

Congress Review

29 August — 01 September 2021
MiCo Convention Centre
Milan, Italy

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CONTENTS

- 3** Thanks
- 4** Committees
- 5** Congress Domains
- 6** Facts & Figures
- 7** Plenary Highlights
- 16** State-of-the-art Highlights
- 19** Scientific Highlights
- 24** Domain In Focus: Precision Medicine
- 26** Domain In Focus: Emerging Approaches & Technologies
- 28** ESOT Congress Awards
- 30** Section & Committees Round-up
- 31** ESOT Grants Programme
- 32** Patient Inclusion Activities
- 34** Our Partners

Thank you for Attending the ESOT Congress 2021!

**Thank you everyone for your valuable participation
at the 20th ESOT Congress.**

The meeting truly delivered world-class science, from ground-breaking abstract-based presentations to Think Tank sessions full of debate and discussion. It has been a great opportunity to network once again – both online via our virtual platform and for those onsite in Milan – helping to foster collaboration and future partnerships.

The preparation for this hybrid meeting has required novel technologies, creative imagination, and tremendous collaboration. As a community, these are qualities that we deliver each day in our field, and we hope that the Congress motivated and inspired you to continue to do so to improve the lives of our patients across the world.

The journey does not stop now – we encourage you to continue using our platform to revisit sessions on-demand over the next 12 months and join ESOT in the development of our vision for equitable and sustainable transplantation in Europe and beyond.

With warmest regards,



Luciano Potena
ESOT President
Co-Chair of the Scientific Programme Committee



Umberto Cillo
ESOT Secretary
Co-Chair of the Congress

COMMITTEES

ESOT Congress Chairs

Maria Rosa Costanzo, Umberto Cillo

Scientific Programme Committee

Luciano Potena & Raj Thuraisingham (Co Chairs)

Christian Benden, Ugo Boggi, Stephan Ensminger, Christine Falk, Anna Forsberg, Amelia J. Hessheimer, Martin Hoogduijn, Sarah Hosgood, Ina Jochmans, Julie Kerr-Conte, Katja Kotsch, Pascal Leprince, Fiona Loud, Dominique Martin, Robert Minnee, Rainer Oberbauer, Gabriel Oniscu, David Paredes, Stephen Pettit, Jacopo Romagnoli, Faouzi Saliba, Stefan Schneeberger, Dimitrios Stamatialis, Luca Toti.

The ESOT Executive Committee 2019–2021

Vassilios Papalois (President)
Stefan Schneeberger (Past President)
Luciano Potena (President-Elect)
Gabriel Oniscu (Secretary)
Olivier Thaumat (Treasurer)

With Councillors

Oriol Bestard, John Boletis, Umberto Cillo, Frank Dor, Ina Jochmans, Nicos Kessarar, Hanne Scholz.

And

Ivan Knezevic (ECTTA Chair), Robert Langer (EKITA Chair), Wojciech Polak (ELITA Chair), Steven White (EPITA Chair), Nichon Jansen (EDTCO Chair), Emma Massey (ELPAT Chair), Martin Hoogduijn (ECTORS Chair), Gerald Brandacher (VCA Chair), Katja Kotsch (BSC Chair), Raj Thuraisingham (EC Chair), Anna Forsberg (ETAHP Chair), Sushma Shankar (YPT Chair).

ESOT CEO

Luca Segantini

CONGRESS DOMAINS

The ESOT Congress 2021 was divided into five distinct domains focusing on the most relevant topics in organ transplantation. Sessions and abstracts were all separated into these specific domains, allowing delegates to follow specific topics and map their Congress journey. The five domains were as follows:

Emerging Approaches and Technologies, which focused on:

- Artificial organs
- Organ reconditioning
- Nanotechnology
- Biotechnology
- New techniques
- Minimally invasive approaches



Precision Medicine, which focused on:

- Big data analysis
- Omics
- Biomarkers
- Biomechanisms
- Immunology
- Immunotolerance



