. of surplus organs exported to other countries - Matters of equity addressed in routine reporting by NTO (yes/no)

LBOS1_7 IMPACT OF THE NEW NATIONAL REGULATION ABOUT HEART TRANSPLANT URGENCY CRITERIA ON A SINGLE-CENTRE HEART TRANSPLANT ACTIVITY

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Background: Since February 27th,2020 the national regulation about heart transplant (HTx) urgency criteria has been modified as compared to the older one started in 2016. Aim of this study was to evaluate the impact of this modification on a single-centre HTx waiting list.
Methods: Retrospective analysis on HTx waiting list patients from 2016 to February 2020 (Period1) and since February 2020 until now (Period2).
Results: One-hundred-seventy-eight patients were of Period1 (38 LVAD, 21%), while 92 patients were of Period2 (15 LVAD, 16%). Twenty-nine patients (29%, 8 LVAD, 36%) still were waiting for HTx at February 27th 2020, and constituted a third group (Period 1-2). In Period1, 43 patients were in status-1 (31%), 36 in status-2 (26%), and 60 in status-3 (43%); in Period2 13 patients were in status-1 (16%), 13 in status-2 (16%), and 57 in status-3 (69%) (p<0.001). In Period1 there were 139 Htx (78%), while in Period2 69 HTx (57%). In Period1 median time on waiting list were 82 days, and median time for HTx of 72 days, while in Period2 were 87 days and 41 days, respectively (p=0.7;p=0.036). In Period1, 34 LVAD patients underwent HTx (89%), of whom 59% in status-2, while in Period2, 8 LVAD patients underwent HTx (53%), of whom 75% in status-3 (p<0.001), with median waiting list time of 104 days and 27 days, respectively (p=0.1). About the 29 patients of Period 1-2, 13 (45) underwent HTx; median waiting list time and median time for HTx were 935 days and 554 days, respectively (p<0.001).
Conclusions: The modification of the national regulation about HTx urgency criteria determined a reduction of emergency HTx with a reduction of time to HTx.

	N	Overall, N = 270[1]	Lista 1, N = 178[1]	Lista 2, N = 92[1]	p-value[2]
Weight, kg	270	75 (64, 83)	75 (64, 82)	75 (61, 85)	0.7
Age, years	270	57 (49, 64)	57 (49, 64)	56 (47, 64)	0.5
Gender	270				0.7
Male		210 / 270 (78%)	137 / 178 (77%)	73 / 92 (79%)	
Femail		60 / 270 (22%)	41 / 178 (23%)	19 / 92 (21%)	
Blood Group	270				0.7
0		124 / 270 (46%)	79 / 178 (44%)	45 / 92 (49%)	
A		107 / 270 (40%)	70 / 178 (39%)	37 / 92 (40%)	
B		29 / 270 (11%)	22 / 178 (12%)	7 / 92 (7.6%)	
AB		10 / 270 (3.7%)	7 / 178 (3.9%)	3 / 92 (3.3%)	
LVAD	270	53 / 270 (20%)	38 / 178 (21%)	15 / 92 (16%)	0.3
Status	222				**0.001**
1		56 / 222 (25%)	43 / 139 (31%)	13 / 83 (16%)	
2		49 / 222 (22%)	36 / 139 (26%)	13 / 83 (16%)	
3		117 / 222 (53%)	60 / 139 (43%)	57 / 83 (69%)	
Unknown		48	39	9	
Removed from waiting list	270				**<0.001**
no		29 / 270 (10%)	0 / 178 (0%)	27 / 92 (29%)	
HTx		195 / 270 (72%)	139 / 178 (78%)	56 / 92 (61%)	
Removed due to improvement		4 / 270 (1.5%)	3 / 178 (1.7%)	1 / 92 (1.1%)	
Died		33 / 270 (12%)	26 / 178 (15%)	7 / 92 (7.6%)	
suspended		11 / 270 (4.1%)	10 / 178 (5.6%)	1 / 92 (1.1%)	
Waiting list duration	270	84 (20, 298)	83 (21, 310)	87 (15, 289)	0.7
Time for HTx *	270	58 (13, 214)	72 (18, 253)	41 (9, 109)	**0.036**
Died	270	33 / 270 (12%)	26 / 178 (15%)	7 / 92 (7.6%)	
HTx	270	195 / 270 (72%)	139 / 178 (78%)	56 / 92 (61%)	

[1]Median (IQR); n / N (%)
[2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test
* Only for patients undergone HTx

LBOS1_8 A DEMOGRAPHY OF OPPOSITION: A 15 YEARS ANALYSIS OF NORTH ITALY TRANSPLANT PROGRAM REGISTRY

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Background: Organ shortage has always been one of the most important issues to be addressed in organ transplantation. The denied consent to organ donation remains one of the key factors affecting the number of available organs. Numerous studies have identified targeted information campaigns as a way to increase willingness to donate by both individuals and family members. Those campaigns must be addressed and targeted according to the socio-economic environment to achieve the expected results. Despite this, in literature, studies describing the socio-economic and demographic characteristics of those who decline the consent for donation in Italy are lacking.
Methods: A retrospective study based on the North Italian Transplant Program (NITp) donation registry was performed. Age, state of origin, and residence were analyzed. Census section-level deprivation index was considered as an indicator of socioeconomic hardship and disadvantage to assess the possible association between socioeconomic status and opposition.**Results**: From January 2007 to December 2022, there were 2510 oppositions in the NIT area (represented 25.6% of the reports), 73% were in hospitals not housing a transplant center. The average age is 63 years. 503 of these (20%) were born in foreign countries, of which 65 (2.6%) in EU countries; 91 (3.6%) were resident abroad at the time of death, of which 26 (1%) in EU countries. 1054 people (42%) resided in areas at the 4th quartile of the Italian deprivation index.
Conclusions: This study describes the characteristics of those who expressed opposition to donation in the NITp area over the past 15 years. Although upon preliminary analysis, the prevalence of opposition in areas with high socio-economic deprivation and in hospitals not home to a transplant centre seems prominent. This stratification may enable policymakers to assess opportunities to promote and support organ donation and anticipate possible challenges to confidence in donation policies.

LBOS1_9 FIVE-YEAR KIDNEY FUNCTION AND OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS CONVERTING FROM TWICE-DAILY TO ONCE-DAILY TACROLIMUS

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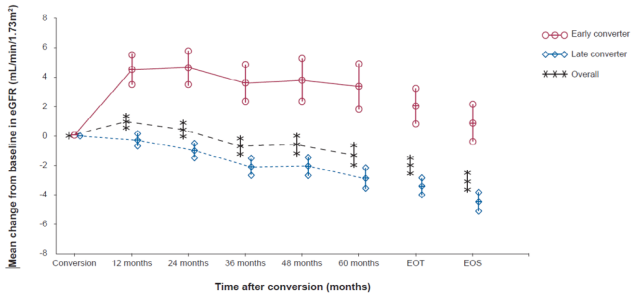
Background: CHORUS (NCT02555787) is a prospective, global, non-interventional study investigating long-term clinical outcomes in kidney transplant recipients (KTRs) who were converted from twice-daily, immediate-release tacrolimus to once-daily, prolonged-release tacrolimus (PRT; Advagraf®, Astellas Pharma Europe, Ltd.) under routine practice conditions.
Methods: The study enrolled KTRs (≥18 years, N=4389) converting to PRT based on the treating physician's judgment. KTRs were grouped by time of conversion post-transplant to early (≤6 months) converters (ECs) and late (>6 months) converters (LCs). The primary endpoint was the change in renal function (measured by estimated glomerular filtration rate, eGFR) from conversion up to 5 years. Secondary endpoints included graft and patient survival, tacrolimus dose and trough levels, emergence of donor-specific antibodies (DSA) and safety.

Results: The full analysis set (FAS) included 4028 KTRs (1060 ECs; 2968 LCs). Most patients (60.5%) were male, with a mean age of 50.9 years and a mean eGFR of 56.05 mL/min/1.73m^2 at conversion. Most ECs were converted to PRT in <3 months post-transplant, and LCs >24 months post-transplant. eGFR remained stable post-conversion in the overall FAS group, with improvement in ECs (**Figure**). At 5 years post-conversion, the mean dose of PRT was 3.95 mg/day (**Table**). At study end, 66.7% of KTRs had tacrolimus trough levels ≥5 ng/mL and >80% of KTRs had trough level coefficient of variation <35%; both were consistent throughout the study. At 5 years post-transplant, Kaplan-Meier estimate of patient survival was 92.9% for ECs and 98.5% for LCs; graft survival was 88.1% for ECs and 97.5% for LCs. Overall, 4.9% of patients who were DSA negative prior to or at conversion had DSA occurrence post-conversion. At study end, 70.8% of patients remained on PRT. Adverse events (AEs) were reported in 72.4% of enrolled patients; 19.3% had ≥1 PRT-related AE. Serious AEs (SAEs) were reported in 50.6% of patients; 10.4% had ≥1 PRT-related SAE. The discontinuation rate due to AEs was 11.8% and PRT-related AEs was 5.5%.
Conclusions: Results from this large cohort of KTRs showed renal function remained stable overall. Patient and graft survival were high at 5 years post-transplant with no unexpected safety findings, supporting the long-term use of PRT.

Figure. Mean change from baseline in renal function (eGFR)*



Number of patients

Overall	4028	3748	3421	3203	2976	2487	3941	4028
Early converter	1060	969	864	790	749	630	1032	1060
Late converter	2968	2779	2557	2413	2227	1857	2909	2968

Mean eGFR change from baseline is displayed with 95% CI.
*The eGFR values were calculated according to the Modulation Diet in Renal Disease (MDRD)-4 formula
CI, confidence interval; eGFR, estimated glomerular filtration rate; EOS, end of study; EOT, end of treatment.

Table. PRT dose, and tacrolimus trough levels (FAS)*

PRT dose and tacrolimus trough levels in FAS	Early converters (N=1060)			Late converters (N=2968)			Total (N=4028)		
PRT dosage, mg/day	n	Mean (SD)	Median (min–max)	n	Mean (SD)	Median (min–max)	n	Mean (SD)	Median (min–max)
At conversion	1060	7.01 (4.10)	6.00 (0.5–28.0)	2968	3.90 (2.44)	3.00 (0.5–25.0)	4028	4.72 (3.27)	4.00 (0.5–28.0)
60 months post-conversion	521	4.32 (2.58)	3.50 (0.5–18.0)	1591	3.84 (2.19)	3.00 (0.5–18.0)	2112	3.95 (2.30)	3.50 (0.5–18.0)
Tacrolimus trough levels, ng/mL	n	Mean (SD)	Median (Q1 Q3)	n	Mean (SD)	Median (Q1 Q3)	n	Mean (SD)	Median (Q1 Q3)
6 months prior to conversion	150	9.38 (4.75)	8.85 (6.9–11.2)	2537	6.76 (2.81)	6.30 (5.0–8.0)	2687	6.91 (3.01)	6.40 (5.0–8.2)
At conversion	1006	9.16 (3.27)	8.75 (7.0–10.7)	2958	6.56 (2.55)	6.20 (4.9–7.8)	3964	7.22 (2.98)	6.70 (5.2–8.7)
12 months post-conversion	1022	7.07 (2.36)	7.00 (5.5–8.3)	2906	5.78 (2.15)	5.50 (4.4–6.9)	3928	6.12 (2.28)	5.90 (4.7–7.3)
24 months post-conversion	913	6.58 (2.11)	6.41 (5.2–7.9)	2672	5.79 (2.14)	5.61 (4.4–7.0)	3585	5.99 (2.16)	5.90 (4.6–7.2)
36 months post-conversion	838	6.53 (2.27)	6.3 (5.2–7.5)	2563	5.76 (2.05)	5.60 (4.5–6.9)	3401	5.95 (2.14)	5.80 (4.6–7.0)
48 months post-conversion	798	6.3 (2.09)	6.1 (4.9–7.4)	2406	5.76 (2.05)	5.60 (4.4–6.9)	3204	5.89 (2.07)	5.70 (4.6–7.0)
60 months post-conversion	677	6.16 (1.97)	5.9 (4.9–7.2)	2062	5.67 (2.02)	5.50 (4.4–6.7)	2739	5.79 (2.02)	5.60 (4.5–6.9)

*The full analysis set (FAS) comprised all enrolled patients who were converted to PRT, had at least one primary endpoint assessment at baseline and 1 year after conversion or later, and did not violate the terms of the protocol.
FAS, full analysis set; IRT, immediate-release tacrolimus; PRT, prolonged-release tacrolimus; SD, standard deviation.

LBOS1_10 LONG-TERM MORTALITY OF LIVING LIVER DONORS : A SYSTEMATIC REVIEW AND META-ANALYSIS

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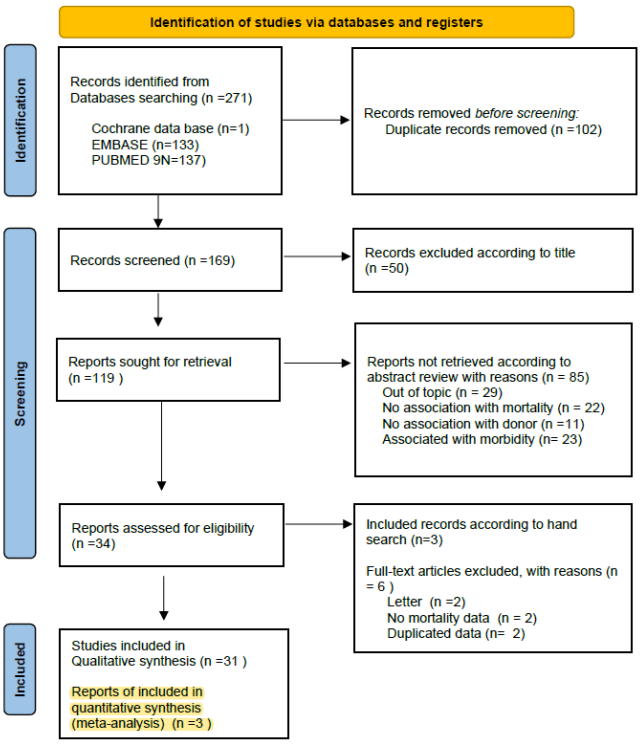
Background: Although the outcome of LDLT recipients has been developed, concerns remain about donor safety and moral issues. The safety of the living donor is the top priority when performing a living liver transplant. Several studies reported donor complications and mortality rate, but the results were short-term, mostly related the operation. Although liver donation is considered safe for healthy people, the donation has lifelong effects. Due to the short history of living liver transplantation, studies of the long-term survival of donors after living donor are lacking. At this point, the justification for living liver transplantation will be established only when there is a long-term result from donors after organ donation. This is a meta-analysis of long-term survival of LDLT donors.
Methods: We searched PubMed, EMBASE, and The Cochrane Library database for studies comparing Living liver transplantation donor with control group published between the date of database creation and June 2021. Statistical analysis was performed using Revman 5.3. We included all data from recent studies and assessed methodological quality using the risk of bias from the Non-Randomized Study of Intervention (ROBINS-I) assessment tool.
Results: Three studies met the eligibility criteria. In the included clinical study, 24,371 patients received living donor surgery. In this paper, we compiled all the data on donors' reported deaths from subsequent published papers on cause of death, including short-lived deaths that may be related to surgery performed within 90 days of donors. In a worldwide survey long-term deaths were reported, with suicide being the most common cause of death. Living donor group have been shown to have reduced long-term mortality rates than healthy group.
Conclusions: This meta-analysis suggests that liver donation is safe and feasible for living donor liver transplantation compared to non-donation people. It is also worth mentioning that regular psychological evaluations of donors by a psychologist before and after donation were mandated. To maintain the LDLT program, careful selection and surgical technique of living liver donors are important for the safety of living liver donors.



LBOS1_11 PROGNOSTIC VALUE IN KIDNEY TRANSPLANTATION OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING

Paloma Leticia Martin Moreno[*1], **Rebeca Echeverria-Chasco[2], Jose Maria Mora-Gutiérrez[1], David Cano[2], Nuria Garcia-Fernandez[1], Maria Fernandez-Seara[2]**

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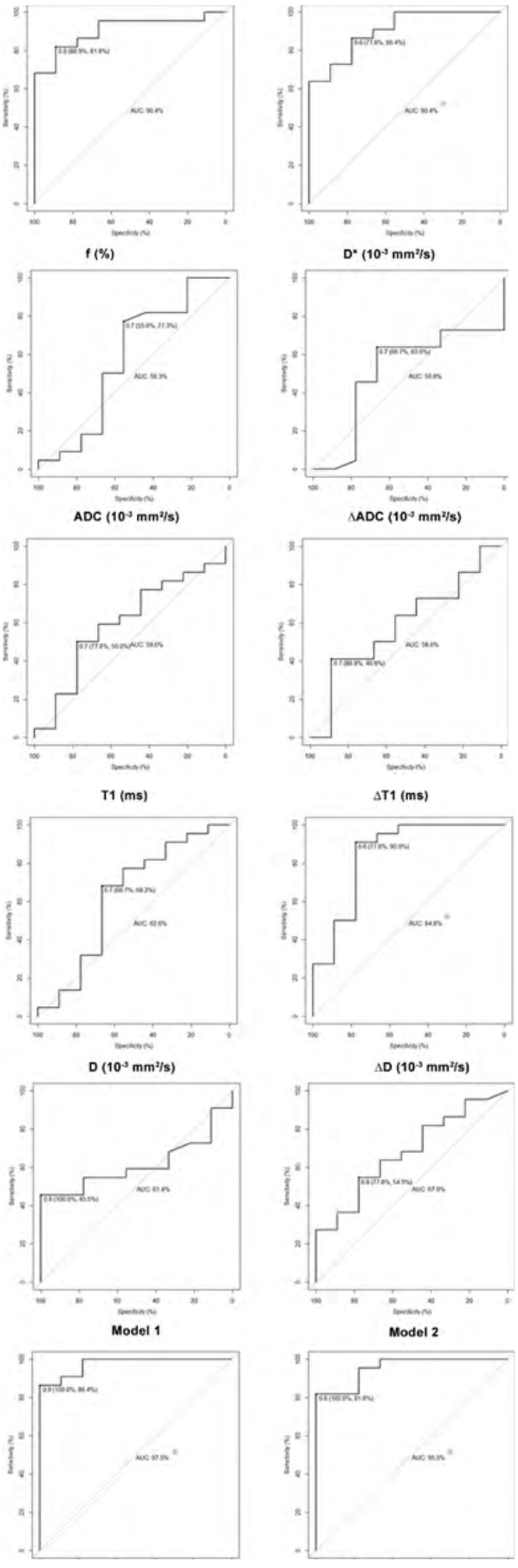
Background: Kidney transplantation is the best therapeutic option in advanced chronic kidney disease. For this reason, it is important to have markers that help to predict its evolution, in order to establish measures that prolong its survival. Multiparametric Magnetic Resonance Imaging (MRI) could safely provide these markers, as it does not require the administration of exogenous contrast. Objective: to study the prognostic utility of the parameters provided by MRI in the assessment of allograft function in a population of kidney transplant recipients.
Methods: Thirty-two kidney transplant recipients who underwent an MRI in the first week post-transplant, including perfusion (RBF), diffusion (f, D*, D, ΔD, ADC, ΔADC) and T1 mapping (T1, ΔT1) sequences, were included. Patients were divided into 2 groups according to estimated glomerular filtration rate (eGFR) measured at 3 months: inferior graft function (eGFR<45 ml/min/1.73 m2, n=10) and superior graft function (eGFR≥45 ml/min/1.73 m2, n=22). Two models were created with the cortical MRI parameters (RBF, f, D*, D, ADC and T1) and cortico-medullary differences (ΔD, ΔADC and ΔT1) and their predictive capacity for eGFR at 3 months was compared with that of the eGFR at the time the MRI was performed. Receiver-operator characteristic (ROC) curves were calculated for univariate models and multivariate models.
Results: In this study, eGFR showed the highest AUC while similar results were found for RBF. The prognostic utility of the model 1 demonstrated in the analysis of ROC curves with an area under the curve (AUC) of 0.9747 (CI: 0.92-1.00), specificity =100% and sensitivity =86%), was better than using only the eGFR (Figure 1).
Conclusions: MRI is a safe diagnostic tool with higher prognostic efficiency than eGFR for determining allograft function in the 3-month period. The use of MRI opens up as a useful tool, which might help to optimize the decision-making in the care of kidney transplant recipients and probably improve graft survival rates.

Prognostic utility of MRI for distinguishing between inferior and superior graft function: Receiver-operator characteristic (ROC) curves calculated for univariate models and multivariate models: model 1, including RBF, D, D CMD, D*, f, T1 and ΔT1 and model 2, including RBF, D, D CMD, T1 and ΔT1. Significant AUCs are marked with '*'



LBOS1_12 REDUCTION OF RENAL GRAFT FIBROSIS WITH VALGANCICLOVIR PROPHYLAXIS FOR CYTOMEGALOVIRUS COMPARED TO PREEMPTIVE THERAPY: A RANDOMIZED CONTROLLED TRIAL

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Background: Prevention of cytomegalovirus (CMV) infection including CMV indirect effects is essential in kidney transplantation. The 12-month results of OVERT Study showed less subclinical rejection and a trend toward lower incidence of acute rejection in recipients receiving valganciclovir prophylaxis compared to preemptive therapy. Here we report long-term results of OVERT Study.
Methods: This was an open-label, single-center, randomized clinical trial of valganciclovir prophylaxis vs preemptive therapy in 140 kidney transplant recipients recruited between June 2013 and May 2018. CMV-seronegative recipients with negative donors (D-R-) were excluded. Patients were randomized 1:1 to receive either valganciclovir prophylaxis for 3 months (or 6 months in D+R-) (n=70) or preemptive valganciclovir for significant CMV DNAemia detected in predefined assessments through month 24 (n=70). The primary outcome was the incidence of moderate to severe interstitial fibrosis and tubular atrophy (IFTA) in protocol biopsy at 3 years. Key secondary outcomes included acute rejection, CMV disease and DNAemia, patient and graft survival.
Results: Among the 127 patients who had a protocol biopsy specimen available at 3 years, 5 (8%) of 66 patients in the prophylaxis group and 14 (23%) of 61 patients in the preemptive group had moderate to severe IFTA (P=0.015). At 3 years the incidence of acute rejection was lower with valganciclovir prophylaxis (13% vs 36%, P=0.052). In spite of 5 (7%) additional patients with CMV DNAemia after month 12 in the prophylaxis group in contrast to none in the preemptive group (P=0.025) the cumulative incidence at 2 years remained lower with prophylaxis (51% vs 75%, P<0.001). Both regimens prevented CMV disease (6% vs 4%, P=0.733). While the 4-year graft survival was comparable (96% vs 93%, P=0.460) patient survival was improved in the prophylaxis group (100% vs 94%, P=0.042).
Conclusions: Among kidney transplant recipients, the use of valganciclovir prophylaxis, compared with preemptive therapy, led to less severe IFTA at 3 years after transplantation.

LBOS1_13 ORGAN UTILIZATION RATE (OUR): A NEW APPROACH TO IMPROVE ORGAN ACCEPTANCE RATE?

Franz Immer*[1], Annika Ballmer[1], Michel Tsimaratos[2], Massimo Cardillo[3], Beatriz Dominguez-Gil[4], Beatriz Mahillo[4], Marina Alvarez[4], Derek Manas[5], Axel Rahmel[6], Serge Vogelaar[7]

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Background: Availability of organs from deceased donors is the most important limitation for organ transplantation. Many studies focused on the number of deceased donors per million inhabitants (pmp). The issue of organ acceptance by individual centers and transplant professionals involved in decision making for the acceptance of organs for transplantation is another crucial aspect. Organs offered for transplantation may be rejected in one center and being successfully transplanted in another or even exported in a foreign country. The aim of the study is to compare the organ utilization rate (OUR) for heart, lungs, liver and kidney in selected European countries (FRA, GER, AUT, ITA, ESP, POR, NL, UK, CH).
Methods: Data from 2018 to 2021 have been extracted from the Newsletter Transplant, published from the EDQM/Council of Europe and the GODT 2021. The numbers of utilized donors (UTI) were extracted for DBD, DCD and overall. The percentage of donors of 60 years and older reported in 2021 in the GODT has been extracted. Transplantation activity pmp for heart, lungs, liver and kidneys were analyzed and put into relation to the number of UTI-donors to calculate the OUR.
Results: The percentage of donors of 60 year and older in 2021 was the highest in ITA with 57%, followed by ESP with 54%, FRA 50%, CH 48%, POR 46%, NL 44%, GER 43, AUT 42% and UK with 33%. The OUR for kidneys (DBD and DCD) in UTI-donors was in average 75.0%. In France the OUR was the highest with 80% in comparison to Italy with 61%. For livers average OUR was 74.0% with 95.3% for Switzerland and 55.3% in Spain. For the heart, average OUR was 21.0% with 35.8% in Germany compared to 11.8% in Portugal with the lowest OUR. For lungs average OUR was 24.5% with 37% in Germany in comparison to 9.3% in Italy and 9.5% in UK. Similar variations can be found by analyzing DBD- and DCD-donors only.
Conclusions: OUR between 2018 and 2021 shows important variations in all organs. Donor characteristics may vary in terms of the enrollment of older donors and the percentage of DCD- and DBD-donors between the different countries, which has an additional effect on the interpretation of the OUR. Considering that posttransplant outcome are quite similar in these countries one may assume that potentially transplantable organs could be rejected and lost due to restrictive national and/or center acceptance criteria.

LBOS1_14 HEALTH-RELATED QUALITY OF LIFE AFTER LIVING KIDNEY DONATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Stijn van de Laar*[1], Hidde de Heus[1], Emma Massey[2], Robert J. Porte[1], Frank Dor[3], Robert Minnee[1]

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Living donor kidney transplantation (LDKT) is the most effective treatment for end-stage kidney disease, offering superior outcomes compared to deceased donor kidney transplantation or dialysis. The assessment of health-related quality of life (HR QoL) following living kidney donation (LKD) is crucial given that a healthy individual willingly undergoes this procedure. Complication rates of LKD are low, however, there is conflicting evidence regarding the post-donation HR QoL. It is unclear whether post-donation physical- and physiological functioning levels (including fatigue and chronic pain) return to pre-donation levels. Furthermore, we compared the HR QoL of LKD to other relevant populations, such as the general population and healthy controls. Comprehensive searches were conducted in Embase, MEDLINE, CENTRAL, Web of Science, and Google Scholar up to the 16th of June 2023. Our primary outcome measures included the SF-36 and composited mental- (MCS) and physical component summary (PCS), comparing post-donation HR QoL to baseline or other relevant populations. A total of 69 studies encompassing 12,523 donors were included in this study. The MCS was not significantly different at 3, 6, and 12 or more months post-donation compared to baseline (Figure 1), with a standard mean difference (SMD) of -0.04 (95% CI: -0.14 - 0.06, p = 0.75). However, the PCS was significantly lower at 3 months post-donation (Figure 2). Nonetheless, no difference was observed at 6 and 12 months post-donation, with an SMD of -0.07 (95% CI: -0.20 - 0.05, p = 0.09). Both PCS and MCS were significantly higher compared to the general population. Furthermore, the separate domains of the SF-36 were significantly decreased at 3 months post-donation. However, these domains were significantly increased at 12 months post-donation, with an SMD of 0.63 (95% CI: 0.60 - 0.66, p < 0.001). Compared to the general population, SF-36 domains were significantly higher at 3, 6, and 12 months post-donation, with an SMD of 0.14 (95% CI: 0.10 - 0.18, p < 0.001). Based on the available evidence, HRQoL appears to be diminished shortly after LKD but does not exhibit a significantly decrease after 6 months or longer post-donation. Furthermore, LKD have significantly higher HRQoL compared to the general population, which is encouraging to expand LDKT programmes.

LBOS2_1 IMPACT OF DONOR-DERIVED CELL-FREE DNA ASSESSMENT IN MONITORING KIDNEY TRANSPLANT RECIPIENTS: INTERIM REPORT OF A PROSPECTIVE LONGITUDINAL STUDY

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Background: Donor-derived cell-free DNA (dd-cfDNA) is a promising non-invasive biomarker for monitoring kidney transplant (KT) recipients. We aim to evaluate its clinical utility in a prospective cohort of 500 cases.

Methods: Since July 2022, we prospectively collect plasma from each KT recipient immediately prior to renal biopsy, to measure dd-cfDNA, using a locally implemented standardized assay (AlloSeq cfDNA, CareDx, CA), and correlate %dd-cfDNA with allograft and recipient status.

Results: Of the 292/500 samples collected so far, dd-cfDNA has been already measured in 229, with 92.1% of samples passing quality control. The %dd-cfDNA <14 days post-TX (0.71% [0.53-0.85]) was significantly higher than >14 days post-TX (0.21% [0.12-0.32]; $p=5.3x10^{-7}$, Fig.1A). Dd-cfDNA was increased in deceased donor (DD) kidneys, both DBD (0.24% [0.16-0.38]; p=0.004) and DCD (0.24% [0.12-0.4]; p=0.03), compared to living donation (LD) (0.13% [0.1-0.25], Fig.1B), but not different between DBD and DCD kidneys. The difference between DD and LD kidneys persisted >14 days post-TX (DBD 0.21% [0.15-0.31]; DCD 0.22% [0.11-0.32]; LD 0.13% [0.10-0.25]). Dd-cfDNA was significantly higher at the time of indication biopsies (0.41% [0.26-0.85]) than at surveillance biopsies (0.18% [0.11-0.30]; $p=2.8x10^{-10}$). 13.3% of cases had (borderline) allograft rejection (AR). Dd-cfDNA was higher in AR (0.80% [0.47-1.64]) versus no rejection (0.31% [0.25-0.70]; p=0.016, Fig.1C) in indication biopsies only, which also showed more cases of full-blown AR than surveillance biopsies (17% vs 3%, respectively). Within 14 days post-TX, the inherently higher %dd-cfDNA masked the association between dd-cfDNA and AR. In indication biopsies performed >14 days post-TX, AR was associated with higher %dd-cfDNA (1.19% [0.32-2.00] vs 0.28% [0.23-0.44] in AR vs no rejection, Fig.1D).

Conclusions: Awaiting study completion by end-2023, this interim analysis indicates that, when measured >14 days post-TX, dd-cfDNA could guide whether to perform an indication biopsy. However, within <14 days post-TX, the injury/healing process occurring after TX masks the ability of dd-cfDNA to uncover ongoing AR. The impact of donor type on %dd-cfDNA persists >14 days post-TX. The clinical utility of dd-cfDNA for subclinical AR will be addressed upon study completion.

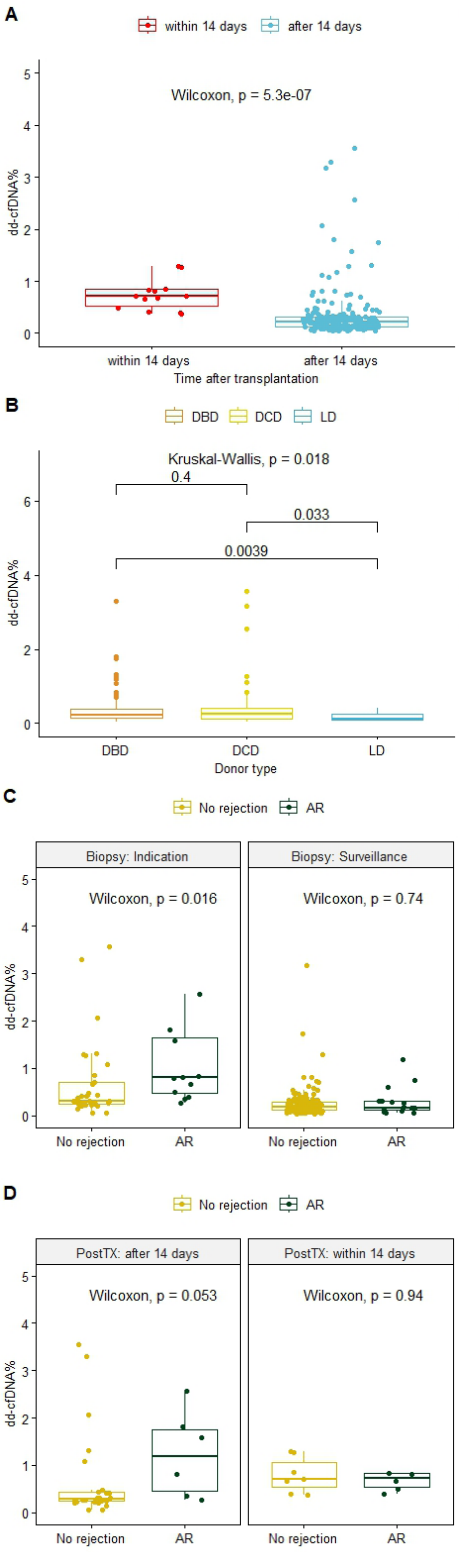

Figure 1: A. Box and whisker plot showing %dd-cfDNA median levels within and after 14 days post-transplantation. **B.** Box and whisker plot showing %dd-cfDNA median levels in kidney transplant recipients from deceased (DBD and DCD) and living (LD) donation. **C.** Box and whisker plot showing %dd-cfDNA median levels in patients with and without allograft rejection (AR) at the time of indication and surveillance biopsies. **D.** Box and whisker plot showing %dd-cfDNA median levels in patients with and without allograft rejection at the time of indication biopsies performed within and after 14 days post-transplantation. DBD=donor after brain death; DCD=donor after cardiac death.

LBOS2_2 HYBRID RENAL REPLACEMENT THERAPY: A NEW APPROACH TO IMPROVE QOL OF CKD PATIENTS WITH AN IMPLANTABLE ARTIFICIAL KIDNEY

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Background: While the number of CKD patients requiring dialysis treatment is significantly increasing, current dialysis patients face the demanding schedule of thrice-weekly, four-hour-long dialysis sessions, high/low blood pressure before/during the treatment, and strict restriction of water intake. Our group proposed "hybrid" renal replacement therapy, where an implantable artificial kidney, or a nano-filtering device, "i-Azinzo", continuously removes adequate amount of fluid from blood while the excessive waste products are removed by the conventional dialysis treatment. Consequently, this hybrid therapy reduces the dialysis treatment frequency down to once a week or less (depending on the residual kidney function) and maintains the body fluid amount while allowing the patients to drink 1.5 L of water per day. Since i-Azinzo is used in the implanted manner, the long-term dialysis and antithrombotic performance needs to be investigated.
Methods: i-Azinzo is a layered filter comprised of a polyethersulfone (PES) dialysis membrane and micro-sized blood flow and filtrate flow channels arranged alternately. It is equipped with two artificial blood vessels connected to the artery and vein and works at blood pressure without an external pump. In this study, we designed i-Azinzo tailored for miniature pigs weighing between 20 to 25 kg(n=3) (Figure_1). They were then connected to the pigs' neck arteries and veins using medical-grade tubing. 6-hour ex vivo experiments were conducted to evaluate the filtration performance and antithrombotic properties of the device.
Results: Throughout the 6-hour experiments, the filtrate volume remained consistent without any decline (Table_1). After the experiment, the device was disassembled to observe the internal blood flow channels, and there were no blood clots present. This verified the device's high antithrombotic properties.
Conclusions: We have successfully conducted 6-hour ex vivo experiments to validate the performance of i-Azinzo. Currently, our focus is on achieving the target implantation period of 6 months for i-Azinzo. Up to this point, evaluations have been conducted for a period of 96 hours.

Figure_1. i-Azinzo: implant artificial kidney that filters blood to remove water from blood.

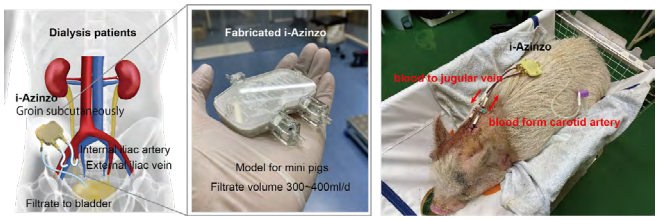

Table_1. Filtrate volume in 6-hour ex vivo experiments.

Time(hour)	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6
Device 1 Filtrate volume [ml/30min]	5.4	5.6	6	5.4	7.6	7	7	6.2	6	5.8	5.6	6.4
Device 2 Filtrate volume [ml/30min]	5.6	6.6	6.3	7	6.4	6.8	6.8	7.2	7.4	7.2	7.4	7.3
Device 3 Filtrate volume [ml/30min]	5.6	6.7	6.2	7.1	6.6	7	6.9	7.1	6.9	6.9	7.3	7.2

LBOS2_3 CONCURRENT PORTAL VEIN THROMBOSIS IN PAEDIATRIC LATE LIVER RE-TRANSPLANTATION: A MULTICENTRE STUDY

Riccardo Cirelli*[1], Stefania Camagni[2], Francesco Cavallin[3], Domenico Pinelli[2], Paola Stroppa[4], Luisa Pasulo[5], Ruben De Kleine[6], Mark Meerdink[6], Marco Spada[1], Stefano Fagiuoli[5;7], Lorenzo D'antiga[4], Robert J. Porte[6], Vincent E. de Meijer[6], Michele Colledan[2;7]

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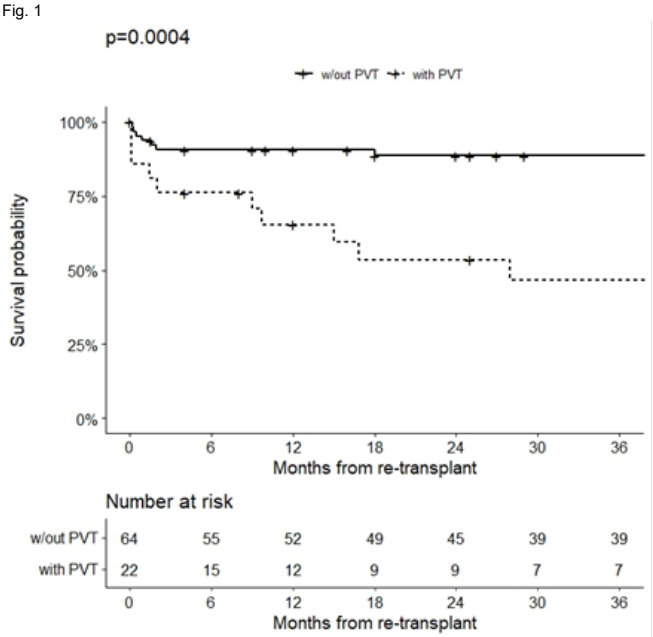
Background: Pediatric liver transplantation success rates have improved over time, but graft loss remains a challenge. Retransplantation (reLT) is the second most common indication for liver transplantation in children. Paediatric late reLT (L-reLT) with concurrent portal vein thrombosis (PVT) can be challenging due to portal inflow alteration, which often needs complex surgical restoration. The study aim is to investigate the impact of concurrent PVT during paediatric L-reLT on longterm outcomes.
Methods: L-reLT performed at two Italian and one Dutch transplantation centers have been retrospectively analyzed from 1998 - 2022 and divided into two groups based on concurrent PVT, defined by the need for at least portal thrombectomy at L-reLT. Prognostic impact was evaluated by looking at patient survival (PS), graft survival (GS), hospital course complications (HC), and post-discharge follow-up. PVT incidence after L-reLT was evaluated in both groups to detect any PVT recurrence.
Results: 91 L-reLT were performed, 22 with concurrent PVT. Three surgical management techniques for PVT were performed: thrombectomy, jump-graft anastomosis or porto-renal anastomosis. The median follow-up was 54 months (IQR 15–110). At the time of analysis, GS at 12–24–36 months was 84.5-80.3–78.6%. Concurrent PVT was associated with lower GS (HR 4.29, 95% CI 1.89 to 9.72; p = 0.0004; **Fig. 1**). PS at 12–24–36 months was 86.7-85.2–82.4% and was lower in the PVT group (HR 1.37, 95% CI 0.44–4.18; p = 0.58). HC was slightly worse in PVT patients with a higher CCI (59 vs 52, p = 0.27); the surgical reoperation rate was also higher in that group during the hospital stay (64% vs 48%; p = 0.20). Furthermore, a significant PVT recurrence after L-reLT was recorded in PVT group (18% vs 2%; p = 0.02).
Conclusions: This study suggests that concurrent PVT at L-reLT has a significant negative impact on GS. Any attempt to reduce the incidence of PVT after pediatric LT should be performed with prevention, prompt diagnosis, and treatment to limit as much as possible a L-reLT with this concurrent condition. Furthermore, in this study, PVT seems to be prone to recurrence, and proper post-operative surveillance is suggested for any L-reLT with concurrent PVT.

Fig. 1



LBOS2_4 LUNGGUARD BREAK THE GOLDEN STANDARD OF SIX HOURS COLD ISCHEMIC TIME

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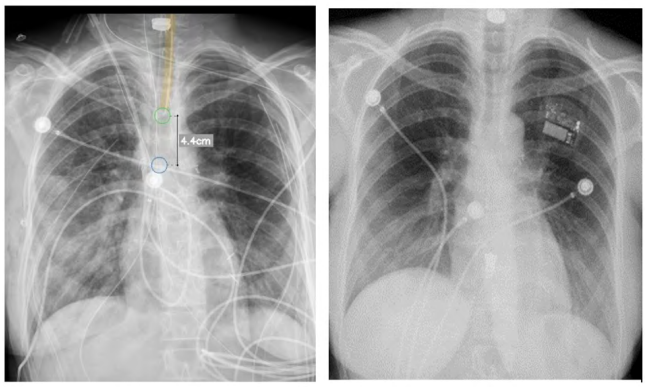
Background: The current maximum cold ischemic time for donor lung transplant is around 8 hours. Six hours is the commonly accepted limit of cold ischemic time at most transplant centers in United States. Now Paragonix LUNGguard™ system brings a new technology to donor lung transportation and extends the cold ischemia time to even longer than 8 hours without compromise the quality of the donor lungs. We review our experience of LUNGguard at our institute.
Methods: A total of 45 donor lungs were procured and stored in LUNGguard at our institution between April 2022 and July 2023. Recipient's demographic, clinical diagnoses, and morbidity are analyzed. 30-day survival is reviewed.
Results: The demographics of the recipients is in table 1. 45 donor lungs (15 single lung, 30 double lungs) were flushed with Perfadex solution and stored in LUNGguard. Among 45 cases, 42 donors were DBD, 3 donors were DCD. Total cold ischemic times were grouped as follows: 26 cases <8 hours, 7 cases between 8-10 hours, 12 cases between 10-13 hours. 41 cases had no significant PGD in first 72 hours, only 4 recipients developed PGD 3, but none was on ECMO support. Five recipients received tracheostomy after the transplants (2 patients secondary to reflex and aspiration. 2 patients had right ventricular failure. 1 patient had multi organ failure). Average ICU stay is 10.5 days (range from 3 days to 39 days). There was one death in 30 days due to heart failure (cold ischemic time 401 minutes).
Conclusions: The analysis of this cohort showed that the Paragonix LUNGguard is an advanced organ preservation device, extends cold ischemic time beyond 8 hours and has a good outcome at short-term.

Table 1. Recipient's demographic

Age	Mean 58 years (range 32-76)
Gender	Male 30 Female 15
Race	Caucasian 32 (71%) Black 7 (16%) Other 6 (13%)
BMI	29 cases <25 9 cases <30 7 cases <35
CAS	Mean LAS 49.1 (before 4/1/2023) Mean CAS 23.5

Figure 1. A 54-year-old female receive double lungs transplant with right lung ischemic time 11 hours 28 min, left lung ischemic time 12 hours 43 min. Left chest X-ray was took right after the transplant. Right one shows she discharged home after 18 days.



LBOS2_5 RECOVERY AFTER INTENSIVE CARE UNIT ACQUIRED WEAKNESS AFTER LIVER TRANSPLANTATION. THE ROLE OF PROMPT DIAGNOSIS AND MANAGEMENT

Rita Gaspari[1;2], Giorgia Spinazzola[1], Stefania Postorino[1], Manuel Delli Compagni[1], Teresa Michi[1], Daniele Fachechi[1], Massimo Antonelli[1;2], Alfonso Avolio*[1;2]
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Background: Intensive care unit acquired weakness (ICUAW) syndrome is characterized by the onset of neuromuscular weakness with no plausible causes other than critical illness. ICUAW is rarely reported in patients undergoing liver transplantation (LT). Despite the difficulty of diagnosis due to confounding factors such as diabetes, multiple organ failure or sepsis, its early identification and treatment are essential to improve functional recovery and avoid other complications.
Methods and Materials: All patients admitted to the Intensive Care Unit (ICU) after LT surgery who developed severe limb weakness have been investigated Electromyography (EMG) and nerve conduction studies (NCS) have been used for the diagnosis of ICUAW. Fibrillation potentials at EMG on the deltoid, brachial and rectus femevoris muscles, absence of sensitive potential on sural nerve, and absence of motor response to direct stimulation of median nerve in NCS indicated ICUAW.
Results: Between Jan 2017 and Jun 2023, 219 patients underwent LT from deceased donor. Seventeen of them showed limb weakness. The electrophysiological diagnosis was made in 7 pts, in the remaining 10 pts only muscle deconditioning was found. Clinical characteristics are reported in Table 1. Patients developed ICUAW 9±4 days after LT. Patients' age was 46.5±17 years, BMI 27±5.7, MELD 36.5 ± 4.7, Simplified Acute Physiology Score (SAPS) II 60±11, length of surgery 10.1 ± 2.7 hours. Intraoperative transfusions were: Red Blood Cells 16.7 ± 10.7 units, fresh frozen plasma 10.8 ±6.9 units, and platelets 3.5±3.2 units. ICU length of stay (LOS) was 33.7±26.5 days, and duration of mechanical ventilation (MV) 175.5±86.7 hours. Three pts were tracheostomized, and 2 patients were re-transplanted for primary non-function (PNF) of the graft. All patients developed Acute Kidney Injury treated with continuous veno-venous hemofiltration (CVVH) and contracted infections as reported in Table 1. We treated ICUAW with Nicetile 500 mg im twice a day, Thiamine im 100 mg daily, group B vitamins 1 bottle once a day and intense physiotherapy. All patients had good clinical recovery and are alive 90 days after LT.
Conclusion: ICUAW is rarely reported after LT. Early diagnosis, prompt therapy, intense daily rehabilitation, glycemic control, and control of infections improves prognosis.

Table 1. Characteristics of patients affected by Intensive Care Unit Acquired Weakness (ICUAW)

Parameters	*Pt 1*	*Pt 2*	*Pt 3*	*Pt 4*	*Pt 5*	*Pt 6*	*Pt 7*
Age (y)	64	56	58	38	17	46	56
Gender (M/F)	M	M	F	F	M	M	F
Body Mass Index	26,6	22,2	34,2	33,5	25,6	25,2	26,1
Hyperglycemia	Yes	Yes	Yes	Yes	Yes	Yes	Yes
MELD score	30	38	40	40	40	31	33
D-MELD	810	912	3105	3160	1062	2139	2234
SAPS II score	46	76	49	60	67	67	69
Alchool	No	Yes	No	Yes	No	No	No
Virus	No	Yes	No	No	No	No	No
Hepatocarcinoma	No	Yes	No	No	No	No	No
Other	Cryptogenetic	-	Polycystosis	-	Cryptogenetic	Trauma	Autoimmune
ICU stay before LT (d)	0	4	5	9	6	13	3
Primary Dysfunction	No	Yes	Yes	No	No	No	Yes
Lenght of surgery (h)	11,5	6	9	14	11	9	12
Duration of MV (h)	168	75	144	336	150	180	240
Tracheostomy	Yes	No	No	No	No	Yes	Yes
RBC U IO	36	18	19	11	10	6	4
FFP U IO	23	14	8	5	10	5	3
PLT U IO	9	5	3	2	2	0	1
Norepinephrine	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mycophenolate	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tacrolimus	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Corticosteroids	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Serum CPK (U/L)	74	113	239	< 15	2000	80	120
Rejection	No	No	No	No	No	No	Yes
Infection site	Blood	Blood+BAL	Blood	Urine	Blood+BAL	Blood+Ascites	Blood
ICUAW (days post LT)	14	8	8	8	3	13	9
ICUAW recovery	Yes	Yes	Yes	Yes	Yes	Yes	No
Pre-LT CVVH	No	Yes	No	Yes	Yes	Yes	No
Post-LT CVVH	Yes	Yes	Yes	Yes	Yes	Yes	Yes
LOS in ICU (d)	79	14	20	20	16	53	40
LOS in hospital (d)	187	53	68	85	83	177	40
90 days outcome	Alive	Alive	Alive	Alive	Alive	Alive	Dead

Abbreviations. Pt: patient; MELD: Model for End stage Liver Disease; D-MELD: Donor age for MELD; SAPS-II: Simplified Acute Physiology Score II; LT: liver transplantation; PNF: Primary non function; MV: mechanical ventilation; RBC U IO: intraoperative red blood cells units; FFP U IO: intraoperative fresh frozen plasma units; PLT U IO: intraoperative platelets units; CPK: Creatine Kinase; BAL: Broncho-Alveolar Lavage; PO: post operative; CVVH: continuous veno-venous hemofiltration; LOS: length of stay.

LBOS2_6 TTV GUIDED BELATACEPT CONVERSION AFTER LUNG TRANSPLANTATION: REPORT OF 7 CASES

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Background: Calcineurin inhibitor (CNI) based protocols are still the standard immunosuppressive regimen (IS) after lung transplantation (LuTx), although CNI-related toxic effects may occur. lung transplantation (LuTx), although CNI-related toxic effects may occur. Belatacept, a novel immunosuppressant that blocks a T-cell co-stimulation pathway, is a non- nephrotoxic drug indicated as an alternative to CNIs in kidney Tx. In most of the published reports on the use of Belatacept after lung TX in combination with CNI sparing protocols, the incidence of acute rejection episodes and early CLAD was unacceptable high. This study investigated the use of TTV-guided Belatacept dosing to overcome this problem.
Methods: We reviewed a series of 7 LuTx recipients with conversion to a CNI-sparing Belatacept IS regimen within the first 3 years post-LuTx (n = 7). Belatacept dosing was started according to the protocol used in kidney TX recipients and adapted thereafter based on TTV PCR levels (therapeutic range log7 –log9 TTV –PCR copies)
Results: Use of Belatacept was triggered by severe renal failure in all patients. Time to Belatacept after LuTX was 445±300 days (mean 401 days). Mean estimated glomerular filtration rate after starting Belatacept had significantly improved 6 months after initiation (GFR mL/min/1.73m^2 before start was 29.5±6.1 and GFR after 6mo 41.0±4.7, p=0.039). Tacrolimus dosage was reduced in all patients but not stopped (reduction of target through level to 1.5-2.5ng/ml). There were no episodes of acute cellular (ACR) or humoral rejection (AMR) and none of the patients developed CLAD. One pat died due to pulmonary embolism 101 days after Belatacept start. In 3 patients Belatacept dose had to be adapted according TTV levels (in 2 cases dose had to be increased, in 1 case dose had to be reduced).
Conclusions: Conversion to CNI-reduced Belatacept-based IS with TTV guided Belatacept dosing improved renal function without increasing risk of ACR, AMR or CLAD. Further studies are needed to prove the safety and efficacy of this therapeutic regimen.

LBOS2_7 INTEGRATED COGNITIVE ERGONOMICS OF THE REMOTE EVALUATION OF THE GRAFTS WITH ROBOTICS AND MACHINE PERFUSION TECHNOLOGY IN SOLID ORGAN TRANSPLANTATION

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Background: Big data collected on a real time mode from ESOT's records on 07.11.2017 have the potential to compute crucial risks, sourcing from the damaged organs interrelated with the human-system design of the remote evaluation of the grafts and decision making in the procurement phase of Organ Transplantation (OT) enhanced by Robotic framework and machine perfusion technology and method.
Methods: In a prospective real time experimentation using the Prometheus digital medical device (pn:2003016) applying AI and the Robotic framework ''Stamoulis'' for the remote evaluation of the grafts and the robotic based computational analysis for 189.721 transplants in Europe from 2011 to 2016, computed the expected damaged organs and compared with the expected impact of the applied machine perfusion technology and method for trauma, cancer, infection and injury pathologies.
Results: Robotic cognitive ergonomics integration and simulation of the remote evaluation of the grafts in the procurement phase of OT showed and accuracy for liver, renal, pancreas, uterus, heart and lung grafts that ranged from:90.9%-97.6%)'
Conclusions: The results showed that Robotic cognitive ergonomics integration simulation of the remote evaluation of the grafts in the procurement phase of OT enhanced significantly operational maneuverability and inter-operability to remotely and instantly: a.Minimize damaged or diseased, with infection, trauma and cancer, grafts applying AI and Big Data analytics and computing, for evidenced real time computations and interventions, b. Develop an international clinical surveillance system integrated with cognitive ergonomics of the remote evaluation of the grafts integrated with robotics and machine perfusion technology. Source:GODT 2011-16.

Organ	2011	2012	2013	2014	2015	2016	Total	Expected damaged organs
Heart	1980	1960	2037	2146	2235	2254	12612	1.261
Lung	1677	1756	1825	1822	1818	1916	10814	1.081
Liver	7006	6845	7173	7390	7694	7762	43870	3.510
Kidney	18712	18854	19227	19670	20102	20638	117203	12.892
Pancreas	859	825	865	818	821	780	4968	696

LBOS2_8 TECHNICAL FEASIBILITY AND OUTCOME OF SALVAGE LIVING DONOR LIVER TRANSPLANTATION AFTER MAJOR HEPATECTOMY

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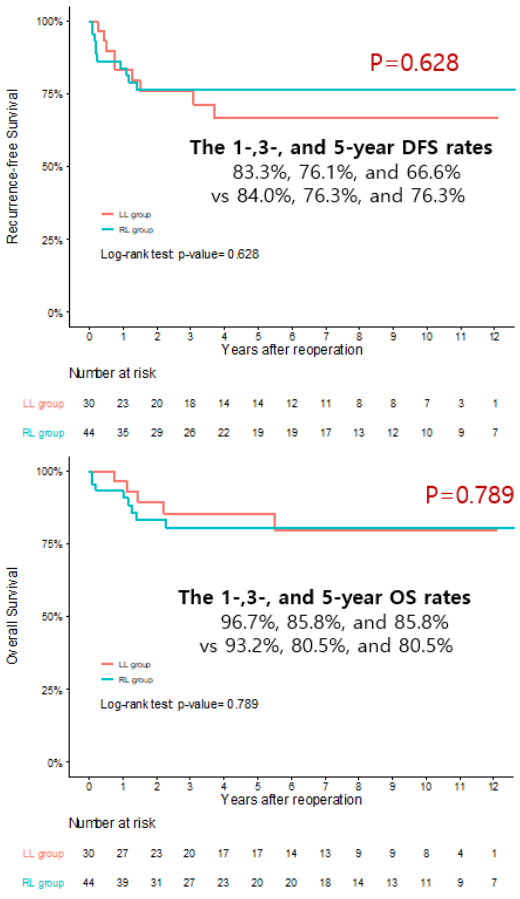
Background: Salvage living donor liver transplantation (LDLT) is technically challenging due to adhesions caused by previous liver resection (LR) in addition to the inherent difficulties short vasculo-biliary stumps and co-existing vasculo-biliary injury. The purpose of this study was to assess the technical feasibility of LDLT after major hepatectomy and determine whether there was a difference in surgical outcome according to the type of LR received previously.
Methods: We retrospectively reviewed the medical records of consecutive 83 patients who underwent LDLT after major hepatectomy from December 2004 and June 2022, at Asan medical center, Seoul, Korea.
Results: Among 83 patients, 74 patients underwent salvage LDLT for recurrent hepatocellular carcinoma. Of the 74 patients, 44 patients received right hemihepatectomy (RL group) and 30 patients received left hemihepatectomy (LL group) prior to LDLT. The operative time longer (mean ±SD, 861.05±151.02 vs. 737.67±94.61 min; p = 0.000) and intraoperative RBC (median (IQR), 8 (2, 19.5) vs. 0.5 (0, 6) units; p = 0.003) and FFP (8.5 (0, 19) vs. 0 (0, 6) units; p = 0.003) transfusion requirements were higher in the RL group. In the RL group, the incidence of postoperative surgical complication was higher significantly (54.6% vs. 30.0% p=0.037). However, no difference was detected regarding survival rate. The 1-, 3-, and 5-year overall survival rates were 93.2%, 80.5%, and 80.5%, respectively, for the RL group, and 96.7%, 85.5%, and 85.5%, respectively, for the LL group (P=0.789). The 1-, 3-, and 5-year disease-free survival rates were 84.0%, 76.3%, and 76.3%, respectively, for the RL group, and 83.3%, 76.1%, and 66.6%, respectively, for the LL group (P=0.628).
Conclusions: Salvage LDLT can be safely performed for patients with recurrence or deterioration of liver function even after major hepatectomy. However, salvage LDLT is technically demanding procedure, it should be performed by experienced transplant surgeon.



LBOS2_12 QUANTIFICATION OF GLOMERULAR FILTRATION RATE BY STANDARD RENAL COMPUTED TOMOGRAPHY: A NEW AND SIMPLE METHOD TO ASSESS KIDNEY FUNCTION

Helena Genberg*[1;2], Kristoffer Huitfeldt Sola[3], Torkel Brismar[3]

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Background: Gold standard for measuring glomerular filtration rate (mGFR) is the iohexol clearance test. Simple non-invasive estimation of GFR by computed tomography (CT) may hence be achievable when iohexol is used as contrast medium. This study therefore aimed to develop a simple and precise technique to quantify GFR from clinical renal CT by segmentation of the renal pelvis and bladder.
Methods: Medical records of adult living kidney donors operated 2013-2022 and patients considered for neoadjuvant cisplatin prior to cystectomy 2019-2022 were reviewed. Inclusion criteria were renal CT obtained before and 7-13 minutes after administration of contrast medium and an iohexol clearance test within three months from the imaging. Estimated GFR (eGFR, mL/min) derived from cystatine C ($eGFR_{cystatine\ C}$) and creatinine using both the Cockroft-Gault formula ($eGFR_{Cockroft-Gault}$) and the Revised Lund-Malmö formula ($eGFR_{LMR18}$) within 3 months of the CT scan was additionally obtained. To determine GFR from renal CT scans ($eGFR_{CT}$), renal pelvis and bladder were segmented on CT images. $eGFR_{CT}$ was calculated by: renal volume (ml) * Δ radiodensity (HU) * contrast medium (grams) / time (minutes). A multivariate linear regression analysis comparing $mGFR_{iohexol}$ to age, body surface area and the CT measurements was performed.
Results: Out of 339 screened patients, 104 were included in the analysis (mean age: 50 ± 13 years; 61% women. Main reason for exclusion (n=99) was a CT at different voltage than 120 kV.Multivariate linear regression analysis combining GFR_{CT} with body surface area and age gave an adjusted R-square correlation of 0.56 to $GFR_{iohexol}$ (p <0.001). GFR_{CT} had the strongest relationship to $GFR_{iohexol}$ with a mean average error (MAE) of 9.8 mL/min, while $eGFR_{cystatine\ C}$ gave an MAE of 15.7 mL/min, $eGFR_{Cockroft-Gault}$ MAE of 15.1 ml/min and $eGFR_{LMR18}$ an MAE of 12.1 mL/min. Figure 1.
Conclusions: Renal function can be estimated with high precision using standard renal CT. This method might be of special relevance in the assessment of both living and deceased kidney donors as well as in the planning of urologic therapies. However, $eGFR_{CT}$ could potentially be used in any clinical setting where a precise estimate of kidney function and multiphase contrast-enhanced abdominal CT is required. A prospective study is underway.

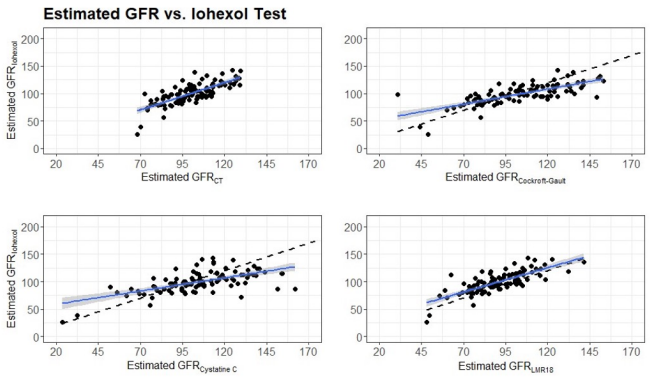

Figure 1. Comparing the estimated GFR to that derived from iohexol . The trend line (in blue) is compared to the best fit line (dashed black line). Trend line of GFR_{CT} overlaps the best fit of $GFR_{iohexol}$ in the top left panel and the latter is consequently not visible.

LBOS2_13 EXPLORATION OF NORMOTHERMIC MACHINE PERFUSION STRATEGIES IN RAT KIDNEY

Tong Chen*[1], Shuangjin Yu[1], Haiwei Chen[1], Yu He[1], Guodong Chen[1], Xiaoshun He[1], Jiang Qiu[1]

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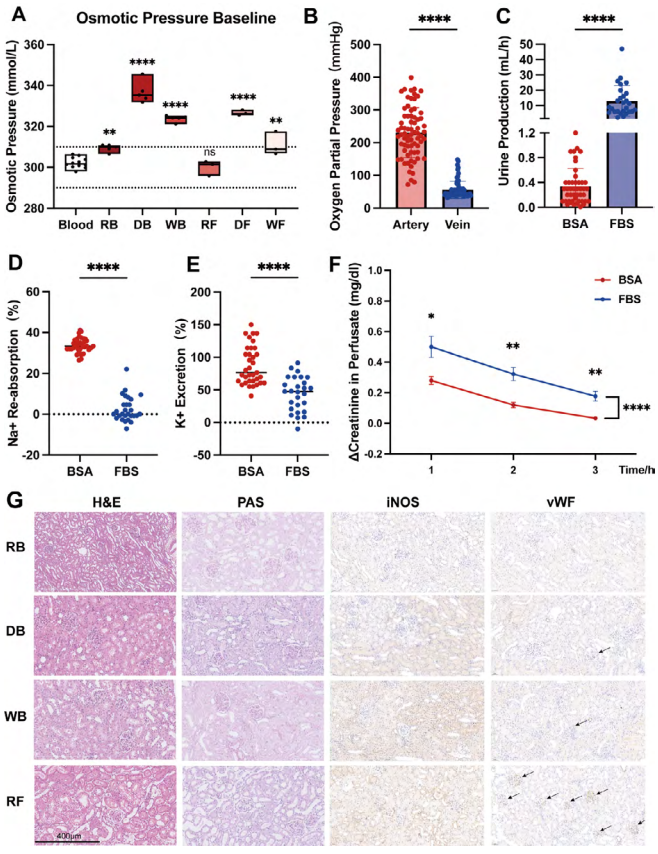
Background: To establish a novel rat kidney normothermic machine perfusion (NMP) model and explore the perfusion efficacy of different perfusates.
Methods: The NMP was initiated at 37ºC under the pressure of 80-100mmHg once the renal artery and vein were canulated. Based on rat peripheral blood, 6 different perfusate formulates were developed by adding different components: RPMI 1640 + BSA (RB), DMEM/F12 + BSA (DB), William's E + BSA (WB), RPMI 1640 + FBS (RF), DMEM/F12 + FBS (DF), William's E + FBS(WF). Urine production, metabolic parameters of both perfusate and urine were record for analysis. In addition, creatine clearance capacity and Na+ reabsorption rate were also compared between groups. Finally, renal biopsies were obtained at the end of NMP.
Results: The osmotic pressure of RB group (309.5±1.775mmol/L) was the closest to physiological state. As anticipated, the pO2 of perfusate was significantly lower in the renal vein than artery, which suggested the aerobic metabolism of kidneys. During NMP, all kidneys were able to produce urine, and the groups with FBS produced more urine than BSA groups (13.09±10.06ml/h vs 0.34±0.29ml/h, P<0.0001). Interestingly, the BSA group showed significantly higher Na+ re-absorption than FBS group (33.81±3.49 % vs 2.30±6.10%, P<0.0001), and similarly in K+ excretion (87.58± 29.47% vs 44.19±26.26%, P<0.0001). All the kidneys showed excellent creatine clearance capacity during NMP. Consistently, the histology staining exhibited physiological tissue structure in all kidneys. Additionally, RB shows the least injury in activation of inflammatory marker (iNOS) and endothelial activation (vWF) compared with other groups.
Conclusions: Our results demonstrated a safe and effective short-term rat kidney NMP procedure. More importantly, perfusate consist of rat peripheral blood, RPMI 1640 and BSA showed the best osmotic pressure and Na+ reabsorption than other perfusate strategies. This novel NMP strategy in small animal models may facilitate basic studies related to organ preservation in future.

Figure 1 Comparison of perfusion parameters among different perfusates and histology of perfused kidneys, including H&E staining, PAS, iNOS and vWF.



LBOS2_14 FAECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT URINARY TRACT INFECTIONS IN KIDNEY TRANSPLANT RECIPIENTS: PROMISING RESULTS WITH RESEARCH IMPLICATIONS

Changliang Cao[*1], **Yongguang Liu**[1], **Jianmin Hu**[1], **Ming Zhao**[1]
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Background: Kidney transplant recipients (KTRs) are highly susceptible to infections due to immunosuppressive therapy, with urinary tract infection (UTI) being the most prevalent. The rising antibiotic resistance rates among urinary isolates in KTRs pose significant treatment challenges. According to reports, over 70% of UTIs in kidney transplants are caused by Gram-negative bacilli, predominantly Escherichia coli. Additionally, early post-transplantation, extended-spectrum β-lactamase (ESBL)-producing *Enterobacter cloacae* is prevalent, whereas ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* dominate after the third month. In response to the escalating antibiotic resistance challenge, faecal microbiota transplantation (FMT) emerges as a potential treatment.
Methods: Eight KTRs with diagnosed recurrent UTIs and associated symptoms underwent FMT treatment. The procedure involved administering frozen capsulized microbiota obtained from healthy donors. Urine culture and urinalysis were performed both before and after the FMT intervention. Additionally, one patient with a complex condition underwent metagenomic next-generation sequencing (mNGS) before and after the FMT intervention to gain deeper insights.
Results: Prior to FMT, seven KTRs were affected by ESBL-producing *E. coli*, and one by ESBL-producing *K. pneumoniae*. During the 15 to 31-month follow-up after FMT, all patients displayed a positive response to the treatment, with six out of eight showing no symptoms of UTIs. Two patients experienced symptoms, including one patient with infrequent urination once during the 27-month follow-up and another with fever once during the 20-month follow-up. Both of these symptoms were effectively resolved with sulperazone treatment.
Conclusions: FMT holds promise as an intervention for recurrent UTIs in kidney transplant recipients with ESBL-producing *E. coli* and *K. pneumoniae* infections. However, further research is indispensable to comprehend its underlying mechanisms and optimize therapeutic efficacy in this vulnerable patient population.

LATE BREAKING E-POSTERS

LBP01 EXPLORING PERSPECTIVES ABOUT THE PSYCHOSOCIAL FACTORS INFLUENCING ACCESS TO KIDNEY TRANSPLANTATION AND TRANSPLANT OUTCOMES FOR CHILDREN

Ji Soo Kim*[1;2;3], Stephen D Marks[2], Jo Wray[1]

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Background: Kidney transplantation is often seen as the optimal form of kidney replacement therapy for children and young people (CYP) with stage 5 Chronic Kidney Disease (CKD-5). Psychosocial factors have been cited to delay their access to a kidney transplant, however it is unclear what these factors are. We undertook a multi-centre qualitative study that explored the range of psychological and social factors that CYP, their carers and their paediatric nephrology multi-disciplinary team (MDT) perceived to influence how soon a CYP with CKD-5 accesses a kidney transplant. This included factors that were perceived to influence kidney transplantation outcomes or deemed important to patients and their families in terms of their quality of life (QoL).
Methods: Across 8 paediatric nephrology units in the United Kingdom, semi-structured interviews were conducted with CYP, their carers and their paediatric nephrology MDT. These interviews were reviewed for pertinent themes using thematic analysis following the approach of Braun and Clarke.
Results: A total of 37 interviews were conducted with 13 families and 17 members of the paediatric nephrology MDT. The majority of participating families identified as White (57.1%), followed by Black (21.4%) or Asian (21.4%). The following themes were perceived as important to accessing kidney transplantation and post-transplant outcomes: health beliefs; relationship with and trust in healthcare; support networks; family relationships; socioeconomic circumstances; culture and race; and mental health and coping strategies. Specific challenges from living with CKD-5 and living through the COVID-19 pandemic were also discussed due to their impact on QoL and accessing a kidney transplant.
Conclusions: There are a wide range of psychosocial factors that are perceived to influence a CYP's access to kidney transplantation. Longitudinal and prospective studies are needed to fully assess the relationship between these psychosocial factors and a CYP's access to, and outcomes of, kidney transplantation.

LBP02 THE RISK OF MICROBIAL INFECTION IN RECIPIENTS OF DONOR LIVERS THAT UNDERWENT HYPOTHERMIC OR NORMOTHERMIC MACHINE PERFUSION

Bianca Lascaris*[1], Chikako Endo[1], Isabel M.A. Brüggenwirth[1], Jan Roggeveld[1], Hans Blokzijl[1], Vincent E. de Meijer[1], Edwina Doting[1], Robert J. Porte[2]

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Background: Ex situ machine perfusion is increasingly used to preserve and assess donor livers prior to transplantation. Compared to traditional static cold storage (SCS), machine perfusion exposes livers to an additional risk of microbial contamination. However, information on the risk of microbial transmission after machine perfusion is scarce. We aimed to determine the risk of infection after liver transplantation following either hypothermic oxygenated machine perfusion (HOPE) or normothermic machine perfusion (NMP).
Methods: Retrospective observational study of patients who underwent liver transplantation after HOPE or NMP preservation between 2014-2022. We examined the microbial transmission from SCS preservation fluid to the machine perfusion solution, and the subsequent recipients. The standard machine perfusion fluid for HOPE did not contain antibiotics, while cefazolin and metronidazole were added per protocol to the NMP perfusion fluid.
Results: A total of 155 patients were included, of which 102 patients received a liver after HOPE, and 53 patients after NMP. Although SCS preservation fluid cultures prior to HOPE and NMP were positive for at least one microorganism in 54% and 58%, respectively, machine perfusion fluid cultures were positive in only two cases after either HOPE or NMP. One case of de novo contamination occurred during HOPE. In one recipient of a NMP liver (1.9%), the same E. coli strain was grown from abdominal drain fluid, as was grown from SCS preservation fluid prior to NMP. This patient was otherwise asymptomatic but treated with antibiotics for 14 days. No other cases of microbial transmission after HOPE or NMP were found.
Conclusions: The risk of microbial transmission after machine perfusion is generally very low (1.9% after NMP); however, it is not entirely absent. We observed no difference in the risk of microbial contamination and transmission during and after either HOPE or NMP, despite the fact that NMP inherently carries a higher risk due to the perfusate composition (e.g., red blood cells) and the applied temperature of 35-37ºCC. We recommend implementation of routine sampling of machine perfusion fluid at the end of the procedure for microbiological analysis to enable prompt initiation of antibiotics in recipients if indicated.

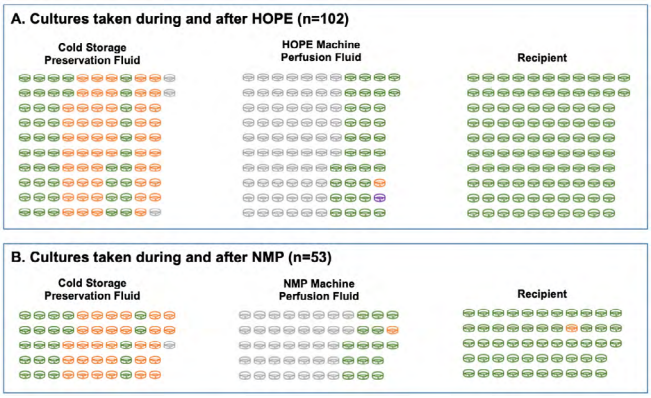
Table 1. List of microorganisms identified in the cold storage preservation fluid

Organism	Origin	Pathogenic*	Frequency n (%)
Actinomyces radingae	Skin		1 (0.8)
Alistipes onderdonkii	Gut		1 (0.8)
Alloscardovia omnicolens	Gut/Oral		1 (0.8)
Bacillus cereus	Gut (soil)		1 (0.8)
Bacteroides thetaiotaomicron	Gut		1 (0.8)
Bifidobacterium spp.	Gut		2 (1.5)
Candida spp.	Skin/Gut/Oral	Yes#	7 (5.3)
Clostridium perfringens	Gut	Yes	1 (0.8)
Collinsella aerofaciens	Gut		1 (0.8)
Corynebacterium spp.	Skin		2 (1.5)
Enterococcus spp.	Gut	Yes#	6 (4.5)
Escherichia coli	Gut	Yes	8 (6.0)
Finegoldia magna	Gut		1 (0.8)
Hafnia alvei	Gut	Yes#	1 (0.8)
Klebsiella pneumoniae	Gut	Yes	1 (0.8)
Kocuria spp.	Skin/Oral		1 (0.8)
Lactobacillus spp.	Gut		6 (4.5)
Other CNS	Skin		22 (16.5)
Pediococcus pentosaceus	Gut		1 (0.8)
Prevotella salivae	Gut		1 (0.8)
Propionibacterium spp.	Skin		3 (2.3)
Serratia marcescens	Gut	Yes	1 (0.8)
Staphylococcus epidermidis	Skin		33 (24.8)
Staphylococcus warneri	Skin		23 (17.3)
Streptococci spp.	Skin/Gut/Oral		6 (4.5)
Veillonella atypica	Gut		1 (0.8)

* All microorganisms can be potentially pathogenic when they enter the bloodstream.

Pathogenic in immunocompromised patients

Figure 1. Graphic overview of all samples available for microbiological analysis during HOPE (Panel A) or NMP (Panel B) procedures.



LBP03 PERFUSION PRESSURES, INTRAHEPATIC PERIVASCULAR EDEMA, AND PARADOXICAL WEIGHT LOSS DURING NORMOTHERMIC MACHINE PERFUSION OF HUMAN DONOR LIVERS

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Background: Normothermic machine perfusion (NMP) is increasingly used to preserve and assess donor livers prior to transplantation. NMP, however, may also cause adverse effects. We investigated the effect of perfusion pressures during NMP on the development of intrahepatic peri-portal edema (IPE) after transplantation.
Methods: All donor livers transplanted after a NMP procedure (Liver Assist; XVIVO, the Netherlands) between March 2019 and March 2022 were included. Data on perfusion settings, perfusate composition, and clinical outcome were collected. Livers were weighed before and after NMP. CT scans performed in the first week post-transplantation were reviewed for the presence of IPE, defined as increased fluid around the in the Glisson's capsule.
Results: A total of 36 livers were transplanted after NMP. Initially, post-transplant CT scans frequently showed increased IPE. This prompted us to lower NMP perfusion pressure settings in a two-step fashion. Group T1 had the initial pressures with a median (IQR) of 47 mmHg (42-54 mmHg) for the hepatic artery (HA) and 8 mmHg (7-10 mmHg) for the portal vein (PV). In group T2 we mainly decreased the HA pressure to 44 mmHg (35-50 mmHg), and in group T3 we decreased both pressures to 34 mmHg (30-39 mmHg) for the HA and 7 mmHg (6-8 mmHg) for the PV (Table 1). This change led to a reduction of IPE noted on CT scans but did not negatively affect the venous saturation, lactate clearance, or hepatocellular injury markers during NMP. Instead of developing IPE, most livers lost weight during NMP. Paradoxically, weight loss increased with decreasing perfusion pressures and subsequent reduction of IPE (Table 1). The rate of reduction in liver weight was inversely correlated with the applied PV pressure during NMP (r = -0.52, p = 0.005) and the HA flow (r = -0.38, p = 0.045).
Conclusions: NMP of human donor livers is associated with IPE development. Despite this, livers lose weight during NMP, which is more pronounced when a low PV pressure is applied. To avoid IPE, we advocate to apply the lowest perfusion pressures possible to achieve adequate flows and oxygen delivery during liver NMP. The precise mechanisms leading to liver weight loss during NMP require further research.

LBP04 QUALITY OF LIFE OF LIVING KIDNEY DONORS AT CHO RAY HOSPITAL:THE SHORT-FORM 36-ITEM HEALTH QUESTIONNAIRE SURVEY

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Background: This study aimed to identify the psychological and social effects of kidney donors after kidney donation by using the short-form 36-item health survey (SF-36) as the quality-of-life questionnaire.
Methods: A cross-sectional study was conducted on living kidney donors in the Cho Ray hospital's outpatient department. The donors were assessed their quality of life based on the SF-36 from May 2022 to November 2022.
Results: The SF-36 questionnaire about donor satisfaction were completed by 281 donors (144 women and 137 men; mean age 49.9±9.8 years). The follow-up ranged from 12 to 264 months after donor nephrectomy (10.7% of kidney donors over 10 years). Most kidney donors had a good quality of life, and 87.5% of the donors would make the same choice again. 10.7% of donors experienced financial hardship, and 8.9% reported negative occupational consequences.
Conclusions: The quality of life for kidney donors was not affected by nephrectomy for donation. Living kidney transplantation is safe and suitable for the rescue of patients with end-stage renal disease.

LBP05 HEPATIC ARTERY COMPLICATIONS AFTER LIVER TRANSPLANTATION IN CHILDREN

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Background: Hepatic artery complications (HAC) are the most frequent vascular complications and the main cause of graft disfunction and loss after liver transplantation in pediatric population. Its management is still matter of debate.
Methods: We retrospectively analysed all the pediatric liver transplantations performed at Our Institution from January 2006 to December 2022. The aim of this study is to evaluate incidence, risk factors, treatment and outcomes after HAC in children transplanted with different type of grafts. Diagnosis was based on ultrasound, clinical and biochemical variations.
Results: 470 patients have been studied. HAC occurred in 58 cases (12.3%): 37/300 left lateral segments (LLS), 10/28 right extended grafts (R-Ext) and 11/52 whole liver (WL) grafts. Intraoperative HA thrombosis occurred in 10 LLS grafts, successfully treated by Redo-anastomosis, Fogarty embolectomy and RTPA in 8 cases. 2 of them were re-transplanted after thrombosis recurrence. The arterial flow was not restored in 2 cases and the patients were retransplanted. We observed 48 postoperative HAC: 23 thrombosis (17 with early onset, < 14 days), 24 stenosis and 1 HA anastomosis damage. Interventional radiological approach was preferred in 40 HAC (83%). It was effective in 6 of 16 thrombosis (0 grafts lost) and in 22 of 24 stenosis (4 grafts lost) but failed in 10 thrombosis (7 grafts lost) and in 2 stenosis (0 grafts lost). HAC risk was associated with retransplantation (p=0.004) and R-Ext grafts (p=0.004) and was closely statistically significant for WL grafts (p=0.05). Neither vascular anatomy of donor and recipient nor the number of anastomoses influenced the HAC incidence (p=0.20). Concomitant biliary complications occurred in 17 cases (29.3%). 22 of the 58 patients with HAC were re-transplanted (37.9%). Graft failure was directly related to HAC in 17 cases. At the multivariable analysis, HAC was confirmed to be an independent risk factor for graft loss (p=0.0002), with graft survival of 84-81.6-79.9% at 12-24-36 months respectively, but not for patients' overall survival (p=0.19).
Conclusions: The occurrence of HAC was associated with retransplantation and right extended grafts. Radiological treatment is safe and effective in most cases. HAC impact significantly on graft survival but didn't affect patients' survival.

LBP06 REVERSIBILITY OF DECEASED DONOR KIDNEY INJURY FOLLOWING DONATION AFTER CARDIOPULMONARY RESUSCITATION: A NATION-WIDE POPULATION-BASED COHORT STUDY

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Background: Donors that had received cardiopulmonary resuscitation (CPR) are frequently used for transplantation. Duration of cardiac arrest and quality of CPR are likely to contribute to the degree of organ ischaemia, and these factors are often difficult to determine at the time of organ offer. The aim was to compare the outcomes for kidney grafts from cardiac arrest donors to those from non-cardiac arrest donors, stratified by the degree of renal dysfunction at the time of donation.
Methods: A nation-wide population-based cohort study was performed using prospectively collected data from the National Health Service Blood and Transplant service in the United Kingdom between January 2016 and December 2020 for all deceased donor renal transplants. Kidneys were stratified into three groups depending on terminal creatinine of the donor (normal = <100 µmol/L, raised= 100-200µmol/L and high = >200 µmol/L). Analyses were performed using general linear models. Creatinine levels were log10-transformed when treated as the dependent variable to improve model fit; the resulting coefficients are summarised using percentage differences or geometric means.
Results: A total of N=6,239 kidney donors were included, of whom 43.6% (N=2,718) suffered cardiac arrest, with median CPR duration of 25 minutes. Donor terminal creatinine was found to increase progressively with duration of CPR (p<0.001) by an average of 6.0% (95% CI: 5.3%-6.8%) per 10 minutes

of CPR (approximately equivalent to 4-5 µmol/L per 10 minutes). However, for the N=11,375 recipients, there was no significant association between donor CPR duration and 12 month creatinine levels (gradient: -0.6% per 10 minutes of CPR, 95% CI: -1.3%, +0.2%, p=0.131). Recipients from cardiac arrest donors had significantly better 12 month creatinine in all three subgroups of donor terminal creatinine, with this being most pronounced in the high terminal creatinine subgroup (geometric mean: 113 vs. 126 µmol/L, p=0.002).
Conclusions: Our study demonstrates that, whilst duration of CPR correlates with the degree of acute donor renal dysfunction, there is no such association with functional outcomes for recipients. This provides reassurance that raised donor creatinine after cardiac arrest is reversible and appears more favourable than raised donor creatinine due to other causes.

LBP07 ISCHEMIC PRECONDITIONING AMELIORATES MOUSE RENAL ISCHEMIA-REPERFUSION INJURY THROUGH ACTIVATING THE NRF2/HO-1 PATHWAY ENHANCED AUTOPHAGY

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Background: Ischemic preconditioning (IPC), which is a brief and nonlethal episode of ischemia, confers protection against subsequent ischemia-reperfusion (I/R) through the up-regulation of endogenous protective mechanisms. Recent studies have reported that the activation of autophagy is associated with IPC. However, there is not fully unveiled the underlying mechanisms involving in giving rise in this IPC. In this study, we investigated the role of IPC in renal I/R injury and demonstrated that IPC could ameliorate renal I/R injury by activating the Nrf2/HO-1 pathway and induction of autophagy.
Methods: In order to gain insights into IPC-induced alterations at the cellular level, an in vitro model for IPC was designed using the human proximal tubule epithelial cell line HK-2. IPC was performed by a 10 min period of incubation of cells under mineral oil followed by a 30 min recovery period prior to the 120 min ischemic insult and reperfusion, along with the treatment of 3-Methyladenine (3-MA) for inhibit autophagy. In a renal I/R injury model, mice were subjected to 30 min of renal ischemia followed by 24 h of reperfusion. IPC was produced by 5 min of ischemia followed by 10 min of reperfusion prior to sustained ischemia.
Results: IPC markedly improve renal I/R injury by attenuating renal apoptosis, reducing reactive oxygen species (ROS) levels and inflammatory responses. We found that IPC increased LC3-II and Beclin-1 levels and decreased SQSTM/p62 and cleaved caspase-3 levels during renal I/R injury, as well as increased the number of intracellular double-membrane vesicles in injured renal cells. IPC-induced renal protection was efficiently attenuated by pretreatment with 5mM 3-MA. Also, IPC dynamically affected the expression of Nrf2/HO-1 signaling components. Moreover, Nrf2 antagonist brusatol significantly suppressed LC3-II and Beclin-1 levels, increased SQSTM/p62 and cleaved caspase-3 levels, and abolished the protective effect of IPC against I/R-induced renal damage.
Conclusions: In conclusion, the results of the present study indicate that IPC protects against renal injury induced by IR through activation of autophagy and Nrf2/HO-1 pathway.

LBP09 EXPERIENCE AND BURDEN OF POST-TRANSPLANT CYTOMEGALOVIRUS INFECTION AND TREATMENT FROM THE PATIENT'S PERSPECTIVE

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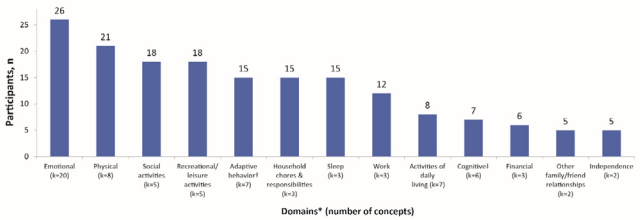
Background: Patient-reported data on how cytomegalovirus (CMV) infection in transplant recipients impacts patients' health, well-being, and daily activities are limited. This study based on qualitative interviews is the first, to our knowledge, to examine signs/symptoms and impact of post-transplant CMV from a patient perspective.
Methods: Participants were adults (≥18 years) with a past or current clinician-confirmed difficult-to-treat CMV infection (eg, intolerance to treatment, resistant, refractory, and/or recurrent infection; or presence of co-morbidities) following solid organ or allogenic hematopoietic stem cell transplant (SOT or HSCT; within the last 5 years prior to recruitment; 2015–2022). Participants were recruited via outreach to recruitment agencies, clinical sites, advocacy groups, and patient organizations. Participant informed consent and ethics approval were obtained. Semi-structured, qualitative, virtual, 60-minute, 1:1 interviews with participants were conducted by trained interviewers to describe signs/symptoms, impact, and disease/treatment burden of post-transplant CMV. Transcribed audio-recordings were anonymized, coded, and analyzed using qualitative data analytic methods, including concept frequency, clarification (eg, symptom severity and related impacts), and bothersome analyses. Concepts were organized into a patient-centric CMV conceptual model.
Results: 28 participants from the US (n=16), Germany (n=5), France (n=4) and the UK (n=3) were interviewed between May 2021 and September 2022. Participants had a mean±SD age of 51.8±13.1 years; 60.7% (n=17) male. The majority (78.6%; n=22) were SOT recipients. Refractory CMV was the most common type of difficult-to-treat CMV (n=11; 39.3%). CMV infection was reported as moderate to very severe by 17 (60.7%) participants. Of 26 CMV-related signs and symptoms (table) and 80 impact on life (table/figure) concepts, participants reported tiredness (60.7%), fever (53.6%), lack of physical energy (64.3%), and anxiety (42.9%). A further 23 and 20 concepts were related to disease or treatment burden, respectively.
Conclusions: Further research is needed on the impact of more effective and tolerable anti-CMV therapies on patients' perspectives of symptoms and emotional, physical and social well-being.

Table. Most frequently reported, most important to improve and most bothersome concepts describing signs and symptoms and impact of difficult-to-treat post-transplant CMV, as reported during semi-structured interviews

Number (%) of participants reporting concepts (N=28)*	Signs and symptoms (26 concepts)		Impact (80 concepts across 17 domains)	
Most frequently reported†	Tiredness	17 (60.7)	Lack of physical energy	18 (64.3)
	Fever	15 (53.6)	Unable to complete household chores	13 (46.4)
	Stomach pain	13 (46.4)	Anxiety	12 (42.9)
Most important to improve‡	Stomach pain	4 (14.3)	Anxiety	4 (14.3)
	Tiredness	3 (10.7)	Need to take precautions	3 (10.7)
	Vomiting	3 (10.7)	Lack of physical energy	2 (7.1)
	Nausea	3 (10.7)	Limited activities	2 (7.1)
			Unable to participate in social activities	2 (7.1)
Most bothersome§	Tiredness (n=17)	11 (64.7)	Unable to complete household chores (n=13)	5 (38.5)
	Stomach pain (n=13)	8 (61.5)		
	Body aches (n=11)	6 (54.5)	Anxiety (n=12)	4 (33.3)
	Fatigue (n=9)	6 (66.7)	Lack of physical energy (n=18)	3 (16.7)

*The denominator for Most bothersome differs between concepts as only those participants who reported a particular symptom were also asked to report on the bothersomeness of that symptom. †3 most frequently reported concepts. ‡4–5 most frequently reported 'most important to improve' concepts. §4 most frequently reported 'most bothersome' concepts, rated 7–10, on a scale of 0-10, where 10 is most bothersome.

Figure. Number of participants (out of 28 total) reporting impact of difficult-to-treat post-transplant CMV by domain



*Excludes data for following 4 domains with concepts reported by <5 participants: partner/spouse relationships, sexual function, caregiver responsibilities, ability to enjoy life. †Adaptations required to daily activities (eg, need to take precautions, change diet). ‡Impact on cognitive function (eg, difficulty thinking, unable to focus). CMV, cytomegalovirus; k, number of concepts.

LBP10 CAN CT ANGIOGRAPHY REPLACE RENAL SCINTIGRAPHY FOR PREDICTION OF SPLIT RENAL FUNCTION IN PREOPERATIVE LIVING KIDNEY DONOR ASSESSMENT?

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Background: In living donor kidney transplantation, the decision regarding which donor kidney to retrieve is based on anatomy and split renal function (SRF). The study aim was to compare split renal volume (SRV) and SRF measured on CT angiograms (CTA) and that of SRF of renal scintigraphy to predict donor residual single kidney function.
Methods: Retrospective monocentric study including all consecutive patients considered and assessed for living donor nephrectomy between 01/2005 and 05/2022. To determine SRV on CT, regions of interest (ROI) were drawn over kidneys using a semi-automatic interactive algorithm, and SRV was expressed as percentage (%). For each kidney, renal enhancement (E) was calculated as the difference between CT numbers of all ROIs from enhanced and unenhanced series to obtain the SRF (%). SRF was also measured with Tc-99m-MAG scintigraphy. Correlations between these measures were evaluated by linear regression analysis (Pearson correlation coefficient).
Results: A total of 393 patients were included. Mean age was 53 years (SD 12), mean BMI was 25.0 kg/m2 (SD 3.6), and 130 (39.2%) were male. The right kidney was chosen in 185 (47%) cases for donation, because of better function or vascular anatomy. The correlations between CT-SRV/CT-SRF and scinti-SRF of the preserved kidney were low (respectively r=-0.089 and r=0.032). The mean absolute difference of predonation SRF between preserved and donated kidney was lower for CTA than renal scintigraphy (2.4 vs 6.8%, p<0.001).
Conclusions: Morphology (SRV) and function (SRF) derived from CTA alone should not replace functional data (SRF) provided by renal scintigraphy in order to determine which donor kidney to retrieve. These results suggest that kidney volume does not necessarily correlate with kidney function, and each potential donor should benefit from both investigations for anatomy and relative function.

LBP11 OPTIMIZATION OF HLA MATCHING IN KIDNEY ALLOCATIONS, WITH MINIMAL EFFECT ON QUEUE

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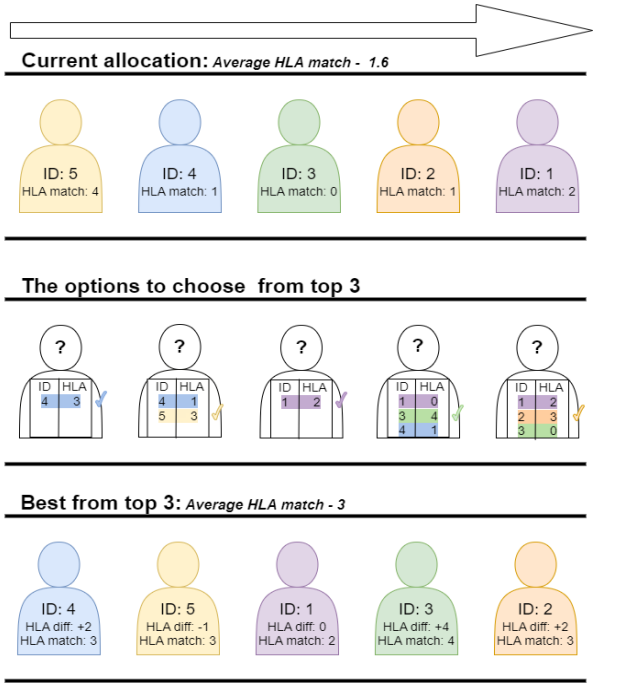
Background: HLA matching between the donor and the recipient can extend the lifespan of the transplanted kidney, and prevent the emergence of donor-sensitized antibodies. In Israel, kidney donations have three origins: altruistic or paired living donations and diseased donors. In all three, the HLA match is only considered as a minor contribution to the allocation score.
Methods: We analyzed recent altruistic, deceased, and paired living donations from two hospitals, with a total of 172, 35, and 28 pairs, respectively. Sensitive recipients were not studied. We computed the match assuming optimal pairing, considering the blood type and age of the donor and recipient, using a linear programming solution. Such a match requires extensive changes to the order. To maximize the match, with a minimal effect on the kidney allocation queue (Top-K method), we tested the optimal match allowing only a choice between the K top candidates of the queue, (K=2 -10), ensuring blood type and age matching. A patient that waited more than K-1 positions automatically receives the next blood type and age matched transplant. We further tested whether it is possible to improve the HLA matching for related donor-patient pairs, by allowing crossover in chain transplants.
Results: In altruistic and disease donors, the optimal matching level is 3-4 times higher when testing either HLA-B&DRB1, or only class II or all 5 loci (Optimal vs Current in table), and keeping into consideration blood type and age limitation. Even when we limit the perturbation, and ensure no one is moved more than 10 positions in the queue, the match level is twice higher, with practically no change to the queue (Top10 in table). The same occurs for related pairs.
Conclusions: Minimal modifications of the kidney allocation queue can improve the HLA match. This method can accommodate any HLA alleles combination that is desired to maximize their match.

		5 loci	Class II	B&DRB1
Altruistic	Current	1.76	0.83	0.44
	Optimal	4.68	2.5	1.92
	Top10	2.51	1.4	0.93
Deceased	Current	2.4	1.26	0.8
	Optimal	3.56	2.03	1.41
	Top10	2.74	1.31	1.11
Paired	Current	3.96	1.6	1.46
	Optimal	4.57	2.28	1.89
	Maximal	10	4	4



Top K method (K = 3). ID is the position in the current queue (1 is top current queue in first row). Middle row – Current donors and their HLA match to each patient. Bottom row rearranged queue by Top3 method.

LBP12 ARTIFICIAL INTELLIGENCE IN PREDICTING PATIENT AND GRAFT SURVIVAL FOLLOWING DECEASED DONOR LIVER TRANSPLANTATION

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Background: Although the Model for End-stage Liver Disease (MELD) score is commonly used to prioritize patients awaiting liver transplantation, previous studies have indicated that MELD score may fail to predict well for the postoperative patients. Similarly, other scores (D-MELD score, balance of risk score) that have been developed to predict transplant outcome have not gained widespread use. These scores are typically derived from linear statistical models. The aim of this study was to compare the performance traditional statistical models with machine learning approaches in predicting survival following liver transplantation using multi-center data.
Methods: Data came from 785 deceased donor liver transplant recipients enrolled in the Korean Organ Transplant Registry (KOTRY, 2014~2019). Five machine learning methods and 4 traditional statistical models were compared for the prediction of survival.
Results: Of the machine learning methods, random forest (RF) yielded the highest area under the receiver operating characteristic curve (AUC-ROC) values (1 month = 0.94, 3 month =0.97, 12 month = 0.92) for predicting survival. The AUC-ROC values of Cox regression analysis was 0.80, 0.89 and 0.84 for 1month, 3month and 12 month posttransplant survival, respectively. However, the AUC-ROC values of the MELD, D-MELD and BAR score were all below 0.70.
Conclusions: Machine learning algorithms such as random forest was superior than conventional cox regression and previously reported survival scores in predicting 1 month, 3month 12 month survival following liver transplantation. Therefore, artificial intelligence may have significant potential in providing assistance with clinical decision making during liver transplantation including matching donors and recipients.

LBP13 PREVALENCE AND CLINICAL SIGNIFICANCE OF PANCREATIC CYSTIC LESIONS IN IMMUNOSUPPRESSED PATIENTS WITH SOLID ORGAN TRANSPLANTATION

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Background: Solid organ transplant recipients have an increased risk of cancer due to immunosuppressive therapy. Pancreatic cystic lesions (PCLs) are increasingly being detected, some with malignant potential. We aimed to determine the prevalence of these lesions and describe their clinical course in these patients.
Methods: We identified the presence of pancreatic cystic lesions in a retrospective cohort of 804 consecutive solid organ transplant recipients from 2009 to 2019 and compared lesion characteristics at initial and follow-up imaging, when available. We also compared these features with an immunocompetent control group encompassing patients under surveillance for greater than 12 months and were matched for age and sex.
Results: There were 15 patients in the study group and 60 patients in the control group. Among the solid organ transplant recipients with PCLs, there were 7 and 8 patients undergoing liver and kidney transplantation, respectively. Lesion prevalence was 1.86% (15/805). Median diameter of the largest lesion was 20 mm (range: 0.2–60 mm) and most lesions were benign (9/15, simple cyst or pseudocyst). During follow-up imaging, the cysts size remained stable in 79.7%, increased in 6.6%, and decreased in 13.7%. Among patients diagnosed with IPMN (6/15), worrisome features was noted in one patient at the time of cyst diagnosis. However, due to multiple comorbidities the patient received only conservative management. There were no significantly different features including the rate of size increase or the development of worrisome features between the study and control group (p<0.05).
Conclusions: Pancreatic cystic lesions are somewhat common in solid organ transplant recipients. In lesions without high-risk features, the development of features worrisome for cancer is rare. These lesions can be managed conservatively, and their presence should not affect transplant eligibility.

LBP14 IMPROVED PRESERVATION BY OMNISOL COMPARED TO RED BLOOD CELL PERFUSATE FOR 6 HOUR NMP OF WARM ISCHEMIA-DAMAGED PORCINE KIDNEYS

Laura Zarnitz[1], Benedict Doorschodt*[2;2], Lisa Ernst[2], Tamara Fechter[2], Alexander Theissen[1], René Tolba[2], Christian Bleilevens[1]
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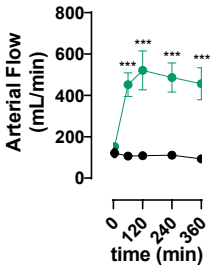
Background: Normothermic machine perfusion (NMP) is increasingly applied in clinical practice since it holds the potential of increasing the viability of marginal grafts. NMP offers the possibility of real-time viability assessment and therapeutic intervention prior to transplantation, in contrast to hypothermic preservation methods. A readily available cell-, albumin- and oxygen carrier-free solution could enhance employment of NMP and potentially prevent adverse effects, such as inflammation transfusion reactions and hemolysis, associated with packed red blood cell (pRBC)-based perfusates.
Methods: In this study, the novel cell- and oxygen carrier-free organ preservation solution Omnisol for cold storage and hypothermic machine perfusion was compared to a clinically established pRBC-based perfusate (pRBC) protocols. In the Omnisol group, porcine kidneys were cold stored in Omnisol for 24 h, followed by NMP using the same solution and compared to NMP using pRBC, directly after explantation. All kidneys sustained 20 min of warm ischemic damage and NMP was applied at 75 mmHg using 1L/min oxygenation at 37°C.
Results: In the Omnisol group, renal blood was over 3-fold higher after 1 h of NMP (p<0.001) and the functional parameters intrarenal resistance, fractional excretion of sodium and potassium were significantly better during 6 h NMP compared to the pRBC group. The damage parameters AST and LDH were over 3-fold lower after 1 h in Omnisol (p<0.001) and oxygenation (arterial pO2) was similar to pRBC.
Conclusions: Omnisol solution demonstrated improved preservation quality for cold storage followed by NMP compared to direct NMP using a pRBC-based perfusate during 6 h NMP of warm ischemia-damaged porcine kidneys.



LBP15 SINGLE-CELL RNA-SEQ REVEALS THE HETEROGENEITY OF MICROENVIRONMENT BETWEEN BKPYVN AND TCMR

Gang Huang*[1], Feng Yang[2], Xutao Chen[1], Hui Zhang[2], Siyan Meng[1], Guodong Zhao[2]

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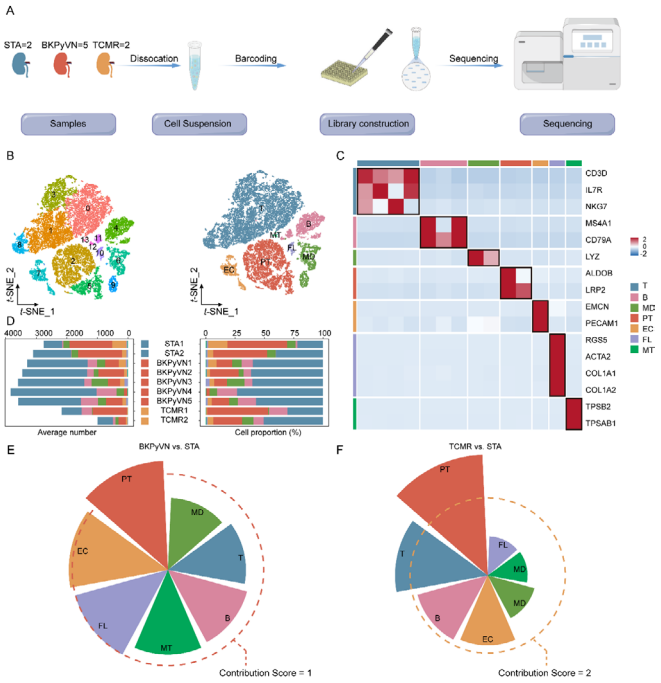
Background: Despite requiring opposite treatments, BKVN and T cell–mediated rejection (TCMR) can exhibit overlapping clinical and histological features, presenting a diagnostic dilemma with significant implications for patient management. Novel tools are thus needed to help confirm the diagnosis and predict response to treatment. Then, we aimed to distinguish the BKPyVN and TCMR from microenvironment by single-cell RNA sequencing (scRNA-seq).
Methods: Single-cell RNA-seq was performed on 2 stable grafts (STA), 5 BKPyVN, and 2 TCMR (Fig. A).
Results: 41,565 single cells were clustered into fourteen major clusters. With marker-based annotations, seven major cell types were identified in STA, BKPyVN and TCMR groups (Figs. B and C). We found that the BKPyVN and TCMR microenvironments had a similar cellular composition (Fig. D). However, there were slight variations in the percentage of cells in each microenvironment. Moreover, we found the PT exhibited the highest contribution score among all subsets, indicating that it was crucial for aggravating disease progression in both BKPyVN (Fig. E) and TCMR (Fig. F). Specifically, in BKPyVN, we noticed that EC and stromal cells tended to play a subdominant role, while immune cells took on that role in TCMR. These results suggested that we could distinguish the BKPyVN and TCMR from heterogeneity of microenvironment.
Conclusions: The microenvironment heterogeneity bears significant implications for distinguishing BKPyVN and TCMR, despite the clinical convergence of their phenotypes. These findings presented a substantial advancement in diagnostic tools, ultimately facilitating the precise identification and management of these intricate kidney transplant-related disorders.



LBP16 OUTCOMES FOR DECEASED DONOR KIDNEY TRANSPLANT FOLLOWING DONOR CARDIAC ARREST: A NATION-WIDE POPULATION-BASED COHORT STUDY

Dimitra Limnatitou[1], Angeliki Kosti*[1], Ffion Dewi[1], Christine Biela[2], Kamlesh Patel[3], Adnan Sharif[3], James Hodson[4], Jay Nath[1], Vasileios Mavroeidis[1]

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Background: Kidneys from donation after cardiac arrest (DACA) donors are frequently used for transplantation. However, whilst DACA is generally considered a detrimental transplant marker, there is currently limited evidence for this hypothesis. As such, the aim of this study was to determine whether DACA is an independent risk factor for outcomes in deceased donor kidney transplant.
Methods: A nation-wide population-based cohort study was performed using prospectively collected data from the National Health Service Blood and Transplant service in the United Kingdom between January 2016 and December 2020 for all deceased donor kidney transplants. The effect of DACA status was determined using multivariable Cox or binary logistic regression models, which additionally adjusted for potential confounders.
Results: A total of 11,375 transplant recipients (from N=6,155 donors) were included, of whom 43.9% received kidneys from DACA donors. Following cardiac arrest kidneys were significantly more likely to be donated after circulatory death (48.1% vs. 33.5%, p<0.001), but were significantly less likely to be extended criteria organs (29.1% vs. 46.8%, p<0.001). After adjustment for confounders, DACA was not found to be a significant independent predictor of either death-censored graft survival (hazard ratio [HR]: 0.83, 95% CI: 0.67-1.02, p=0.075), or patient survival (HR: 1.04, 95% CI: 0.88-1.23, p=0.644). Rates of initial graft dysfunction (i.e. delayed graft function or primary non-function) were similar for DACA and non-DACA recipients on univariable analysis (25.0% vs. 25.2%, p=0.123). However, after adjustment on multivariable analysis, rates were found to be significantly lower in DACA recipients (odds ratio: 0.84, 95% CI: 0.75-0.94, p=0.002).
Conclusions: There is no evidence on this nation-wide population analysis that donor cardiac arrest is a marker of poor outcome for kidney transplant, which could provide reassurance to clinicians. However, these results should be interpreted within the context of current transplant organ acceptance practice.

LBP17 SURVIVAL BENEFIT OF KIDNEY TRANSPLANTATION IN PATIENTS WITH END-STAGE KIDNEY DISEASE AND PRIOR ACUTE MYOCARDIAL INFARCTION

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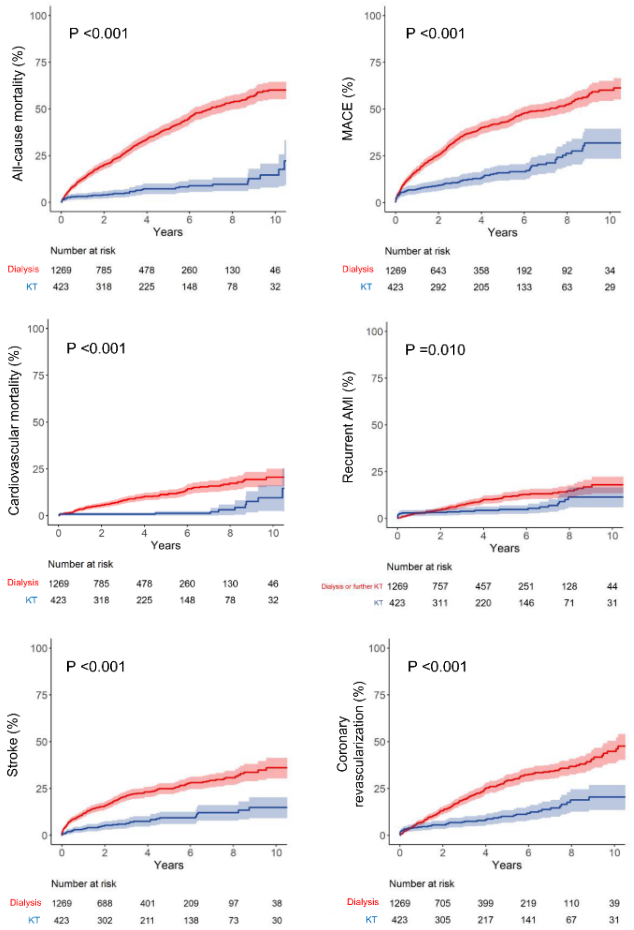
Background: Patients with end stage kidney disease (ESKD) and a previous acute myocardial infarction (AMI) have less access to KT.
Methods: Data on ESKD patients with an AMI history who underwent first KT or dialysis between January 2007 and December 2018 were extracted from the Korean National Health Insurance Service. Patients who underwent KT (n=423) were chronologically matched in a 1:3 ratio with those maintained on dialysis (n=1,269) at the corresponding dates, based on time-conditional propensity scores.
Results: The 1-, 5-, and 10-year cumulative incidences for all-cause mortality were 12.6%, 39.1%, and 60.1% in the dialysis group and 3.1%, 7.2%, and 14.5% in the KT group. Adjusted hazard ratios (HRs) of KT versus dialysis were 0.17 (95% confidence interval [CI], 0.12–0.24; *P*<0.001) for mortality and 0.38 (95% CI, 0.23–0.51; *P*<0.001) for major adverse cardiovascular events (MACE). Of the MACE components, KT was most protective against cardiovascular death (HR, 0.23; 95% CI, 0.12–0.42; *P*<0.001). Protective effects of KT for all-cause mortality and MACE were consistent across various subgroups, including patients at higher risk (e.g., age >65 years, recent AMI [<6 months], congestive heart failure).
Conclusions: KT is more beneficial than maintenance dialysis in reducing all-cause mortality and MACE in ESKD patients with a prior AMI.

Kaplan–Meier curve analyses for cumulative incidence of each outcome. (A) All-cause mortality, (B) MACE, (C) cardiovascular mortality, (D) recurrent AMI, (E) stroke, and (f) coronary revascularization. Dialysis group data are shown in red and KT group data are shown in blue. MACE is the composite outcome of cardiovascular mortality, non-fatal AMI, and stroke. AMI, acute myocardial infarction; KT, kidney transplantation; MACE, major adverse cardiovascular events.



LBP20 FIVE-YEAR KIDNEY FUNCTION AND OUTCOMES IN ASIAN KIDNEY TRANSPLANT RECIPIENTS CONVERTING FROM TWICE-DAILY TO ONCE-DAILY TACROLIMUS

Jaeseok Yang[1], Su Hyung Lee[2], Hải An Hà Phan[3], Seung Yeop Han[4], Yoshihiko Watarai[5], Mohamed Soliman*[6]

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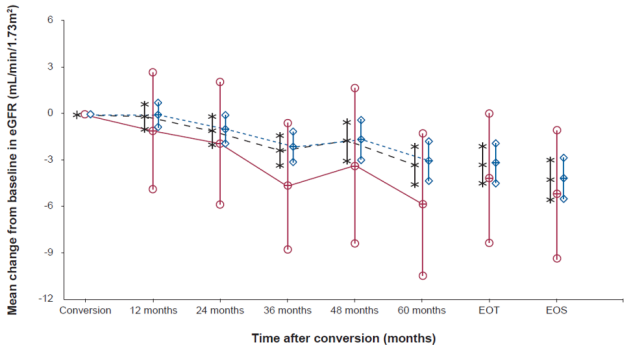
Background: Organ transplantation criteria and capabilities may differ in Asia compared to Europe and North America. Conversion from twice-daily (BID), immediate-release tacrolimus (IRT) to once-daily (OD), prolonged-release tacrolimus (PRT; Advagraf®, Astellas Pharma Europe, Ltd.) is associated with improved short-term outcomes in kidney transplant recipients (KTRs). This subgroup analysis of a prospective, global, non-interventional CHORUS study (NCT02555787) assessed 5-year long-term clinical outcomes in KTRs enrolled in Asian countries who converted from BID IRT to OD PRT.

Methods: The study enrolled KTRs (≥18 years, N=4389) converting to PRT according to the treating physician's judgment. KTRs were grouped by time of conversion post-transplant to early (≤6 months) converters (ECs) and late (>6 months) converters (LCs). The primary endpoint was the change in renal function (measured by estimated glomerular filtration rate, eGFR) from conversion up to 5 years. Secondary endpoints included graft and patient survival, tacrolimus dose and trough levels, emergence of donor-specific antibodies (DSA) and safety.

Results: Of the full analysis set (FAS, N=4028 patients), 887 were from Asian countries (92 ECs; 795 LCs). Most patients (59.0%) were male, with a mean age of 49.5 years and a mean eGFR of 66.80 mL/min/1.73m^2 at conversion. There was a decreasing trend in eGFR post-conversion in the Asian cohort (**Figure**). At 5 years post-conversion, the mean change in eGFR from baseline was -3.35 for the Asian cohort (*vs* -1.36 in FAS). The median PRT dose remained stable at 3.0 mg/day throughout the study. The median tacrolimus trough level was 4.9 ng/mL at 5 years post-conversion (**Table**). At 5 years post-transplant Kaplan-Meier estimate of patient survival was 98.9% and graft survival was 97.8%. Overall, 1.4% of patients who were negative prior to or at conversion had DSA occurrence post-conversion. At study end, 78.2% of patients remained on PRT. Adverse events (AEs) were reported in 58.1% of enrolled Asian patients; 9.1% had ≥1 PRT-related AE.

Conclusions: There was a decreasing trend in renal function in the Asian cohort. Patient and graft survival estimates in the Asian cohort were similar to the overall study group.

Figure. Mean change from baseline in renal function (eGFR)*



Number of patients

Overall	887	820	786	747	713	654	875	887
Early converter	92	81	76	69	67	66	88	92
Late converter	795	739	710	678	646	588	787	795

Mean eGFR change from baseline is displayed with 95% CI.

*The eGFR values were calculated according to the Modulation Diet in Renal Disease (MDRD)-4 formula
CI, confidence interval; eGFR, estimated glomerular filtration rate; EOS, end of study; EOT, end of treatment.

Early converter
Late converter
Overall

Table. PRT dose, and tacrolimus trough levels (FAS, Asian cohort)*

Asian cohort	Early converters (N=92)			Late converters (N=795)			Total (N=887)		
PRT dosage, mg/day	n	Mean (SD)	Median (min–max)	n	Mean (SD)	Median (min–max)	n	Mean (SD)	Median (min–max)
At conversion	92	4.07 (2.28)	4.00 (1.0–10.0)	795	3.12 (1.60)	3.00 (1.0–11.0)	887	3.21 (1.71)	3.00 (1.0–11.0)
60 months post-conversion	59	3.26 (1.75)	3.00 (1.0–9.0)	528	3.44 (1.84)	3.00 (0.5–12.0)	587	3.42 (1.83)	3.00 (0.5–12.0)
Tacrolimus trough levels, ng/mL	n	Mean (SD)	Median (Q1–Q3)	n	Mean (SD)	Median (Q1–Q3)	n	Mean (SD)	Median (Q1–Q3)
6 months prior to conversion	10	10.47 (8.47)	7.00 (6.5–12.4)	733	5.84 (2.44)	5.50 (4.2–7.1)	751	5.95 (2.82)	5.50 (4.2–7.2)
At conversion	91	7.27 (2.67)	7.00 (5.2–9.5)	795	6.00 (2.74)	5.60 (4.3–7.2)	886	6.14 (2.76)	5.70 (4.4–7.4)
12 months post-conversion	91	5.28 (2.23)	4.80 (3.9–6.4)	792	4.87 (2.08)	4.80 (3.5–5.9)	883	4.91 (2.09)	4.80 (3.5–6.0)
24 months post-conversion	82	4.93 (2.09)	4.45 (3.6–5.6)	753	4.79 (1.94)	4.70 (3.4–5.9)	835	4.80 (1.96)	4.70 (3.4–5.9)
36 months post-conversion	75	5.05 (2.28)	4.70 (3.6–5.9)	730	4.94 (1.97)	4.70 (3.6–6.0)	805	4.95 (2.00)	4.70 (3.6–6.0)
48 months post-conversion	73	5.15 (2.02)	4.90 (3.6–6.2)	707	4.91 (1.87)	4.70 (3.7–6.0)	780	4.93 (1.88)	4.80 (3.7–6.0)
60 months post-conversion	72	5.46 (2.14)	5.10 (4.3–6.5)	638	5.07 (2.12)	4.80 (3.7–6.2)	710	5.11 (2.12)	4.90 (3.7–6.2)

*The full analysis set (FAS) comprised all enrolled patients who were converted to PRT, had at least one primary endpoint assessment at baseline and 1 year after conversion or later, and did not violate the terms of the protocol.
FAS, full analysis set; IRT, immediate-release tacrolimus; PRT, prolonged-release tacrolimus; SD, standard deviation.

LBP21 NO NUMBER TOO HIGH FOR KIDNEY TRANSPLANT RECIPIENTS - UNVEILING THE IMPACT OF A SIXTH MRNA VACCINE DOSE

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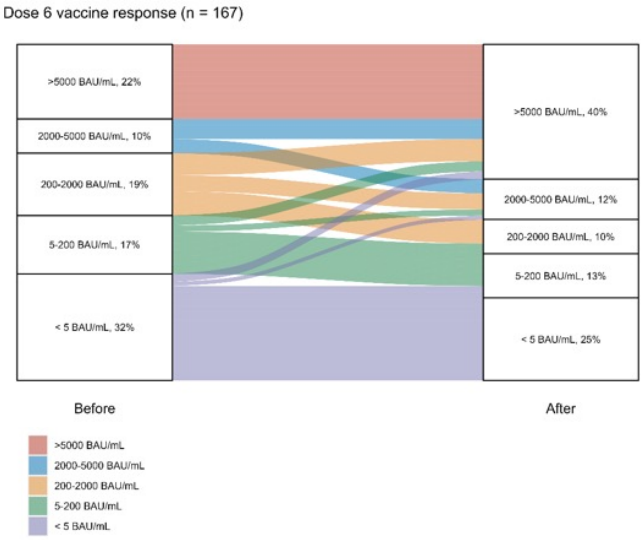
Background: During the initial phase of the persisting COVID-19 pandemic mortality was very high in kidney transplant recipients (KTR). In the general population, vaccines were the most important efforts in stopping the pandemic. In KTR a low humoral response to primary vaccination against SARS-CoV-2 was soon detected and additional booster-doses were recommended. However, a significant proportion of KTR remain vaccine unresponsive or with very low measurable antibody (AB) levels even after receiving up to five previous doses. Should we continue vaccinating KTR with additional doses? We here demonstrate the impact of a sixth vaccine dose on humoral vaccine response in KTR.
Methods: We included KTR (>18 years) who had previously received five doses of the mRNA-based vaccines Spikevax® (Moderna) or Comirnaty® (Pfizer) with no physician- or self-reported infection with SARS-CoV-2. The level of SARS-CoV-2 IgG anti-S AB were quantified by an in-house flow cytometry method 4-6 weeks after vaccination. The measured AB response after dose 5 was used as a baseline for evaluating the effect of dose 6. All patients were on a triple immunosuppressive regimen consisting of calcineurin-inhibitors, mycophenolate, and prednisolone.
Results: Of the 1168 KTR with measured vaccine response after dose 5, we included 167 whom so far have received dose 6 and measured response after 5 [4, 6] weeks. This cohort had a median [IQR] age of 70 [63, 75] years, 59% male, and were 8 [4, 15] years post-transplantation (66% with deceased donor). Following the sixth dose, median AB concentration increased from 261 [1, 3733] to 2268 [2, 12039] binding antibody units per milliliter (BAU/mL), and the proportion of individuals with no previous vaccine response (<5 BAU/mL) was reduced from 32% to 25% (Figure 1). Additionally, there was a substantial increase in the proportion of individuals with high response (>5000 BAU/mL) from 22% to 40%. No adverse events to vaccination were reported.
Conclusions: Our study reveals that a sixth dose of the mRNA-based COVID-19 vaccines may further protect KTR by decreasing the proportion with no humoral vaccine response and enhance the response in previous low or poor responders. This is in line with previous observations following dose 3, 4, and 5, and as such we recommend continued vaccination in non- to low-responders.



LBP22 EXPLORING THE MOLECULAR PATHWAYS OF INTRACRANIAL ANEURYSM FORMATION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE USING PROTEOMIC ANALYSIS

Jin-Myung Kim*[1], Sung Shin[1], Hye Eun Kwon[1], Joohee Jung[1], Hee-Sung Ahn[2], Kyunggon Kim[2,3], Hyunwook Kwon[1], Youngmin Ko[1], Young Hoon Kim[1]

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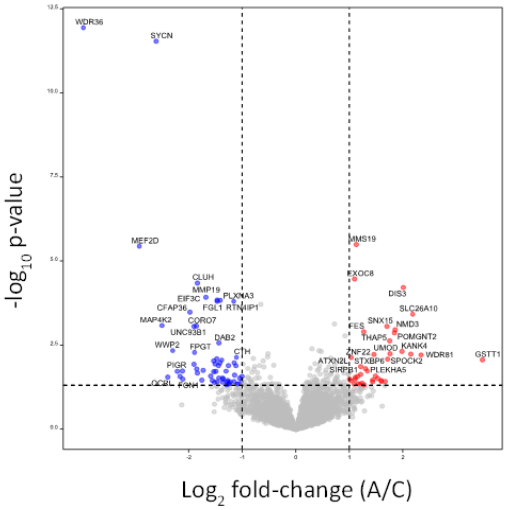
Background: Intracranial aneurysm (IA) frequently coincides with autosomal dominant polycystic kidney disease (ADPKD), exhibiting incidence rates nearly 10 times higher than the general population. However, the exact mechanism of how these two conditions are related remains unclear. This study aims to identify mechanisms behind IA occurrence in ADPKD patients using proteomics and to discover potential protein biomarkers for early diagnosis.
Methods: Pre-kidney transplantation ADPKD patients underwent cranial CT and/or MR angiography, with findings dictating assignment to either a control group (ADPKD without IA, n=20), an IA group (ADPKD with IA, n=7), or an indeterminate group (n=2). During transplantation, bilateral nephrectomy was performed and native renal arteries were sampled for proteomic analysis via mass spectrometry. Differentially expressed proteins were subjected to bioinformatic analysis and a protein-protein interaction network analysis.
Results: Seven proteins showed significant variation between IA and control groups, with three proteins upregulated (DIS3, MMS19, EXOC8) and four downregulated (CLUH, SYNC, MEF2D, WDR36) in IA group (Log_2 fold change (FC) >2 and false discovery rate [FDR] q-value <0.05). One protein, RAB6A, showed increased expression in indeterminate group (Log_2 fold-change of 1.97 and an FDR q-value of 0.048). These proteins correlated with pathways implicated in IA development, such as exocytosis, inflammation, extracellular matrix remodelling, and apoptosis. Additionally, links were found between protein expression and clinical measurements (bilirubin, prothrombin time, platelet count), suggesting potential as early diagnostic markers.
Conclusions: This study is the first to employ renal artery samples to study underlying mechanisms for IA in ADPKD patients by proteomics. We identified novel candidate markers that are either upregulated or downregulated in the IA group compared to the control group. These candidate proteins will undergo further validation through Western blot and immunohistochemistry analysis and may ultimately be used as biomarkers of disease progression in clinical trials.

Figure 1. A volcano plot based on fold change (Log2) and P value (Log10) of all proteins identified in the analysis.



LBP26 ADVANCED MULTIPLEX FLUORESCENCE MICROSCOPY OF AN EXPERIMENTAL PORCINE LUNG TRANSPLANT MODEL

Sandra Lindstedt[1], Qi Wang[1], Anna Niroomand[1], Martin Stenlo[1], Leif Pierre[1], Snejana Hyllen[1], Franziska Olm[1], Nicholas Bechet*[1]

[1]BMC - Biomedical Center, Lund, Sweden

Background: Experimental lung injury and transplantation models in large mammals are an important translational tool for exploring novel lung therapies. However, understanding the complex spatial and morphological changes that arise in injury, after transplantation, and after a given treatment, is a challenge. Current imaging readouts lack the sensitivity, resolution and multiplex capacity to explore lung spatial biology, particularly in human and large animal models.
Methods: Lung tissue biopsies were taken from porcine lung tissue after acute lung injury with gastric aspiration, ex vivo lung perfusion and transplantation to a recipient. These tissues were used to develop an advanced light imaging pipeline to generate more advanced morphological readouts and build on our understanding of the pulmonary environment after each of these processes.
Results: Through high resolution imaging of the bronchoalveolar scaffold we have developed a novel alveolar morphology readout capable of extrapolating the precise changes that occur in alveolar wall thickness and circularity after injury and transplantation. Furthermore, we have developed the first multiplex advanced imaging pipeline compatible with porcine tissue which reveals discerning quantitative architectural changes across several proteins.
Conclusions: These data represent the inception of a more detailed means to study the molecular mechanisms of acute lung injury and transplantation. Application of this pipeline to broader human and large mammalian transplant research will serve to help us better understand how our exploratory therapies improve graft survival and guide the development of future therapies.

LBP27 "EDTCO" - HOW WE MANAGE THE CRITICAL DONOR AND RECIPIENT SITUATION AFTER THE COVID-19 ERA FROM THE POINT OF VIEW OF A COORDINATOR

Nóra Kovács*[1], Éva Héder[1], Ildikó Madurka[2], Nóra Schönauer[2], Dóra Nagy[1], Levente Bogyó[1], Balázs Gieszer[1], Klára Török[1], Péter Radeczky[1], Áron Ghimessy[1], Anikó Bohács[3], Zsuzsanna Kováts[3], Lajos Kovács[4], Réka Gajdócsi[5], Zoltán Örlős[6], Ferenc Rényi-Vámos[1]

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Background: This presentation focuses on the results of our Lung Transplantation Program from its beginning and what innovations we performed to rebuild our Program after the coronavirus pandemic: We have centralised recipients' evaluation and have simplified the referral process. We also implemented personal visits to the pulmonology clinics and wards as a new feature.
Methods: We made retrospective data analysis of all transplanted patients and all donors between 12.12.2015-27.04.2023. We extracted data from healthcare software, Eurotransplant Statistics Library, Donordata and our transplantation (Tx) databases. We also used data from the National Blood Transfusion Service.
Results: After an uneventful beginning, the Program was still relatively young when a pandemic coronavirus disease spread all around the World. There was a dramatic shortage of donors, and the recipients' condition worsened. The recipients' evaluation process stopped. After the end of the COVID-19 pandemic, it was necessary to reorganise both the recipient and donor sides. In our centrum, we deal with recipient coordination. The donor coordination is organised centrally. Related to this problem on the recipient side, we have visited pulmonologists dealing with end-stage lung patients (148 pulmonology centres). We have simplified the referral protocol for appearing before the Lung Transplant Committee. We have centralised the evaluation process to shorten the examination time and register the recipients on the waiting list as soon as possible. In the last years, we had to accept extended criteria donors (4 other criteria in addition to age), so the Program slowly started again. As a result of these necessary steps, our Program has been restarted after a five-month no-transplant period: the next 1.5 years, we performed 18 transplantations.
Conclusions: As a coordinator, we have a determinant connecting role between the evaluating pulmonology departments and our medical team. We take a crucial part in the recipients' evaluation process and the Lung Transplant Committee from the beginning. We took an important role in centralising and rebuilding our Program. In addition to visiting pulmonology centres, the centralisation of the evaluation process is the solution for having significantly more recipients on our waiting list.

LBP28 EFFECTS OF HYPOTHERMIC MACHINE PERFUSION ON THE ENDOTHELIUM IN HUMAN KIDNEYS

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Background: Despite beneficial effects of hypothermic machine perfusion (HMP) for kidney preservation, HMP may cause injury to the endothelium and the glycocalyx (eGC) that could potentially be detrimental to graft outcomes. This study aimed to assess the extent of endothelial and eGC injury during HMP.
Methods: In this retrospective, observational study (January 2015-December 2021), HMP perfusate and pre-implantation biopsies of HMP-preserved (n=40) and statically cold-stored (SCS)-preserved kidneys (n=20) were collected. Endothelial cell (EC) detachment in perfusate samples was assessed using flow cytometry. Endothelial glycocalyx and -injury markers hyaluronan, syndecan-1, and soluble VCAM-1 were determined in HMP perfusates. Furthermore, glycocalyx-staining wheat germ agglutinin (WGA), CD34, and VE-cadherin were stained in biopsies. Results were compared to SCS-preserved kidneys.
Results: EC-detachment during HMP was limited (0.27% of all living perfusate cells). Endothelial glycocalyx and injury markers hyaluronan (7-fold), syndecan-1 (750-fold), and soluble VCAM-1 (2.5-fold) were significantly increased (all three: $P < 0.001$) at the end of HMP compared to 15 minutes after the start of HMP. Cold preservation time was associated with an increase in hyaluronan ($P = 0.003$) and sVCAM-1 ($P = 0.048$). No correlations were found between the perfusate makers and outcome parameters. Glycocalyx-related WGA positivity in pre-implantation biopsies tended to be lower in HMP-preserved kidneys compared to SCS-preserved kidneys ($P = 0.065$). In addition, WGA was significantly inversely correlated with functional delayed graft function (fDGF; $P = 0.047$).
Conclusions: Although EC detachment seems limited, HMP is accompanied by glycocalyx shedding which is associated with an increased risk of fDGF. However, markers of eGC loss in the perfusate were not associated with graft outcome parameters in this small cohort.

LBP30 HEPATITIS B SURFACE ANTIGEN POSITIVE DONORS FOR LIVER RECIPIENTS WITH HEPATOCELLULAR CARCINOMA: A SINGLE CENTRE EXPERIENCE

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Background: Due to the severe shortage of the donor pool, the use of hepatitis B surface antigen-positive donors is a possible strategy to increase the donor pool, but there are few data about the outcomes in liver recipients with hepatocellular carcinoma (HCC) and their recurrence rate.
Methods: Patients undergoing liver transplantation (LT) between January, 2004, and November 2022, were retrospectively evaluated. 17 patients (1,5%) with HCC, received the graft from hepatitis B surface antigen positive (HBsAg)-positive deceased donors
Results: All patients were male and Milan IN. Median time of follow up was 63±5 months. Median MELD was 16. Seven (41%) recipients had not an HBV-related liver disease. Only one patient before LT had hepatitis B surface antibodies. Three patients had an HBV/HDV cirrhosis. In all recipients HBV DNA was suppressed at the time of LT. Eight (47%) patients did a prophylaxis with HBV-specific immunoglobulins after LT. At 1 – 3 and 5 year in all the recipients, hepatitis B surface antigen positivity was recorded. Only one patient developed hepatitis B surface antibodies but was immunized before LT. HBV DNA was detected in one patient at 1 and 3 years, but they were responsive to antiviral treatment. Only one patient had HCC recurrence. Overall survival at 1-3 and 5 year was 76,5%.
Conclusions: We suggest that the use of HBsAg positive donors is safe and in our cohort of HCC transplanted patients, only one experienced HCC recurrence. Moreover, it would be fundamental to immunize all patients before LT.

LBP31 ACTIVE PARTICIPATION DURING THE EDUCATIONAL PROCESS OF DONATION AFTER CIRCULATORY DEATH AT EXTRA CORPOREAL MEMBRANE OXYGENATION INTENSIVE CARE UNITS

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Background: Participatory Action Research (PAR) is a theoretical approach offering experimentation with evidence-based and people-based inquiry and are promoting the grounding of knowledge in human agency and social history. Intervention research examines the effects of an intervention with an outcome of interest, in this case how active participation from ICUnurses can frame a feeling of participation, secureness and curiosity for the caring team in the complex caring situation of Donation after Circulatory Death (DCD) at Extra Corporeal Membrane Oxygenation (ECMO) - ICU:s.
Methods: Aim: Evaluate active participation during the education process of DCD, and if active participation can frame a feeling of comfortability and secureness for the ICU nurses in the caring situation of an potential DCD donor patient with on-going ECMO-treatment. • Can active participation from the ICUnurse during educational process lead to an experience of comfortably and secureness in the complicated process of DCD and ECMO-treated patients? • Can a specific made education plan lead to a feeling of participation, secureness and curiosity for the complex process of DCD and ECMO-treated patients. A quasi-experimental, nonequivalent two group design. One experimental group and one active control group. A quantitative non-standardized questionaries will collect data before and after the intervention
Results: Caring of a potential organ donor patient is described as a complex and multidimensional situation. ICUnurses' cares for the patient as a patient with an extreme need of intensive treatment. When treatment goes from lifesaving for the patient himself to a situation with focus on medical treatment for the organs for someone else, the dimension of caring changes, and a deeper level with a need for reflection and contemplation for the ICUnurse is illuminated.
Conclusions: The DCD-process and ECMO-treatment is an un-explored area, which leads to a huge need for further dissemination of this type of studies worldwide. By create an education plan managed by ICUnurses', for ICUnurses' by using their active participation, the process hopefully manage a new way to avoid ethical challenges and dilemmas during implementation of complicated processes at ECMO-ICU:s' worldwide in the future.

LBP32 CHANGES IN ENDOGENOUS PEPTIDES IN DCD KIDNEY BIOPSIES ASSOCIATE WITH PROLONGED WARM ISCHAEMIA

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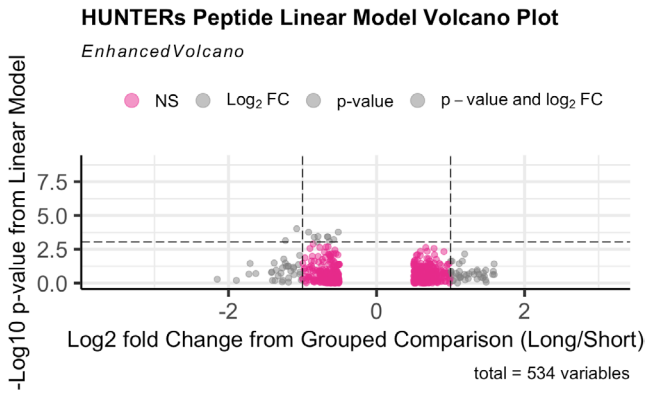
Background: Warm ischaemia (WI) is an inherent part of the donation after circulatory death (DCD) pathway. Functional WI (fWIT) starts when donor blood pressure drops below 50 mmHg until *in-situ* cold perfusion, and associates with organ hypoperfusion, and a switch to anaerobic glycolytic metabolism. DCD kidneys have increased incidence of delayed graft function and early graft loss posttransplant, however the molecular implications of WI on kidney quality remains under-explored. Here, we investigate protein degradation and biological dysregulation in pretransplant kidney biopsies from DCDs with prolonged fWIT.
Methods: Pretransplant kidney biopsies (n=42) from DCDs were selected from the Quality in Organ Donation (QUOD) biobank. Two experimental groups were defined as short (<25 minutes; n=15) and long (30-120 minutes; n=27) fWIT. Biopsies were analysed using High-efficiency Undecanal-based N-TERmini enrichment (HUNTER) degradomics. Endogenous peptide sequences were used to identify probable degraded proteins and cleaving proteases, using MaxQuant, Uniprot and the MEROPS database. Reactome pathway analysis was used to compare degradome data between long and short fWIT groups.
Results: Degradomics mass spectrometry analysis identified 2,563 peptides matched to 1,053 proteins. Peptide cleavage sites linked to 63 proteases, likely causing protein degradation and generation of the identified peptides. Comparison of peptide and protease activity between long vs short fWIT groups indicate that 78 proteins were differentially degraded and signposts to the activity of 7 key proteases. Differences in protein cleavage patterns and protease activity indicate that dysregulated pathways include metabolism and oxygen transport, catalytic activity, and degradation of cytoskeletal and extracellular matrix (ECM). Correlation analysis of peptidomes against the continuum of fWIT suggest that anchoring of cytoskeletal and ECM proteins, markers of proximal tubule injury, glycolysis, and kidney repair were impacted (Fig 1).
Conclusions: Our results provide evidence that prolonged fWIT associates with protein degradation that may alter the kidney ECM and cytoskeleton. Further mapping of tissue protein degradation will provide novel insights into the impact of hypoxic injury on donor kidneys.

Figure 1



LBP34 440 CONSECUTIVE HAND-ASSISTED-RETROPERITONEOSCOPIC-DONOR-NEPHRECTOMIES(HARP). A COMPREHENSIVE ANALYSIS OF THE INTRAOPERATIVE CHALLENGES

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Background: This analysis highlights the various pitfalls and challenges encountered in living kidney transplantation. This study aims to evaluate the outcomes and trends within an established living kidney program, providing valuable insights into the effectiveness and advancements in this area of transplantation.
Methods: A retrospective analysis was conducted on a cohort of living kidney transplant recipients who underwent transplantation at a specialized german transplant center between 06/2010 and 06/2023. Relevant data, recipient demographics, donor characteristics, surgical details, post-transplant outcomes, and long- term follow-up, were extracted from prospective database. Statistical analyses were performed to assess graft survival, patient survival. Complications were categorized in vascular, urinary tract associated, device- and donor associated pit falls.
Results: A total of 440 living kidney transplant procedures were included in the study. The mean age of the recipients was 52.8 ± 11 years, with a slight female predominance 58.5% female. All kidney grafts were taken out with hand assisted total retroperitoneous nephrectomy (HARP). 65% (286) were left kidneys. No conversion surgery had to be performed. Time of kidney explantation was 108.4 ± 27.9 min, time of the whole donation surgery 130 ± 27.5 min, warm ischemic time during kidney harvest was 122 sec ± 57, blood loss of the recipients was 49.2 ± 42 ml, 64 donors 16.4 % had multiple arteries and veins. In 228 (51.8%) cases potential pit falls were detected. 102 Vascular-(58.1%), 5 urinary tract- (2.2%), 46 donor- (25.9%) and 13 device associated pit falls (2.9%). If pit falls or deviating procedure were pointed out time of kidney explantation was longer 113 ± 28.52 p <0.001, warm ischemic time during kidney harvest was longer 143 ± 70 sec p <0.001 and blood loss was significant higher 60.1 ± 54.4 p<0.001.
Conclusions: The importance of blood loss, warm ischemia time, and operative time.By addressing these pitfalls, we can strive to improve the overall success and long-term outcomes of living donor renal transplantation and enhance the quality of life for transplant recipients.The importance of blood loss, warm ischemia time, and operative time

LBP36 INCREASED PERCENTAGES OF CD8+DR+ T-CELLS IN PATIENTS WITH DIFFICULT TO CONTROL CMV INFECTION IN SOLID ORGAN RECIPIENTS: A NEW BIOMARKER?

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Background: CMV infection is a barrier to long-term survival after solid organ transplantation (SOT). Although most cases are adequately controlled with antivirals (ganciclovir, valganciclovir, letermovir, maribavir), control of infection is sometimes difficult. The identification of potential immune mechanisms of difficult to control CMV infection (DC-CMV) is of the greatest interest since it can be used to assess biomarkers to detect patients at special risk to evaluate specific therapeutic interventions.
Methods: In a prospective observational study, the immunophenotype of CD4+, CD8+ CD19+, and NK T cells was evaluated in patients diagnosed with DC-CMV (n=20, heart n=9, liver n=6, kidney n=4, lung n=1). The polyfunctional activity of CD4+, CD8+ and NK+ T cells producing IFN-gamma and TNF-alpha was evaluated after stimulation with CMV peptides. The immunophenotypic study included the evaluation of CD8+ T cell activation markers and the maturation status of B lymphocytes. Multiparametric flow cytometry was used. The DC-CMV definition included one or more of the following: Persistent CMV infection, recurrent CMV infection, CMV infection with neutropenia secondary to antivirals, refractory CMV disease or resistant CMV disease. As controls, 14 patients with SOT who were free of any type of infection in the first 3 months after transplantation were included. Study time was at the time of diagnose of DC-CMV after SOT or similar time in controls.
Results: Patients with DC-CMV showed a tendency to a lower percentage of CD8+IFN-gamma+ T cells to CMV IE1 vs controls (0.20 vs 0.53%, p=0.10). The percentage of CD8+DR+ T cells was significantly higher in these patients (60.2 vs 35.9%, p=0.0002). The level of naive B cells was similar in both groups (52 vs 57, p=0.577). In logistic regression CD8+ DR+ >50% was associated with high risk of DC-CMV.
Conclusions: The level of CD8+DR+ cells in peripheral blood could serve as a biomarker of risk for development of DC-CMV post-SOT. Future studies are warranted to validate the potential role of this biomarker in multicentre studies.

LBP37 IMPACT OF DONOR-DERIVED CELL-FREE DNA ASSESSMENT IN MONITORING KIDNEY TRANSPLANT RECIPIENTS: INTERIM REPORT OF A PROSPECTIVE LONGITUDINAL STUDY

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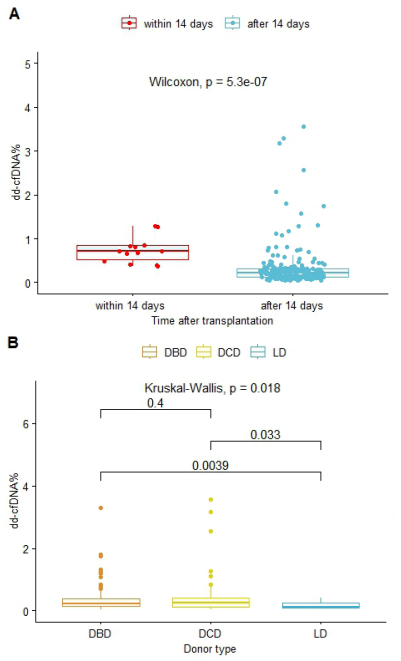
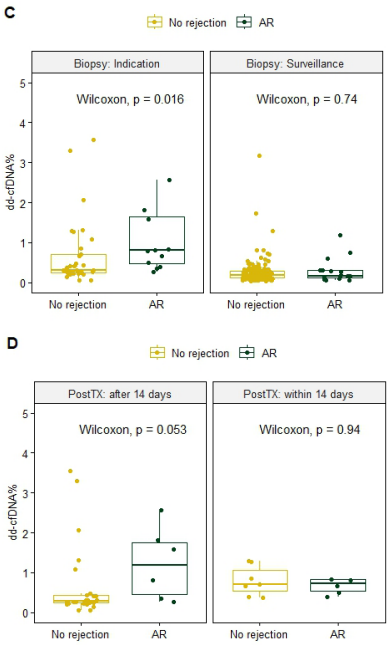
Background: Donor-derived cell-free DNA (dd-cfDNA) is a promising non-invasive biomarker for monitoring kidney transplant (KT) recipients. We aim to evaluate its clinical utility in a prospective cohort of 500 cases.
Methods: Since July 2022, we prospectively collect plasma from each KT recipient immediately prior to renal biopsy, to measure dd-cfDNA, using a locally implemented standardized assay (AlloSeq cfDNA, CareDx, CA), and correlate %dd-cfDNA with allograft and recipient status.
Results: Of the 292/500 samples collected so far, dd-cfDNA has been already measured in 229, with 92.1% of samples passing quality control. The %dd-cfDNA <14 days post-TX (0.71% [0.53-0.85]) was significantly higher than >14 days post-TX (0.21% [0.12-0.32]; $p=5.3x10^{-7}$, Fig.1A). Dd-cfDNA was increased in deceased donor (DD) kidneys, both DBD (0.24% [0.16-0.38]; p=0.004) and DCD (0.24% [0.12-0.4]; p=0.03), compared to living donation (LD) (0.13% [0.1- 0.25], Fig.1B), but not different between DBD and DCD kidneys. The difference between DD and LD kidneys persisted >14 days post-TX (DBD 0.21% [0.15-0.31]; DCD 0.22% [0.11-0.32]; LD 0.13% [0.10-0.25]). Dd-cfDNA was significantly higher at the time of indication biopsies (0.41% [0.26-0.85]) than at surveillance biopsies (0.18% [0.11-0.30]; $p=2.8x10^{-10}$). 13.3% of cases had (borderline) allograft rejection (AR). Dd-cfDNA was higher in AR (0.80% [0.47-1.64]) versus no rejection (0.31% [0.25-0.70]; p=0.016, Fig.1C) in indication biopsies only, which also showed more cases of full-blown AR than surveillance biopsies (17% vs 3%, respectively). Within 14 days post-TX, the inherently higher %dd-cfDNA masked the association between dd-cfDNA and AR. In indication biopsies performed >14 days post-TX, AR was associated with higher %dd-cfDNA (1.19% [0.32-2.00] vs 0.28% [0.23-0.44] in AR vs no rejection, Fig.1D).
Conclusions: Awaiting study completion by end-2023, this interim analysis indicates that, when measured >14 days post-TX, dd-cfDNA could guide whether to perform an indication biopsy. However, within <14 days post-TX, the injury/healing process occurring after TX masks the ability of dd-cfDNA to uncover ongoing AR. The impact of donor type on %dd-cfDNA persists >14 days post-TX. The clinical utility of dd-cfDNA for subclinical AR will be addressed upon study completion.

Figure 1: A. Box and whisker plot showing %dd-cfDNA median levels within and after 14 days post-transplantation. **B.** Box and whisker plot showing %dd-cfDNA median levels in kidney transplant recipients from deceased (DBD and DCD) and living (LD) donation. **C.** Box and whisker plot showing %dd-cfDNA median levels in patients with and without allograft rejection (AR) at the time of indication and surveillance biopsies. **D.** Box and whisker plot showing %dd-cfDNA median levels in patients with and without allograft rejection at the time of indication biopsies performed within and after 14 days post-transplantation. DBD=donor after brain death; DCD=donor after cardiac death.





LBP38 JOINT ALLOTRANSPLANTATION: A SYSTEMATIC LITERATURE REVIEW AND EXPERIMENTAL EXAMINATION OF IMMUNE REJECTION OF CARTILAGE

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Background: Joint allotransplantation (JA) offers substantial promise for the functional and non-prosthetic reconstruction. However, the clinical application of JA is restricted due to immune rejection commonly associated with all forms of allotransplantation. This study aims to offer a comprehensive understanding of the current JA landscape through a systematic review. Additionally, considering cartilage as a critical component of JA, the immune rejection of cartilage was specifically analysed in a porcine VCA model.
Methods: We executed a systematic literature review in line with the PRISMA guidelines, sourcing relevant articles from PubMed. The results were thoroughly analyzed and potential prospects were discussed in-depth. Within the swine heterotopic VCA model, cartilage, including the articular cartilage and meniscus, was collected. Immune rejection of cartilage was analysed.
Results: Our systematic review included 14 articles detailing pertinent developments in JA. At present, most JA research utilizes small animal models, showcasing graft survival and functional restoration with short-term immunosuppression. In human patients, only six knee allotransplantations have been carried out to date, all of which ultimately failed. In our experimental study, histologic examination of cartilage samples showed infiltration of inflammatory cells and tissue destruction, particularly in the meniscus. However, tissue damage was less severe compared to the rejected skin and muscle. Transmission electron microscopy confirmed tissue damage and necrosis in cartilage, skin, and muscle. Immunofluorescent staining highlighted the activation of both innate and adaptive immune systems, with an up-regulation of cell death biomarkers in the rejected cartilage.
Conclusions: Over the past 20 years, research on joint allotransplantation has rarely been pursued due to the scarcity of clinical applications, the complexity of surgical procedures, and the unpredictable outcomes resulting from immune rejection. Our experimental results suggest that cartilage does not possess immunological privilege and undergoes immune rejection alongside skin and muscle in the VCA model, albeit with less severe inflammation, particularly in articular cartilage.

LBP39 ACCESS TO AND RESULTS OF TRANSPLANTS IN CATALONIA; REVIEW FROM THE STANDPOINT OF GENDER

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Background: Different studies have described the existence of inequality based on sex and gender at each stage of the transplant process: Access to the transplant waiting list, Access to transplant once the patient is on the waiting list, and the result of the transplant. Our objective is to review the tendencies in access to and results of transplants in Catalonia, by sex and type of solid organ.
Methods: We evaluated the tendencies in access to solid organ transplant through the correlation between the proportion of recipients and the proportion of active patients on the waiting list for men and women in 4 periods (2014-2015; 2016-2017; 2018-2019; 2021-2022). The results of solid organ transplants were calculated on the basis of survival models; time elapsed from transplant until graft loss, death or end of study (31st of December 2021). The hazard ratios for women were obtained (in comparison with those for men) for each solid organ using the Cox model adjusted for potential confounding factors: donor age, transplant indication, period, urgency and recipient age.
Results: Slight disparities were found in the access of women to transplant among the candidates on waiting list and these were substantially greater among women awaiting a lung transplant in the first period (2014-2015).
Patient survival among recipients of solid organ transplants is higher, in general, for women. In contrast, in the study of graft survival in renal transplant the results were best for men in the age group between 45 and 59 years old (HR=1.26; p=0.049).
Conclusions: In Catalonia there exists a slight disparity in access to lung transplant between men and women, as with the transplant results.
We consider it a priority to continue working on the analysis of the activity and results of donation and transplantation, from a gender perspective.

Table. Patients active on waiting list (WL), transplanted from deceased donors and effective donors by organ type and sex (Woman-W; Man -M), period 2014-2022.

Organ	2014-2015				2016-2017				2018-2019				2021-2022			
	WL[1]	TX[2]			WL[1]	TX[2]			WL[1]	TX[2]			WL[1]	TX[2]		
		Recipient	Donor	Ratio[3]		Recipient	Donor	Ratio[3]		Recipient	Donor	Ratio[3]		Recipient	Donor	Ratio[3]
Kidney	2202	926			2488	1217			2695	1399			2739	1369		
W (%)	36,9	34,7	44,1	0,94	36,9	35,3	42,2	0,96	35,5	34,7	40,0	0,98	37,5	37,6	40,2	1,00
M (%)	63,1	65,3	55,9	1,04	63,1	64,7	57,8	1,03	64,5	65,3	60,0	1,01	62,5	62,4	59,8	1,00
Liver	549	303			534	313			568	371			468	359		
W (%)	28,8	31,0	43,9	1,08	26,0	26,2	45,4	1,01	26,2	27,5	41,5	1,05	29,5	27,6	38,2	0,94
M(%)	71,2	69,0	56,1	0,97	74,0	73,8	54,6	1,00	73,8	72,5	58,5	0,98	70,5	72,4	61,8	1,03
Heart	189	122			172	115			182	141			165	108		
W (%)	21,2	26,2	41,8	1,24	21,5	27,8	46,1	1,29	22,5	22,7	33,3	1,01	25,5	25,9	29,6	1,02
M(%)	78,8	73,8	58,2	0,94	78,5	72,2	53,9	0,92	77,5	77,3	66,7	1,00	74,5	74,1	70,4	0,99
Lung	213	126			236	162			293	224			259	192		
W (%)	45,5	39,7	44,4	0,87	46,2	48,1	51,9	1,04	43,7	45,1	50,4	1,03	44,8	43,2	59,4	0,97
M(%)	54,5	60,3	55,6	1,11	53,8	51,9	48,1	0,96	56,3	54,9	49,6	0,98	55,2	56,8	40,6	1,03

[1] Total of patients active on waiting list at start of period (1st of January) and patients on list throughout the whole period.
[2] Transplants performed during the whole period.
[3] Ratio between percentage of transplanted patients and percentage of patients on waiting list.

LBP40 GRAFT FAILURE AND DEATH AMONG OLDER PRIMARY DECEASED DONOR KIDNEY RECIPIENTS IN THE UNITED STATES

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Background: Induction choice varies widely in older transplant recipients, especially with the challenging senescent immune system. Herein, we report on the association between different types of induction and outcomes of older deceased donor recipients in the United States.
Methods: Between 2000-2022, we analyzed the Scientific Registry of Transplant Recipients for all primary deceased kidney recipients 55 years of age or older. We excluded those who received an unusual induction regimen or were discharged on a regimen other than tacrolimus and mycophenolate mofetil with or without steroids. All transplants were HLA and ABO compatible and received one of the following induction: rabbit anti-thymocyte globulin rATG (n=43097), alemtuzumab (n=20948) or interleukin-2 receptor antagonist IL-2RA (n=16106). Kaplan-Meier curves were generated for death-censored graft failure and recipient survival through ten years from transplantation. The association between induction and outcomes of interest were examined in multivariable Cox Proportional hazard models. Models were adjusted for clinically pertinent donor and recipient factors, while the center was included as a random effect.
Results: Induction with rATG increased while IL-2RA and alemtuzumab use declined (Figure 1). In the univariable Kaplan-Meier analyses (Figure 2), alemtuzumab was associated with the lowest probabilities of death-censored graft survival (log-rank p <0.0001) and recipient survival (log-rank p=0.008). In the multivariable models, compared to rATG, alemtuzumab was associated with 20% increased risk of graft loss [HR 1.20, 95% C.I. (1.12, 1.29), p<0.001] and 7% increased risk of mortality [HR 1.07, 95% C.I. (1.02, 1.12), p<0.001]. IL-2RA was not associated with worse recipients or graft survival compared to rATG.
Conclusion: In this large cohort of older deceased donor kidney recipients, compared to rATG induction, alemtuzumab but not IL-2RA was associated with worse long-term recipients and graft survival.

Figure 1

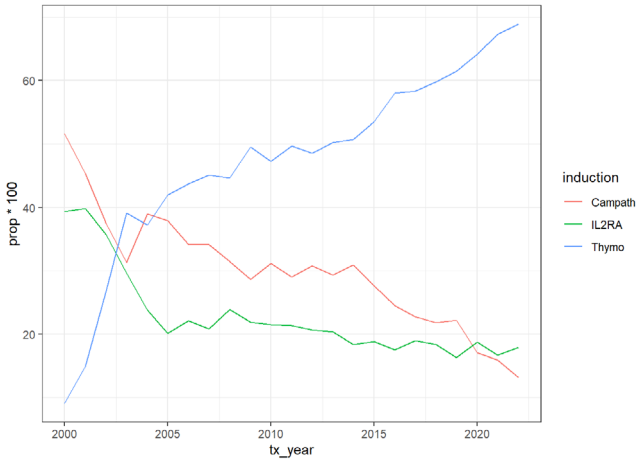
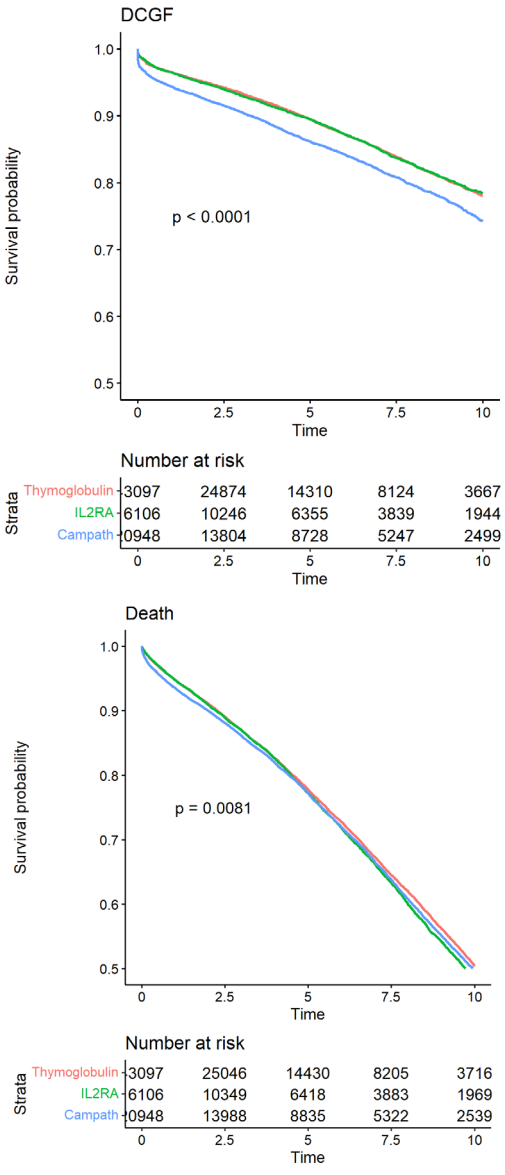


Figure 2



LBP42 ISCHEMIA-FREE LIVER TRANSPLANTATION AS A NOVEL APPROACH TO OPTIMIZE TRANSPLANT OUTCOME IN THE ACUTE-ON-CHRONIC LIVER FAILURE SCENARIO

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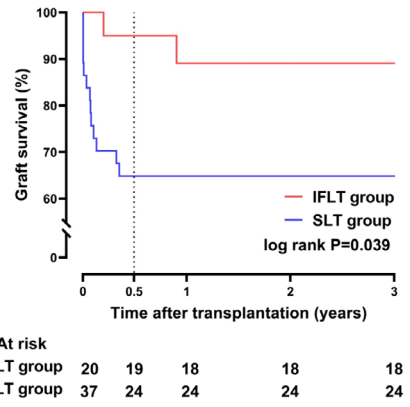
Background: Acute-on-chronic liver failure (ACLF) is a global epidemic in hospitalised patients with high short-term mortality. This study was performed to assess the transplant benefit of ischemia-free liver transplantation (IFLT) in patients with ACLF compared to standard liver transplantation (SLT).
Methods: In this retrospective study, 20 patients received IFLT and 92 patients received SLT were chosen for the entire cohort between July 2017 through October 2022. A 1:2 propensity score matching was performed, 20 IFLT recipients and 37 matched SLT patients were enrolled in propensity-matched cohorts. Donor and recipient characteristics, intraoperative and postoperative outcome between two groups were assessed.
Results: Both in the entire cohort and propensity-matched cohort, patient in the IFLT group had lower incidence of post reperfusion syndrome, faster recovery of coagulation function and consciousness, shorter fasting time, earlier extubation, and shorter intensive care unit stay. Lower incidence of early allograft dysfunction was observed in the IFLT group. What's more, in the propensity matched cohort, the patients in the IFLT group had lower incidence of acute kidney injury grade 3 and less application of renal replacement therapy within 14 days. No primary non-functionoccurred in patients in the IFLT group. In the Kaplan–Meier analysis, the 6-month and 3-year graft survival in the IFLT group were significantly higher than those in the SLT group (P=0.039).
Conclusions:IFLT largely prevent IRI of liver grafts when performed in patients with ACLF, resulting in good transplant outcome with intraoperative stable hemodynamics, less remote organ injury and acceptable survival benefits.

TABLE 4 Postoperative outcome in IFLT and SLT groups before and after propensity score matching

Characteristics	Entire cohort			Propensity-matched cohort		
	ILFT (n=20)	SLT (n=92)	P-value	ILFT (n=20)	SLT (n=37)	P-value
ICU stay time (h)	63.15±16.12	113.50±11.48	0.015	63.15±16.12	136.60±22.64	0.011
Duration of invasive mechanical ventilation (h)	38.20±13.14	82.48±10.50	0.011	38.20±13.14	97.44±21.14	0.021
The time of full consciousness recovery(h)	14.30±4.43	28.19±4.00	0.024	14.30±4.43	32.25±6.88	0.033
Fasting time (d)	4.60±0.68	6.20±0.35	0.039	4.60±0.68	6.82±0.73	0.037
Need vasoconstrictors more than 12 hours, n(%)	2 (10)	45 (49.5)	0.003	2 (5)	20 (54.1)	0.001
Need CRRT within 14 days, n(%)	1 (5)	24 (26.1)	0.079	1 (5)	13 (35.1)	0.028
Peak ALT (U/L)	272.65±42.72	707.23±81.45	<0.001	272.65±42.72	649.78±140.86	0.011
Peak AST (U/L)	545.90±93.14	1950.32±276.21	<0.001	545.90±93.14	2142.53±564.38	0.008
Peak GGT (U/L)	198.95±31.01	255.27±19.26	0.194	198.95±31.01	225.06±29.23	0.564
Peak creatinine (umol/L)	105.10±10.57	125.40±8.99	0.150	105.10±10.57	137.38±14.69	0.080
POD7 bilirubin (mmol/L)	104.68±24.37	179.18±15.98	0.035	104.68±24.37	177.20±27.24	0.053
POD7 INR	1.191±0.040	1.192±0.035	0.994	1.191±0.040	126.24±14.86	0.637
Peak pro-BNP (pg/ml)	1336.40±337.22	2493.61±271.14	0.048	1336.40±337.22	2219.07±308.47	0.068
Peak TnT (ng/ml)	0.05±0.03	0.11±0.21	0.226	0.05±0.03	0.16±0.50	0.052
Bile duct complications, n(%)	4 (20)	21 (22.8)	1	4 (20)	9 (24.3)	0.968
Clinical acute rejection, n(%)	2 (10)	12 (13)	1	2 (10)	4 (10.8)	1
Vascular complications, n(%)	1 (5)	7 (7.6)	1	1 (5)	3 (8.1)	1
AKI, n(%)	6 (30)	44 (47.8)	0.228	6 (30)	20 (54.1)	0.101
AKI grade 3, n(%)	1 (5)	23 (25)	0.094	1 (5)	12 (32.4)	0.043
EAD, n(%)	2 (10)	46 (50)	0.002	2 (10)	17 (45.9)	0.008
PND, n(%)	0	5 (5.4)	0.583	0	2 (5.3)	0.540

Data are presented as mean ± standard error and n (%).

Abbreviations: AKI, acute kidney injury; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EAD, early allograft dysfunction; GGT, y-glutamyl transpeptidase; ICU; intensive care unit; IFLT, ischemia-free liver transplantation; INR, international normalized ratio; NT-pro BNP, N-terminal fragment of the pro brain natriuretic peptide PNF, primary non-function; POD, postoperative day; SLT, standard liver transplantation; TnT, troponin T



The graft survival by Kaplan-Meier survival analysis for patients transplanted for ACLF between the IFLT and SLT groups for 3 years' follow-up in the propensity-matched cohort

141x129mm (300 x 300 DPI)

LBP43 SUCCESSFUL REPLANTATION OF PORCINE FORE-LIMBS 33 HOURS AFTER AMPUTATION USING 24-HOUR EX VIVO PERFUSION

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Background: Delay in replantation or transplantation of limbs after amputation can lead to severe ischemia reperfusion injury (I/R injury), causing extensive muscle tissue damage in the affected extremity, even systemic inflammatory response syndrome and even multiorgan failure. In vascularized composite allotransplantation (VCA) of limbs, I/R injury will lead to an increased allorejection due to priming of the adaptive immune response by inflammation.
Methods: Landrace pigs were used for this study. The left forelimb was surgically amputated and the main artery as well as two large veins were cannulated. The limbs were kept for 9 hours at room temperature and then connected to ECP for 24 hours. ECP was performed at 8°C with a modified histidine-tryptophan-ketoglutarate solution (HTK) solution containing 5% autologous red blood cells. After ECP, the amputated limbs were orthotopically replanted to the pig and perfused with in vivo for 12 hours before euthanasia. Throughout the study, clinical data, blood samples and tissue samples were collected.
Results: Our preliminary data is able to prolong the time window from amputation to replantation to 33 hours while effectively controlling I/R injury. Notably, all replantation surgeries were managed successfully, and the amputated limbs showed significant improvement after 12 hours of in vivo perfusion. Moreover, all the pigs survived without experiencing acute organ failure symptoms. The histological examination and transmission electron microscopy revealed partial edema, but no myofiber necrosis was observed. The ongoing analysis of immune response in tissue and plasma will provide further insights into our findings.
Conclusions: Using cold ECP for 24 hours, we successfully established an animal model for preserving limbs from amputation to replantation for up to 33 hours. As ECP can also be performed during road- or air transportation, this setting makes transplantation of limbs possible, which are procured at very distant locations from the center which performs the VCA and where the graft recipient resides. This will allow donor-recipient matching across countries and even continents and increase the chance for potential VCA recipients to receive an optimally suitable graft.

LBP44 EX VIVO CHARACTERIZATION OF KIDNEY TRANSPLANT TUBULAR EPITHELIAL CELL CO-STIMULATORY AND -INHIBITORY MOLECULE EXPRESSION DURING INFLAMMATION

Constantin Thieme*[1], Ayda Bilehjani[1], Daniel Gaetzi[1], Luka Queitsch[1], Julian Autrata[1], Mira Choi[2], Jasmin Jaeger[3], Panagiota Zgoura[4], Richard Viebahn[5], Timm H. Westhoff[4], Nina Babel[1;6]

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Background: Direct allorecognition is generally regarded as a result of antigen presentation and activation of recipient T cells by donor professional antigen presenting cells. However, tubular epithelial cells contribute the vast majority of cells in the kidney transplant, and their contribution to alloreactions despite being targets of cytotoxic T cells is not well understood.
Methods: We collected urine samples of healthy donors, kidney transplant patients, and living donors of kidney transplants and isolated and cultivated urine-derived kidney tubular epithelial cells. To ensure transplant origin, we characterized blood and epithelial cells of living donors and the respective recipients by chimerism analysis. After treatment with cytokines IFNγ, TNFα, IL-1β, IL-6, IL-17A, and IL-22, as well as with 1% oxygen hypoxia, we performed a flow cytometric characterization of over 20 markers.
Results: Chimerism analysis of living donor and recipient pairs revealed a near total transplant origin of the cultivated tubular epithelial cells (median 100% donor origin, minimum 96%, n=6 living donor-recipient-pairs). Inflammatory treatment with IFNγ, TNFα, and IL-1β resulted in an upregulation of MHC-I and -II, costimulatory molecules CD40, CD70, ICAM-1, and ICOS-ligand, the immunomodulatory molecule HVEM and/or PD-L1. Other molecules, such as CD80/CD86, 4-1BBL, CD48, and CD58, only showed little expression and/or modification by inflammatory treatment. Treatment with IL-6, IL-17A, IL-22, and hypoxia only caused minimal modulation of immunomodulatory molecule expression.
Conclusions: Taken together, human kidney transplant tubular epithelial cells can be isolated ex vivo and studied without invasive procedures. We used this tool to characterize the immunomodulatory potential of tubular epithelial cells under inflammatory conditions, which are present during ischemia-reperfusion injury and rejection episodes. Tubular epithelial cells express not only MHC-I, but also MHC-II and a multitude of important immunomodulating molecules. Thus, they can significantly contribute to the activation and modulation of alloreactive CD4+ and CD8+ T cells.

LBP45 SURFACE MOLECULE EXPRESSION OF KIDNEY TUBULAR EPITHELIAL CELL DERIVED EXTRACELLULAR VESICLES – A NEW PERSPECTIVE ON THE MODULATION OF ALLOIMMUNITY?

Luka Queitsch*[1], Ayda Bilehjani[1], Daniel Gaetzi[1], Mira Choi[2], Timm H. Westhoff[3], Nina Babel[1;4], Constantin Thieme[1]

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Background: Alloimmunity is one of the leading causes of a limited short- and long-term graft survival. Extracellular vesicles (EVs) have recently been recognized to hold a key role in immune processes in many conditions. They could therefore also impact alloimmunity, for example through the expression of surface proteins that in- or decrease adaptive immune cell reactivity after inflammatory or hypoxic episodes. Kidney parenchymal cells are an important source of EVs in kidney transplantation. Thus, we aimed to shed light on the immunomodulatory molecule expression of renal tubular epithelial cells (rTECs) derived EVs in the pathophysiology of alloreactivity.
Methods: rTECs of healthy probands and kidney transplant patients were isolated from urine using a protocol established by our group. We compared different immunomodulatory cytokines (IL1β, IFNγ, TNFα, IL6, IL17A, and IL22) and hypoxic conditions regarding their impact on EV-production and EV surface marker expression. EVs were isolated from cell-culture supernatants by ultracentrifugation. Quantity and size distribution was analyzed by nanoparticle tracking analysis and EV phenotype was confirmed by electron microscopy. Surface expression of tetraspanins, MHC and immunomodulatory molecules such as PDL-1, ICAM-1, and ICOS-L was analyzed by flow cytometry. Finally, functional impact of EV incubation on T cell activation was studied.
Results: EV production capacity of cells varies between probands and conditions, with IL1β stimulation enhancing vesicle production strongly. Surprisingly, IFNγ and TNFα only moderately increased the quantity of EVs, despite their regular use as EV-production stimulants. Furthermore, we could show that rTEC – Evs potentially influence T cell activation via immunomodulatory surface molecules. This was further tested in functional analysis of T cell activation after co-culture with EVs by flow cytometry.
Conclusions: Taken together, we showed that rTECs can have immunomodulatory effects via the production of EVs, leading to new insights into alloimmunity after ischemia-reperfusion injury and intragraft inflammation.

LBP46 UNSUPERVISED ANALYSIS OF KIDNEY BIOPSY TRANSCRIPTOMES FROM DONORS AFTER BRAINSTEM OR CARDIAC DEATH

Rachel Thomas*[1], Tobias Bohnenpoll[2], Ricardo Castro[2], Maria Kaisar[3], Maria Letizia Lo Faro[3], Georg Ebeling[3], Sadr Shaheed[3], Lente Lerink[3], Nelly Mostajo Berrospi[2], Rayan Daou[2], Tim Blokker[2], Olivier Radresa[2], Uwe Andag[2], Gabriel Oniscu[4], Rutger Ploeg[3]

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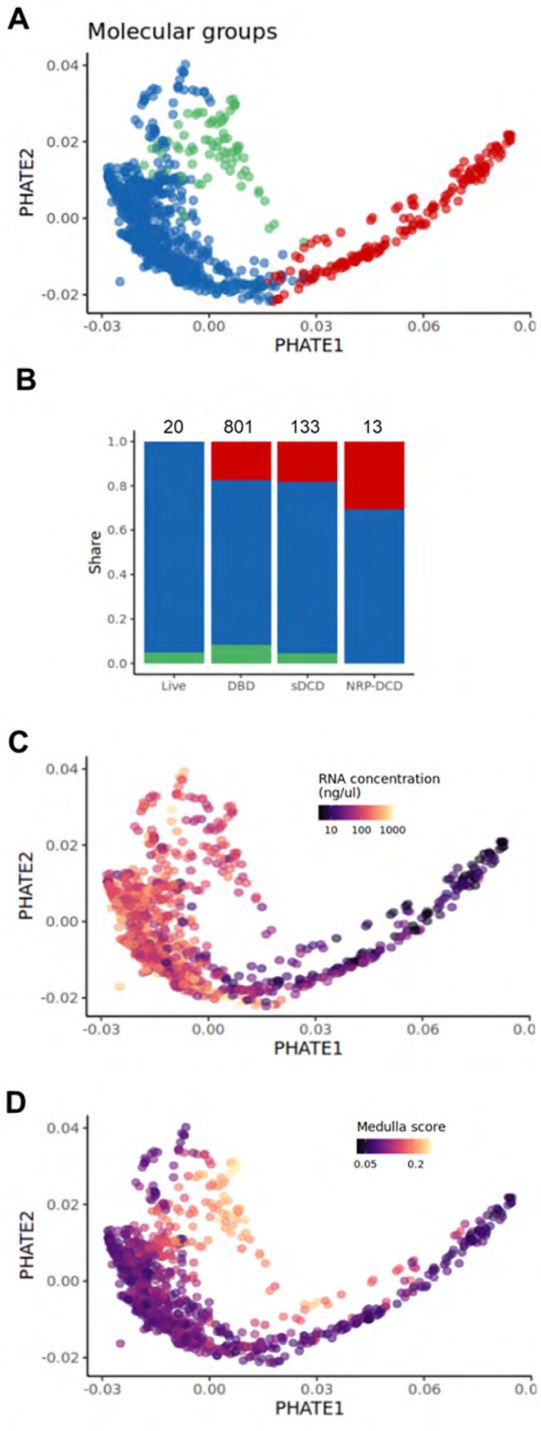
Background: Brainstem and cardiac death result in profound cellular and molecular changes in donor kidneys, that adversely impact graft function and clinical outcome. Here unsupervised methods were used to characterise biopsy transcriptomes from different donor types with aim to improve mechanistic understanding of organ quality, injury and repair.
Methods: Kidney biopsies from live donors (n = 20), donors after brainstem death (DBD, n = 801) or standard cardiac death (sDCD, n = 133) or normothermic regional perfusion (NRP-DCD, n = 13) were obtained from a biobank and processed for RNA sequencing. Transcriptomes were clustered by similarity via self-organizing maps (oposSOM) and further explored via dimension reduction (PHATE) to integrate technical, clinical and molecular data.
Results: Unsupervised clustering of biopsy transcriptomes revealed three molecularly distinct groups of different sizes (Fig. 1A), labelled blue (n = 724), red (n = 170) and green (n = 75). Interestingly, molecular clustering did not separate DBD from DCD, highlighting molecular similarities largely independent of donor type (Fig. 1B). Integration of clinical and technical variables using a decision tree approach suggested that red and green clusters could be explained by RNA quality and biopsy type (core needle vs. punch), respectively. RNA concentration showed a gradient separating the red cluster from high-quality samples (Fig. 1C). Variability in sampling procedures affected biopsy composition, with the green cluster enriched for needle biopsies and characterised by a stronger medullary signal (Fig. 1D). Importantly, initial exploration of high-quality transcriptomes with comparable tissue composition (cluster blue) revealed gradients of tubular damage and metabolic adaptation, and stromal and immune activation, underlining the potential of the dataset to study mechanisms of kidney injury and repair.

Conclusions: Unsupervised analysis of biopsy transcriptomes revealed technical variability in RNA quality and tissue composition, potentially confounding biological signals. Data-driven selection of high-quality transcriptomes with comparable tissue composition will enable the study of kidney injury-repair mechanisms across major transplant conditions.

Fig 1: Unsupervised analysis of biopsy transcriptomes. (A) Transcriptomes clustered into three molecular groups (PHATE dimension reduction). (B) Distribution of donor types across molecular groups. (C) Embedding RNA concentration in PHATE space. (D) Embedding medullary gene expression signature in PHATE space.



LBP49 IMPACT OF PROLONGED NORMOTHERMIC MACHINE PERFUSION ON THE BIOENERGETIC FUNCTION IN PORCINE DBD KIDNEYS

Marlene Pühringer-Sturmayr[*1], **Andras T. Meszaros[1], Silvia Gasteiger[1], Christina Bogensperger[1], Thomas Resch[1], Simon Mathis[2], Gabriel Putzer[2], Martin Hermann[1], Franka Messner[1], Annemarie Weissenbacher[1], Jakob Troppmair[1], Theresa Hautz[1], Hannes Neuwirt[3], Gert Mayer[3], Stefan Schneeberger[1]**

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Background: Lower-quality organs of marginal or donation after circulatory death (DCD) donors accompany greater risk of malfunction after transplantation, which is propelled by ischemia and reperfusion injury (IRI). Emerging technologies like normothermic machine perfusion (NMP) offer the possibility to restore metabolism under near-to-physiologic conditions and thereby assess grafts prior to transplantation. Detailed analysis of mitochondrial respiration may constitute direct and readily available information on organ function. We herein aimed at assessing bioenergetic function in porcine kidney NMP using high-resolution respirometry (HRR).
Methods: Kidneys of a porcine DCD-model underwent NMP for up to 24 h. Tissue integrity and cell viability were assessed in biopsies using real-time confocal microscopy with a scoring system (RTCA) ranging from +3 (100% viable) to -3 (100% non-viable). Mitochondrial respiration was analysed in tissue using HRR for the succinate-linked pathway to analyse oxidative phosphorylation (OXPHOS). Outer membrane damage (cytochrome *c* control) and ATP production *(P-L* control) efficiencies were calculated.
Results: Eight porcine kidneys were perfused for 21.69 ± 4.47 hours (mean ± SD). Intrarenal resistance declined significantly from start (0.32 ± 0.13 mmHg/mL/min) towards end of perfusion (0.17 ± 0.09 mmHg/mL/min), $p = 0.0039$. Renal plasma flow doubled from 217.4 ± 86.6 mL/min to 447.8 ± 201.9 mL/min ($p = 0.0056$) during NMP. No significant changes were observed in lactate levels and plasma creatinine. RTCA score indicated a decrease in cell viability (from 1.6 ± 1.5 to 0.6 ± 2.3). Mass-specific OXPHOS capacity of kidney mitochondria respiring on succinate decreased ($p = 0.0003$). Cytochrome *c* efficiency increased concomitantly ($p = 0.0082$), representing a damage to the outer mitochondrial membrane (OMM). However, no change in the *P-L* control efficiency could be detected, which indicated a sustained efficacy of ATP production.
Conclusions: HRR is a precise and reproducible method to monitor the bioenergetics in the kidney. During prolonged NMP, a decrease in OXPHOS capacity and damage to the OMM, but stable ATP production efficiency was observed. Clearly visible trends in our data underline the suitability of this method and its application in further studies.

LBP51 ANEMIA AFTER KIDNEY TRANSPLANTATION - HOW CAN WE MANAGE?

Ivana Dedinská[*1], **Matej Vnučák[1], Karol Graňák[1], Monika Beliančinová[1], Patrícia Kleinová[1]**

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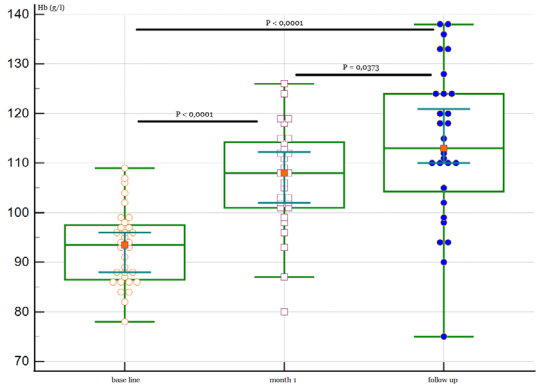
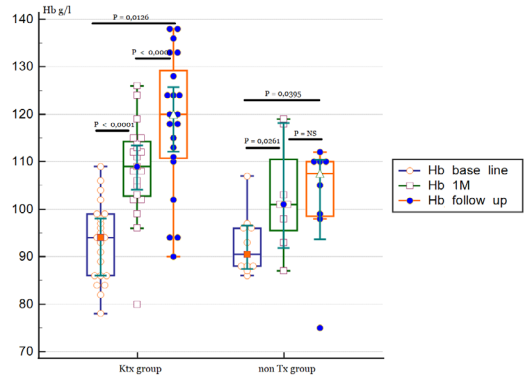
Background: Roxadustat is a recently approved hypoxia-inducible factor prolyl hydroxylase inhibitor that has demonstrated favourable safety and efficacy in the treatment of renal anaemia The goal of this study is to analyse the effect of roxadustat on the level of hemoglobin in a group of patient with chronic kidney disease with or without kidney transplantation.
Methods: This is a monocentric study conducted on the patients of Transplant-nephrology department and/or Transplant-nephrology out-patient clinic of University Hospital Martin, Slovakia who have been treated with roxadusat since August 1st, 2022.
Results: 33 patients were included in the study. The average follow up of treatment with roxadustat was 4,2 months. The following parameters were recorded at the baseline: age, gender, estimated glomerular filtration rate – eGFR (CKD-EPI), treatment with iron and level of iron in serum, level of C-reactive protein, level of hemoglobin, starting dose of Roxadustat. We discovered a significant improvement in the levels of hemoglobin after one month of roxadustat treatment (P < 0,0001) and another significant improvement in follow-up (P ,0,0373). There was no significant difference in eGFR, CRP or iron levels during follow up, so hemoglobin levels were not affected by inflammation or kidney function. In the next step the group of patients was divided based on history of kidney transplantation. Again, we confirmed significant improvement in hemoglobin levels in kidney transplantation group in first month of treatment (P < 0,0001) as well as in follow up (P < 0,0001). There was a significant improvement in hemoglobin levels in the first month of roxadustat treatment in the group of patients who did not undergo kidney transplantation (P = 0,0261). However, there was no significant difference between hemoglobin levels in month 1 and follow up in this group.

Conclusions: Roxadustat – as a new treatment option of anaemia for patients with chronic kidney diseases. Our first analysis confirmed that roxadustat is very effective not only in patients with CKD, but also in patients with anaemia after kidney transplantation.



Hemoglobin levels – whole group



Hemoglobin levels – patients after kidney transplantation (KTx group) and with no history of kidney transplantation (non Tx group)

LBP52 THE DETRIMENTAL EFFECTS OF A BK POLYOMAVIRUS INFECTION IN KIDNEY TRANSPLANT PATIENTS

Wouter Moest[1], **Aiko De Vries**[1], **Danny van der Helm**[1], **M.C.W. Feltkamps**[2], **Joris Rotmans***[1]

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Background: BK polyomavirus-associated nephropathy (BKPyVAN) preceded by BKPyV viremia is a well-known complication of kidney transplantantion, which can lead to significant allograft damage and graft loss. The mainstay of prevention and treatment of BKPyVAN is reduction of immune suppression upon detection of viremia, which subsequently carries a risk of allograft rejection. In this single center, retrospective cohort study we assessed the impact of BKPyV viremia detection on kidney allograft outcomes
Methods: All patients with a kidney transplantation between 2011 and 2021, transplanted at Leiden University Medical Center (LUMC) were included. Data on the incidence, management and course of BKPyV viremia were collected whereupon we studied the association between incidence and load of BKPyV viremia and kidney function and episodes of rejection using logistic regression analysis.
Results: In total, 1158 kidney transplant recipients were included of which 273 patients (23.6%) developed BKPyV viremia and 36 (3.1%) were diagnosed with BKPyVAN. On average onset of BKPyV was 7.4 months after transplantation. At 5 years after transplantation, patients that had developed BKPyV viremia had a lower eGFR (45 ml/min/1.73m^2) compared to patients without viremia (50 ml/min/1.73m^2, p <0.001). Development of de novo donor-human leukocyte antigen specific antibodies (dnDSA) was more common in kidney transplant patients with viremia, compared to patients without (OR 2.0, 95% CI 1.0 to 4.1, p=0.043). Rejection was not significantly different between groups.
Conclusions: Kidney transplant patients who develop a BKPyV viremia are more at risk for the development of dnDSAs and have worse kidney allograft outcomes. Risk for developing rejection is similar between the two groups. This might implicate that the reduction of immunosuppression when a BKPyV viremia arises should be less aggressive.

LBP53 ASSOCIATION OF HEMOGLOBIN LEVELS WITH RENAL FUNCTION DURING NORMOTHERMIC MACHINE PERFUSION OF PORCINE KIDNEYS: A RETROSPECTIVE COHORT STUDY

L. Annick van Furth[*1], **Tobias Huijink**[1], **Leonie van Leeuwen**[1], **Hanno Maassen**[1], **Veerle A. Lantinga**[1], **Baran Ogurlu**[1], **Tim L. Hamelink**[1], **Merel Pool**[1], **Rianne Schutter**[1], **Cyril Moers**[1], **Stefan Berger**[2], **Henri Leuvenink**[1], **Rene Posma**[3], **Leonie Venema**[1]

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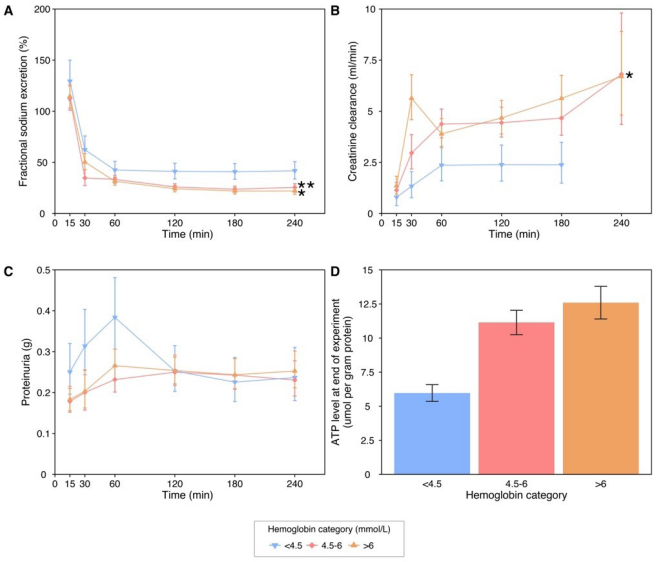
Background: Ex vivo normothermic machine perfusion (NMP) is used to assess and recondition an isolated marginal kidney before transplantation. However, there is no consensus on the optimal conditions such as the oxygen-carrying capacity of the perfusate to support renal function. To investigate the association of hemoglobin level with renal function, a retrospective analysis of porcine kidneys being perfused at our laboratory was performed.
Methods: In total, 228 kidneys underwent 4 hours of NMP with a hemoglobin-containing perfusate between 2015 and 2021. A generalized linear model was used to determine the association of hemoglobin levels with time-weighted means of renal function markers, such as fractional sodium excretion (FENa) and creatinine clearance. These outcomes over time stratified by baseline hemoglobin level (<4.5, 4.5-6, or >6 mmol/L) were modeled with a generalized linear mixed-effects model as well.
Results: Increasing hemoglobin levels were associated with improved FENa and creatinine clearance, with the nadir of FENa and peak creatinine clearance, respectively, both at about 5 mmol/L. A baseline hemoglobin level <4.5 mmol/L was associated with higher FENa rates and lower creatinine clearance ($p<0.001$ and $p<0.05$). Hemoglobin was not significantly associated with proteinuria during NMP, or ATP levels at the end of NMP. Hemoglobin levels exceeding 6 mmol/L do not provide additional benefits in terms of renal function and may even contribute to increased injury.
Conclusions: In conclusion, this study revealed a correlation between baseline hemoglobin levels with parameters of renal function, but not injury, during NMP of marginal kidneys.



LBP55 GROUND BREAKING DECISIONAL ROLE OF TRANSIT TIME DURING A LIVING DONOR TRANSPLANTATION EVALUATED BY A FAST AND FRUGAL TREE

Gianluca Rompianesi*[1;1], Fabiana Rubba[1;1], Giuseppe De Simone[1;1], Rosa Carrano[1], Anna Borrelli[1], Roberto Montalti[1], Teresa Trunfio[1], Giovanni Improta[1], Bruno Buonomo[2], Roberto Troisi[1]

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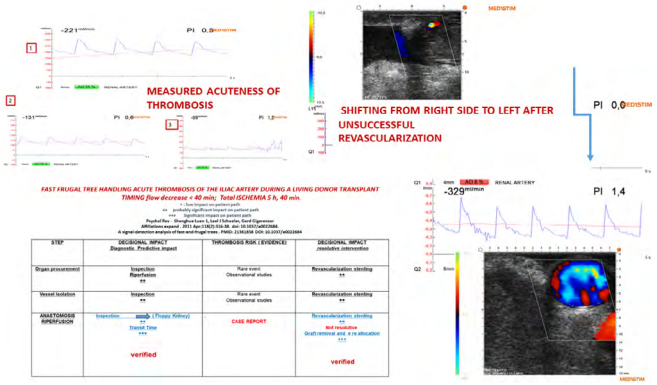
Background: Acute thrombosis of the iliac artery is an extremely rare event during a kidney transplantation and may occur as a complication of traumatic injuries or systemic disorders. We assessed the decision making during a case report of acute and unexpected iliac thrombosis in a living donor transplant for a PKD recipient evaluated by constructing a fast frugal tree (FFT). FFTs are simple algorithms that facilitate accurate decisions based on limited information. FFTs have been successfully exploited to describe decisions and to provide prescriptive guides for effective real-world resolutions, but despite their effectiveness, they are still not widely used.
Methods: We split the three principal phases where iliac thrombosis may occur (organ procurement, vessel isolation, graft reperfusion) according to diagnostic and intervention procedures, weighted for decisional impact and Grade degree of evidence; then we compared the fitting between the occurred decisional steps and the best possible decision making
Results: From observational data, the performed revascularization and removal and reallocation of graft resulted as mandatory interventions in order to preserve the graft when thrombosis occurs unexpected from previous ultrasounds assessments. The used transit time evaluation emerged also with a discriminant decisional power, measuring acuteness of thrombosis (flow reduction 220 to 80 ml/min in < 30 min) and further unsuccessful first try revascularization by resistance index (>3), strengthening fastness in graft removal and reallocation in a different side (shifted from right to left).
Conclusions: FFTs helps the goal of a decision maker to accurately prioritize each step during the transplant critical milieu and at actionable turning points to maximize correct decisions (hits and correct rejections), while minimizing errors (misses and false-alarms) and noise: as learning algorithm used to solve binary classification tasks, they may unlock the full potential of transit time intra operatory measurements.



LBP56 35 YEARS OF PAEDIATRIC HEART TRANSPLANTATION: OUTCOMES AT A VERY LONG TERM FOLLOW-UP

Chiara Tessari*[1], Andrea Cavicchiolo[1], Emma Bergonzoni[1], Valentina Lombardi[1], Giulia Lorenzoni[2], Nicola Pradegan[1], Alessia Cerutti[3], Giuseppe Toscano[1], Giovanni Di Salvo[3], Vladimiro Vida[4], Antonio Gambino[1], Gino Gerosa[1]

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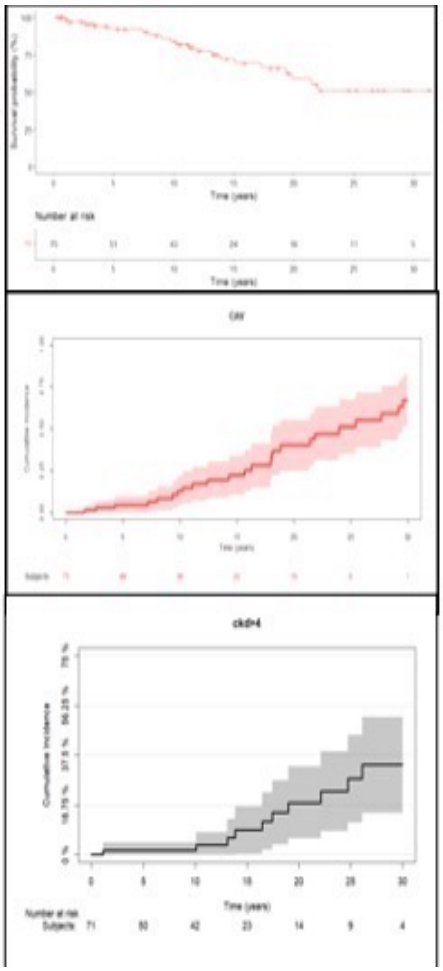
Background: Thirty-five years after the first successful paediatric heart transplantation (pHTx), the long-term outcome of this population is still unknown. The aim of this study is to analyse clinical results in this population in a single centre experience.
Methods: A retrospective analysis of all the patients who underwent Htx in paediatric age was performed. Clinical, laboratory, and instrumental follow-up was completed. Outcomes were survival, severe coronary allograft vasculopathy (CAV), severe chronic kidney disease (CKD). Kaplan-Meier analysis was performed for survival, cumulative incidence functions were applied for incidence of CAV and CKD.
Results: Between 1987 and 2022, 86 paediatric patients underwent Htx. Median age at Htx was 11.9 years. Postoperative mortality was 13% (11 patients). Median follow-up period was 13.7 years, with a cumulative experience of 35 years. Twenty patients died at follow-up (27%), of whom 11 for cardiovascular causes. At 1, 5, 10, 20 and 30-year follow-up survival was 98%, 92%, 84%, 74%, and 60%, respectively. Cumulative incidence of severe CAV at 1,5,10,20, and 30-years follow-up was 4.9%, 12.9%, 40%, 51.2%, 67%, respectively. Cumulative incidence of severe CKD at 1,5,10,20, and 30-year follow-up was 0%, 2%, 5%, 18.75%, and 35%, respectively. At a multivariable analysis, donor age is related with CAV (p=0.004).
Conclusions: Paediatric Htx has good survival and functional outcomes, with a growing cohort of patients approaching their second and third decades. Main causes of death at follow-up were cardiovascular diseases and donor age resulted related with CAV.



LBP58 HEART TRANSPLANTATION (HTX) IN ELDERLY PATIENTS: CROSS-SECTIONAL SINGLE CENTER OBSERVATIONAL STUDY

Agnieszka Kuczaj*[1;2], Szymon Warwas[3], Szymon Pawlak[1;2], Joanna Śliwka[1;2], Michał Zakliczyński[4], Piotr Przybyłowski[1;2], Tomasz Hrapkowicz[1;2]

[1]Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Zabrze, [2]Silesian Center for Heart Diseases, Zabrze, Poland, [3]Students' scientific association affiliated with the Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Faculty of Medical Sciences in Zabrze, Zabrze, [4]Wroclaw Medical University, Department of Cardiac Transplantation and Mechanical Circulatory Support, Wrocław, Poland

Background: The average life expectancy is continuously increasing in developed countries. Simultaneously, the incidence of heart failure is rising with age. In cases of end-stage heart failure, heart transplantation is the treatment method of choice. Therefore, we investigated the outcomes of the elderly patients (over 65 years old) with end-stage heart failure who were treated with orthotopic heart transplantation.
Methods: We investigated the entire group of patients treated with heart transplantation since the beginning of the transplant program in our center (1985) and searching for the subpopulation of patients aged 65 years and older.
Results: Among 1488 patients treated with Htx between November 1985 and June 2023, 60pts (4%), were transplanted at the age ≥65y. In that group the mean age at the time of transplantation equalled 66.3y, IQR 65-67 and 4(15%) pts were women. Among these patients, the heart failure was of ischemic origin in 50% of cases, two pts were bridged with ECMO, 4 with LVAD and 4 with IABP. 21 pts had diabetes, median eGFR was 53ml/min/1.73m^2, IQR: 39-61ml/min/1.73m^2. Median observation period was 23, IQR: 1.75-63months. Baseline immunosuppressive regimen consisted of steroids and: cyclosporine-A with azathioprine (6.7%), cyclosporine-A with mycophenolate (6.7%) and tacrolimus with mycophenolate (81.7%). Acute cellular rejection index (acute cellular rejection according to ISHLT score ≥2 to total number of performed biopsies) was 0.071, IQR:0-0.123. Graft vasculopathy developed 23.3% of pts. One-month survival was 78.3%, one-year survival (conditional on one-month survival) was 85.1%. 25 pts survived 3 years (41.7%), 18 pts (30%) 5 years, and 4 (15%) survived 10 years. 25 pts are still alive and are 69.75, IQR: 68.2-72.2 years old. Among deaths 13 were due to cardiovascular reasons, 5 due to cancer, 8 due to multi-organ failure, 2 due to liver failure, 2 due to respiratory failure, and 5 others non-specified.
Conclusions: Survival outcomes in elderly Htx recipients are poor. However, it seems to be acceptable considering limited survival in elderly general population.

LBP59 PROLONGED EX VIVO KIDNEY PRESERVATION USING SUBNORMOTHERMIC ACELLULAR MACHINE PERFUSION

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Background: In kidney transplantation normothermic machine perfusion can be used to reduce exposure to cold ischaemic injury. This may improve outcomes and allow the technology to extend preservation times and repair marginal kidneys. Subnormothermic acellular perfusion (SNAP) is a new approach proposed to achieve a balance between the cytoprotective effects of reduced cellular metabolism under hypothermia while having sufficient metabolism to allow potential organ repair. Kidneys can be perfused without red blood cells to simplify the procedure, reduce cost and prevent potential harmful effects of hemolysis. The aim of this study was to assess the effects of different durations of SNAP after cold ischaemia in human kidneys.
Methods: Twelve kidneys declined for transplantation were perfused *ex vivo* using SNAP. Kidneys were perfused with a human serum albumin-based solution at 32°C for either 6, 12 or 24h (n = 4 per group). After the preservation phase, kidneys were reperfused *ex vivo* at 37°C for 4 hours using a blood-based perfusate.
Results: The mean donor age was 70±6y, 63±9y and 61±15y in the 6h, 12h and 24h groups, respectively (P=0.530). There was no significant difference in the cold ischaemic time prior to SNAP (6h 892±415, 12h 1203±327, 24h 1042±368 minutes, P=0.523). Throughout SNAP the perfusate flow, mean arterial pressure and acid-base balance remained stable in all kidneys. Kidneys in the 24h group had a significantly lower mean perfusate flow rate compared to the 6h and 12h kidneys (24h 166±45, 12h 266±45, 6h 214±36 ml/min/100g; P=0.008). During reperfusion, kidneys in the 24h group had a numerically lower urine output (24h 27±33, 12h 83±77, 6h 198 ±176ml/h; P=0.074) and lower level of creatinine fall (24h 38±11, 12h 61±23, 6h 59±22%; P =0.298) but this did not reach statistical significance. Renal blood flow was similar in all groups (6h 119±32, 12h 187±55, 24h 146±66ml/min/100g; P=0.243). Histological evaluation showed preserved renal morphology but an increase in ischaemic damage in the 24h group.
Conclusions: This study demonstrates that human kidneys can be successfully perfused with SNAP for up to 12h to extend the preservation period. There was evidence of additional ischaemic injury in the 24h SNAP kidneys which warrants further investigation.

LBP60 PRELIMINARY RESULTS OF CYTOKINE PROFILING AND ADSORPTION DURING SUBNORMOTHERMIC MACHINE PERFUSION OF ECD LIVER GRAFTS

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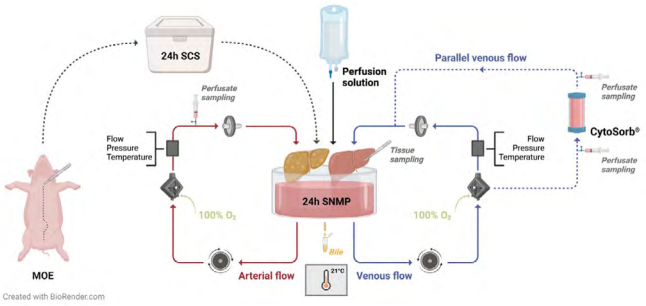
Background: Ex vivo machine perfusion methods have emerged as promising tools for organ preservation, reconditioning and repair. However, the underlying process triggers inflammatory processes. Especially ECD grafts are more vulnerable and therefore cytokines as additional biomarkers may be promising for graft assessment.
Methods: Porcine steatotic (n = 7) and healthy (n = 4) livers were subject to 24 h static cold storage and subsequently perfused for 24 h in a subnormothermic oxygenated perfusion circuit. Throughout perfusion perfusate was collected for analyzing perfusion parameters (pH, glucose, lactate) and snap frozen for post hoc assessment of liver function and cytokine levels. Tissue biopsies were taken every 3 h. The effect of cytokine adsorption was assessed in a follow-up experiment by connecting the CytoSorb® adsorber to the circuit and perfusing additional livers either with (n = 5) or without (n = 3) this adsorber.
Results: Baseline cytokine levels were comparable in all groups. Levels of pro-inflammatory cytokines IL-1 alpha, IL-1 beta, IL-6, IL-18 and TNF-alpha increased over time in steatotic and healthy livers, with a numerically greater increase in the steatotic grafts, reaching statistical significance from 6, 24, 12, 1, 6 h of perfusion onwards, respectively. Anti-inflammatory cytokines IL-1ra and IL-12 showed a similar trend, with significantly higher values in the steatotic grafts. After 24 h pro-inflammatory cytokine levels of steatotic livers were significantly higher compared to the beginning of perfusion. Similarly, IL-8, IL-18 and TNF-alpha levels of healthy grafts were significantly higher at the end of perfusion compared to 1 h. Liver parameters AST and ALT were numerically, and LDH significantly lower in healthy livers, however converging after 24 h to levels comparable to steatotic grafts. The follow-up experiment showed numerically lower levels of pro- and anti-inflammatory cytokines throughout perfusion in the CytoSorb® group.
Conclusions: These preliminary results provided first insight into cytokine dynamics during subnormothermic perfusion. Especially, long term machine perfusion of 24 hours significantly increased pro-inflammatory cytokine levels. The inclusion of an adsorption device is feasible and has the potential to reduce elevated cytokine levels.



LBP63 DONATION AFTER CIRCULATORY DEATH INCREASES OVERALL ORGAN DONATION AND TRANSPLANTATION IN SWEDEN, BUT NOT WITHOUT NEW CHALLENGES

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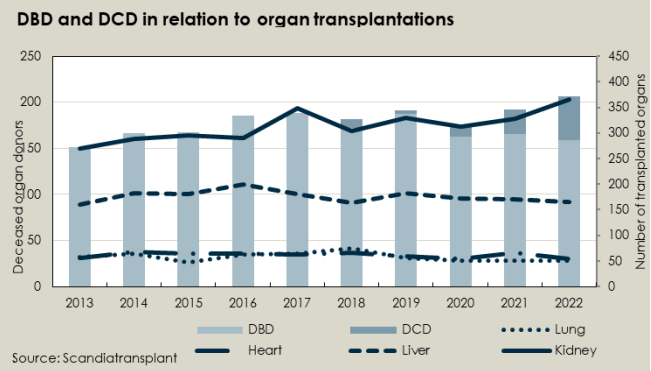
Background: Donation after Circulatory Death (DCD) was introduced in Sweden 2019, aimed to increase organ transplantation. Focus of DCD implementations impact on transplantation in Sweden, and the Intensive Care Units (ICUs) perception as well as number of donors and accomplished transplantations will be presented.
Methods: A survey was sent to all (*n* = 84) Swedish ICUs in January 2023, aimed to follow up on the implementation of DCD. Non-respondent units, *n* = 22 (26%), are not included in the result. The number of donors and transplant statistic were retrieved from the Swedish Intensive Care Registry (SIR) and Scandiatransplant. Descriptive statistics are presented from the survey.
Results: Overall, 61 % of the respondent ICUs declared implementation of DCD at their unit. In 2023, DCD implementation differs depending on national localisation; university hospitals (81%), county hospitals (57%) and local hospitals (46%).Implementation of DCD in Sweden was successful. An increase of deceased donations was seen in Sweden during this period, but the number of DBD donors and transplantations of liver, heart and lungs decreased. The reasons for the decrease in DBD are unknown. DCD heart donations have not been possible in Sweden, and only eight DCD lungs were transplanted during 2020-2022. There is no consensus on whether normothermic regional perfusion for thoracic organs is in accordance with Swedish ethical standards. Obstacles for implementation were lack of ICU- and OR staff, difficulty staffing DCD-teams, lack of management support or fear of displacement effects. Support from hospital management and enough staff was perceived as facilitating actors. Mobile DCD-teams or phone support were suggested as solutions for hospitals with few donors. National process indicators are necessary to follow the development.
Conclusions: Implementation of DCD has increased overall organ donation in Sweden but is resource demanding, and has not increased liver and heart transplants. Additional efforts, such as considering an ethical framework regarding machine perfusion for thoracic organ donation, or working to prevent a decrease in DBD, are needed to increase access to transplantation for all organs.



Actual donors in Sweden 2020 - 2022

Hospital category	2020 DCD	2020 DBD	2021 DCD	2021 DBD	2022 DCD	2022 DBD	Total DCD 2020-2022	Total DBD 2020-2022
University Hospitals	7	84	21	87	41	82	69	253
County Hospitals	4	60	6	71	10	63	20	194
Local Hospitals	0	20	0	11	1	18	1	49

LBP64 HEART TRANSPLANTATION FROM ANTI-HBCORE POSITIVE DONORS: A SINGLE-CENTER OBSERVATIONAL STUDY

Agnieszka Kuczaj*[1;2], Szymon Warwas[3], Joanna Śliwka[1;2], Szymon Pawlak[1;2], Michał Zakliczyński[4], Piotr Przybyłowski[1;2], Tomasz Hrapkowicz[1;2]
[1]Silesian Center for Heart Diseases, Zabrze, Poland, [2]Medical University of Silesia, Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Zabrze, [3]Students' scientific association affiliated with the Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Faculty of Medical Sciences in Zabrze, Zabrze, [4]Wroclaw Medical University, Department of Cardiac Transplantation and Mechanical Circulatory Support, Wrocław, Poland

Background: Organ transplantation is constrained by the scarcity of available organs, necessitating efforts to increase organ availability while preserving positive recipient outcomes. Extended criteria donors, including HbS(-) and anti-HBcore(+) donors, have emerged as a promising option for individuals on the organ transplant waiting list. This study aimed to assess the long-term safety of heart transplantation (Htx) from anti-HBcore (+) donors.
Methods: Retrospective analysis of heart transplant recipients operated in a single high-volume transplant center between January 2013 and June 2023. In further analyses, HbS(-) recipients with Htx from both HbS(-) and anti-Hbcore(+) donors were identified.
Results: Among the 583 transplanted patients during the analysed period, a total of 29 cases (including 6 females) received Htx from anti-Hbcore (+) and HbS(-) donors. The mean recipient age at the time of transplant was 53.7±12 years. The median observation period equaled 11.25, IQR: 0.9-34.5 months. All except for one recipient declared complete hepatitis B vaccination. Prior to Htx, the anti-HbS antibody level was assessed in three patients, with only one patient showing an antibody level≥ 12mIU/mL. Among Htx recipients, none received Anti-HbS globulin at the time of Htx. As there are no unequivocal guidelines, the decision to use prophylaxis against hepatitis B was at the discretion of the attending physician. One-year prophylaxis with lamivudine was used in four cases. Additionally, up to 3 months, 65.5% of the patients received valganciclovir. In the whole group of recipients, frequent transaminase and HbS controls (every month in the first three months and every three months up to one year and then every 6 months) were performed. In the whole observation period, none of the patients developed HbS antigen. Mean(±SD) ASPAT, ALAT, bilirubin, and GGTP levels were at the one year: 26(12)U/L, 28(24)UI/L, 10(4)umol/L, 103(234)U/L. Mean LVEF at one year, 2, and 5 years was 60(±3)%, 58(±3)%, and 58(±4)% accordingly.
Conclusions: Htx from anti-Hbcore (+) donors in patients vaccinated against hepatitis B seems to be viable and safe option even without the application of additional antiviral prophylaxis.

LBP65 THE IMPACT OF DECEASED DONOR ORGAN PROCUREMENT WORKSHOP ON SURGICAL TRANSPLANT FELLOWS' CONFIDENCE AND COMPETENCE

Samrat Ray*[3], Shilpa Balaji[1;2], Hala Muaddi[1;2], Markus Selzner[1;2], Carla Luzzi[1;2], Aileigh Kay[1], Karolina Gaebe[1;2], Nadia Rukavina[1], Trevor Reichman[1], Chaya Shwaartz[1;2]
[1]University Health Network, Toronto, Canada, [2]University of Toronto, Toronto, Canada, [3]Toronto General Hospital, Ajmera Transplant Center, Toronto, Canada

Background: Deceased donor organ procurement entails complex techniques and meticulous anatomical dissection, and is vital to the success of organ transplantation. In our institution, this surgery is often performed by a surgical transplant fellow. Thus, training transplant fellows in these intricate surgical techniques is imperative, but such opportunities are currently limited in Canada. To address this, we organized a two-day hands-on deceased donor workshop for the abdominal transplant fellows at our institution. The objective of this study is to assess the workshop's impact on fellows' confidence and competence to gauge its overall benefit and to identify areas of improvement.
Methods: The abdominal transplant fellows who attended the workshop were invited to participate in the study. At the beginning of the workshop, the participants were asked to report their exposure to and confidence on various aspects of the organ procurement surgery. The fellows' knowledge on organ procurement were also assessed using multiple choice questions. Participants were asked to complete the questionnaires immediately post-workshop, and at one month and six months following the workshop. Descriptive statistics and t-test or Wilcoxon test were used, as appropriate, to compare the responses of participants pre and post workshop.
Results: Seven transplant fellows participated in the study. The fellows' confidence improved at the end of the workshop (t(6)= -4.05 , p= 0.006), at 1 month (t(6)= - 3.68, p= 0.01) and six months post-workshop (t(6)= - 3.31 , p= 0.016). Participants' competence also increased at the end of the workshop (72.4% vs. 81.6%, p=0.46), at one month (72.4% vs. 85.7%, p=0.06) and six months post-workshop (72.4% vs. 86.7%, p=0.11). All of the participants reported that the course was useful and that they would like to see this course offered in future.
Conclusions: The workshop led to a significant improvement in post-workshop trainee confidence, which remained evident even after six months. Although competence levels did not increase significantly, the results indicate a positive impact on trainees. Future studies will explore alternative measures of technical competence and the impact of regular deceased donor workshops on surgical trainees.

LBP66 DISTINCT CYTOKINE SIGNATURES ACCORDING TO MODEL FOR END-STAGE LIVER DISEASE SCORES AFTER LIVING DONOR LIVER TRANSPLANTATION

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Background: The model for end-stage liver disease (MELD) score is widely acknowledged for prognosis in patients with end-stage liver disease (ESLD) because it represents the severity of liver dysfunction. The score does not consider systemic inflammation and septic complications. We compared the MELD scores to the levels of serum cytokines as immune mediators, which represents the systemic inflammation, and then investigated the usefulness of serum cytokines as representing the functions of the grafted liver in patients who underwent living donor liver transplantation (LDLT).
Methods: We enrolled 232 patients in a retrospective study at our institute between March 2011 and December 2021. Demographic, and biochemical data were obtained using electric medical records system. The levels of seven serum cytokines were collected at the preoperative and immediate post-transplant period: interferon (IFN)-γ, interleukin (IL)-10, IL-12, IL-17, IL-2, IL-6 and tumor necrosis factor (TNF)-α. The MELD scores were calculated on 1 day (D), 2 D, 3 D, 7 D, 10 D, 15 D, and 30 D after post-transplantation. We identified the influences of serum cytokines on the MELD scores based on Pearson correlation coefficient using correlation analysis, and investigated the cut-off value of serum cytokines identifying high MELD scores using area under the receiver operating curve (AUROC).
Results: Four cytokines, viz., IFN-γ, IL-10, IL-6, and TNF-α were significantly correlated with post-transplant MELD scores ($P < 0.05$). The others, viz., IL-12, IL-17, and IL-2 were not correlated with the MELD scores. IL-6 and IFN-γ showed a statistically significant correlation with the MELD scores from 1 D to 30 D after LT. The cut-off value of IL-6 and IFN-γ in predicting high MELD scores after LDLT (> 23) were 7.3 and 14.6 pg/ml, respectively (AUROC = 0.619 and 0.641; sensitivity, 66.7% and 44.4%; and specificity, 62.8% and 83.2%, respectively).
Conclusions: The levels of serum cytokines, viz., IL-6 and TNF-α, which are pro-inflammatory cytokines, are strongly correlated with post-transplant MELD scores. Therefore, IL-6 and TNF-α could be useful predictors of the dysfunction of grafted liver in patients underwent LDLT, and 7.3 and 14.6 pg/ml, respectively, were the cutoff values in predicting high MELD scores (> 23) after LDLT.

LBP67 SURGICAL TREATMENT OF THE PAPILLARY RENAL CELL CARCINOMA IN THE TRANSPLANTED KIDNEY. CASE REPORT

Stefan Hulik[*1], **Rastislav Kalanin**[1], **Janka Katuchova**[1], **Zuzana Lukacova**[1], **Diana Tomasurova**[1], **David Adandedjan**[1], **Igor Gaľa**[1], **Tatiana Baltesová**[1], **Jaroslav Rosenberger**[1], **Luboslav Bena**[1]

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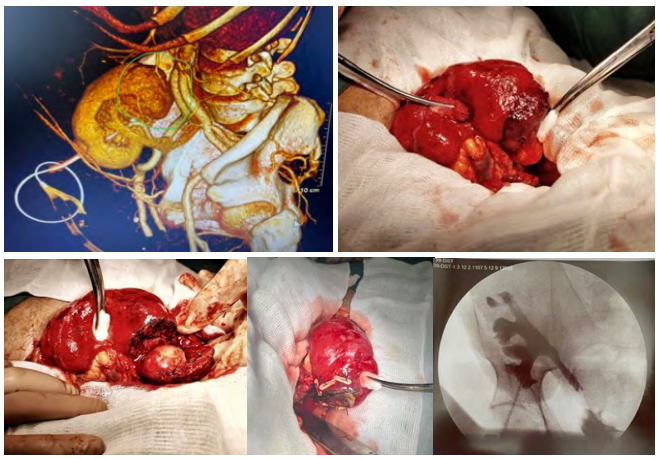
Background: Kidney transplant recipients (KTRs) are at increased risk of developing renal cell carcinoma (RCC). After transplantation, 90% of RCCs are detected in the native kidneys, particularly if acquired cystic kidney disease has developed during prolonged dialysis. The incidence of donor transmitted RCC is unknown. A systematic review on solid masses in kidney allografts found 175 tumors reported in 163 patients, mostly clear- cell RCC (46%) or papillary RCC (42%). The majority were treated with partial nephrectomy (68%), fewer with allograft nephrectomy (19%), radiofrequency ablation (10%), and cryoablation (2%). Cancer recurrence after partial nephrectomy was 3.6% after 3.1 y, which is similar to nontransplanted patients. (Transplantation 2022;106: e52–e63).
Methods: We report a case of a 49y.o. patient, almost 12y. after primary kidney transplantation (KTx) from a brain-dead donor with a permanent nephrostomy as a definitive option after recurrent pyelonephritis of the transplanted kidney with destruction of a graft ureter after three unsuccessful uretero-vesical reimplantations. The patient with otherwise functional graft was referred for a surgery due to incidental ultrasound finding of a tumour mass in the upper pole of the transplanted kidney, confirmed by 3-D CT scan with a high risk for a malignancy, and graftectomy was primarily planed.
Results: Per-operative finding of a very well localised tumour sized up to 4cm in the upper pole of the graft with dominant extrarenal grow was considered by a transplant surgeon as suitable for nephron spearing resection with per operative histological confirmation of negative resection margin. R0 resection of the papillary renal cell carcinoma pT1bNxMx, WHO/ISUP grade 1, was confirmed on definitive histology exam. Clinical oncologist did not recommend adjuvant oncological treatment. Maintenance immunosuppression was switched to mTOR inhibitors. Patient was discharged on POD 12 with maintained graft function – KDIGO G3b.
Conclusions: There are no randomized controlled studies to guide recommendations. Our report is only another one successful case of preferred treatment option for papillary renal cell carcinoma in the transplanted kidney graft. Prospectively collected data and randomized trials are urgently needed.



LBP68 FACTORS INFLUENCING KIDNEY FUNCTION AFTER LIVING DONOR NEPHRECTOMY

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Background: Long-term graft survival is superior when living donors are used for kidney transplantation. As following of increase in the number of live-donor kidney transplantation, many studies have aimed at evaluating risk to the donors and revealed that. kidney donation is a relatively safe procedure with minimal adverse effects. But some reports have described the development of proteinuria and hypertension and decrease kidney function after donation. There are number of reports about safety and good quality of life after living donor kidney transplantation but not enough reports have been published in domestic studies. This study was evaluated factors influence kidney function after kidney donation.
Methods: Between January 2005 and June 2021, we retrospectively reviewed 152 cases of living kidney donor with at least 12months of outpatients clinical follow up with latest follow up laboratory studies. Mean age of kidney donor was 42.2 years (range 17-71). The donors were predominantly male (51.2%). We measured the estimated glomerular filtration rate (GFR), preoperatively relative renal uptake ratios, blood pressure, body mass index, hemoglobin, creatine, cholesterol and assessed prevalence of hypertension, proteinuria.
Results: The average time after donation was 78.9 months (range, 12-406). the left kidney used in 147 patients (96.8%). There was a total complication rate of 8% but serious complication was absent. Proteinuria was found in 8 patients (5.3%), hypertension in 11 patients (11%). Glomerular filtration rate decrease from 106.81±23.68ml/min to 67.67±15.18ml/min(p<0.001).
Thirty-nine patients (25.6%) developed a post-donation e-GFR between 30 and 60ml/min(CKD grade3) and one patient(0.7%) between 15 and 30ml/min(CKD grade4) and two patients(1.3%) developed below 15ml/min(CKD grade5). Factors affected e-GFR after nephrectomy are age at nephrectomy(p<0.001) and pre-nephrectomy e-GFR(p<0.001), other factors such as BMI, underlying disease, sex, laboratory findings did not(p>0.05). male have higher serum creatinine after nephrectomy (p<0.001)
Conclusions: Living kidney donation resulted in a reduced GFR in the donor long term follow-up of living kidney donors. Males are at risk for having higher creatinine following donor nephrectomy

LBP69 DIGITAL DONOR EVALUATION TOOL: A NEW TECHNOLOGY IMPROVES DONOR ENROLLMENT ON INTENSIVE CARE UNIT

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Background: Due to the shortage of organs, contraindications for organ donation are extensively reviewed and in transition. Most of the ICU-doctors are not involved in these discussions and exclude therefore potential donors for medical reasons, which are no longer applicable. In critical urgent patients transplant centers take a higher risk in accepting marginal organs. Swisstransplant implemented a digital donor evaluation tool (DET), which allows the coordinators on the ICU to send a request to the medical advisor (MA) from Swisstransplant before excluding potential donors. Based on the medical condition of the potential donor and the situation on the National Waiting List the MA gives a written feedback to the coordinator of the requesting center.
Methods: All requests in 2022, which have been entered in the DET by coordinators have been analyzed. Patient characteristics, co-morbidities, decision by the MA and final enrollment as potential donor have been analyzed.
Results: 156 requests have been entered in the DET. This is approximatively 20% of the expected potential of DBD- and DCD-donors per year in Switzerland. 117 patients (75%) have been accepted by the MA, out of which 60 patients (51%) have been enrolled as organ donor. In the remaining 57 patients missing consent in 69% was the main cause for not enrolling these patients. Main reasons for using the DET were malignancies (22%), infectious diseases (23%) and age/co-morbidities (22%). Average age of the enrolled donor was with 65.3 years significantly higher compared to the regularly enrolled donors with 56.8 years (p<0.01). In average 1.9 organs have been transplanted in the DET-collective, compared to 3.2 organs in the remaining donors.
Conclusions: The DET is a new technology which allows ICU-doctors in the situation of a discontinuation of therapy to have easy and fast access to a medical expert in the field of organ donation, providing recommendations on the medical suitability for organ donation. Additional examinations can be requested by the MA and the organs, which may qualify for organ donation are defined at an early stage. This allows to reduce the number of examinations and gives the option to have a tailored approach in the discussion with the family, if the number of organs which will be evaluated is limited.

LBP70 RENAL INSUFFICIENCY CAUSES RAPID GROWTH OF PEDIATRIC KIDNEY GRAFT IN A PEDIATRIC-TO-ADULT KIDNEY TRANSPLANTATION RAT MODEL

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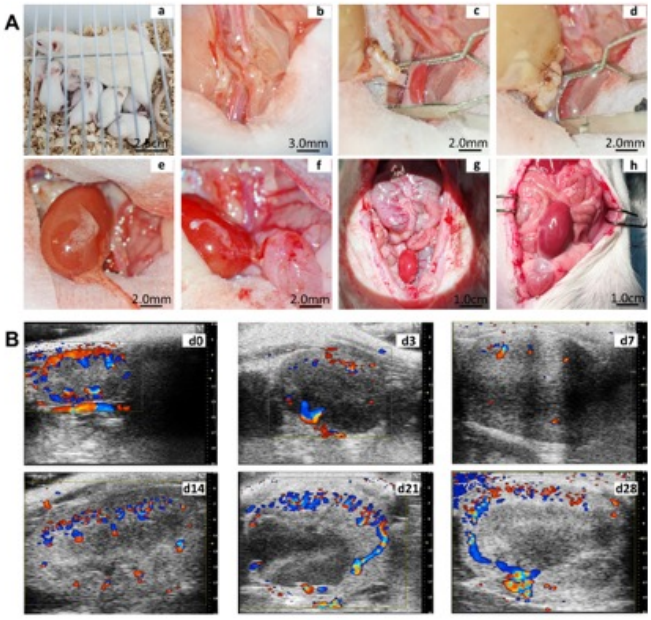
Background: The mechanisms of rapid growth and function improvement of pediatric kidney graft inside adult recipient remain unclear. There is no animal model for conducting relevant studies.
Methods: Syngeneic rats weighed under 50 g and approximately 300 g were used as pediatric and adult animals respectively. They were divided into 4 groups: P-P group, pediatric recipients received pediatric kidneys; A-A group, adult recipients received adult kidneys; P-A group (Figure A) and P-A-intact group, adult recipients received pediatric kidneys. All recipients except the P-A-intact group underwent bilateral kidney nephrectomies. Ultrasonography, biochemical test of serum and urine, blood pressure measurement, transcutaneous measurement of glomerular filtration rate, graft histological analysis by light and electron microscopies, and Ki67 and PAX2 immunohistochemistry were performed.
Results: Grafts in the P-A group grew rapidly to the size comparable with those in the A-A group 7 days after transplantation (**Figure B**). Grafts in the P-P group grew much slower while grafts in the P-A-intact group showed complete growth stasis though no difference was found in postoperative blood pressure among groups of adult recipients. In P-A group, graft function gradually improved until postoperative day 28. On postoperative day 7, graft histology of the P-A group revealed substantial enlargement of the glomeruli, hypertrophy and proliferation of tubular epithelial cells, and thickening of the glomerular basement membrane with podocyte foot process effacement, which signified hyperfiltration injuries. In addition, an increase in Ki67 and PAX2 positive cells implied that there were more intra-graft G1 and progenitor cells in P-A group. Interstitial fibrosis in the graft was comparable between the P-A and the A-A groups on postoperative day 28. Single-cell RNA sequencing of the parenchymal cells in the graft was investigated to unravel the underlying mechanisms.
Conclusions: The P-to-A model first reported here suffices to simulate the clinical P-to-A kidney transplant scenario. This study indicates that relatively insufficient graft function rather than the renal artery hyper pressure plays a key role in driving the rapid growth of a pediatric kidney graft when transplanted in a recipient heavier than the donor.



The pediatric-to-adult (P-to-A) kidney transplantation model in rats and the graft size changes under ultrasonography after surgery. A. Animals and surgical procedures. a. pediatric rats weighed less than 50 g and lactating rat. b-f. A pediatric rat donor kidney was transplanted to an adult rat recipient weighed ~300 g by end-to-side anastomoses of the donor vessels to the recipient common iliac artery and vein and drag-in connection of the ureter graft to the recipient bladder. g-h. Reviews of pediatric donor kidney grafts on day 0 and 28 after surgery. **B. Graft size changes by color doppler ultrasonography on indicated days after surgery.**

LBP71 ATTACHMENT AND PARENTAL BOND: IMPACT ON PSYCHOPATHOLOGY, MENTAL HEALTH AND QUALITY OF LIFE OF KIDNEY TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL STUDY

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Background: Attachment theory represents a reference model for understanding better how pre-existing personality factors can contribute to the development of some chronic conditions. The onset of a chronic disease can represent a "threat" to the relationships between the subject and parental figures according to the type of bond that already exists. The aim of our study was to investigate, in a sample of kidney transplant recipients, attachment style and parental bond, to evaluate the impact on any psychological symptoms and perceived quality of life.
Methods: Fifty transplant kidney recipients were given the following tests: Attachment Style Questionnaire (ASQ) to assess attachment styles, Parental Bonding Instrument (PBI) to assess parental bonding, Short Form Health Survey-36 (SF-36) for perceived quality of life and Middlesex Hospital Questionnaire (MHQ) to detect key psychological symptoms and relevant traits.
Results: The results showed that secure attachment is significantly associated with adequate general health (B= .926; P= .021) and mental health (B= 1.104; p= .002) of the SF-36. Maternal care was also significantly associated with a good SF-36 mental health index (B= .528; p=.021).
Conclusions: The results confirmed the positive role of a secure attachment style and a good parental bond for adequate psychological health. Early identification of patients with dysfunctional attachment styles will make it possible to offer them targeted interventions to improve their ability to accept, adapt and manage the disease and to maintain adequate psychological well-being.

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