Present and Future Transplant Practice, which focused on:

- Real-life clinical approaches
- Case based scenarios
- Ongoing clinical protocol sharing
- Logistics in transplantation
- Telemedicine in transplantation



Regenerative Medicine (Cell Biology), which focused on:

- Stem cell therapy
- Scaffolds/organoids
- RNA interference therapy
- Nanomedicine in regenerative Medicine



Value-based Care, which focused on:

- Patient and population outcomes: endpoints and actions for improvements
- Guideline development: methods, results
- Resource optimisation and cost effectiveness
- Equitable organ allocation systems
- Disparities and unequal access to resources
- Transplant system governance



FACTS & FIGURES

Participants

1,200



Onsite participants

1,475



Online participants

Press & Social

4,412

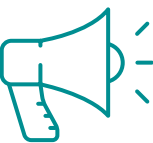
Total posts using #ESOTcongress

14,375,433

#ESOTcongress audience reach

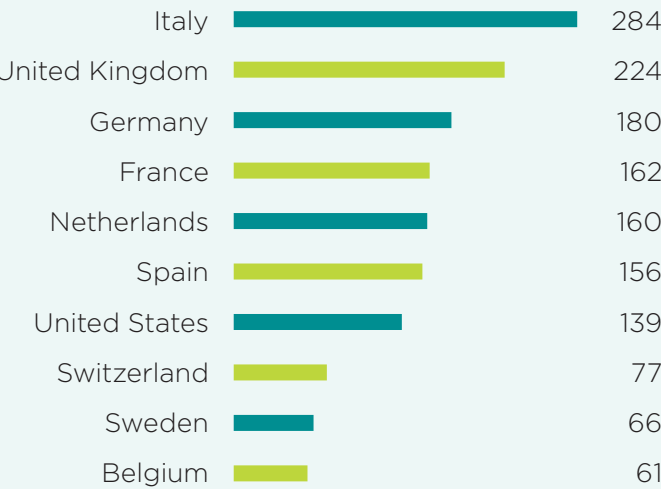
645

Articles in the press



74 COUNTRIES REPRESENTED

Top 10 countries represented:



Industry

30+



Sponsors and exhibitors

14 INDUSTRY SYMPOSIA



Scientific Programme

19 Congress tracks

5 Congress domains

1,220 Abstracts submitted

994 abstracts presented

96 Late-breakers presented

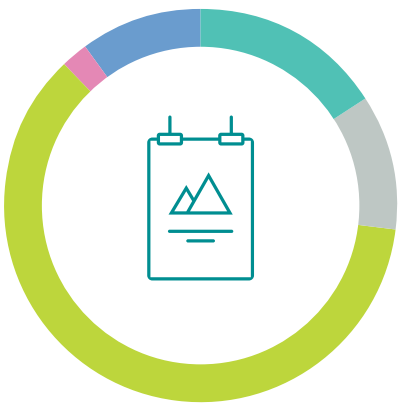
850+ Speakers

830 Presentations

3 Hands-on sessions

Abstract breakdown by domain:

- Emerging approaches and technologies: 16%
- Precision medicine: 11%
- Present and future transplant practice: 61%
- Regenerative medicine: 2%
- Value based care: 10%



PLENARY HIGHLIGHTS

A Call to Action to End Inequalities

ESOT leaders launched a call to action on the opening day the ESOT Congress 2021, as the Opening Session vividly highlighted inequality in healthcare and transplantation.

Congress co-chair Professor Umberto Cillo described it as an “incredible milestone” that this year, ESOT was holding the 20th meeting since the first in Zurich in 1983. As the first ever fully hybrid event, it was “avant-garde”. During the past two decades, he explained that there had been many developments of the highest level in transplantation which should all be celebrated. However, the subject chosen for the opening session – ‘Managing inequalities in healthcare and transplantation’ – demonstrated how inequities such as race and social background must be addressed to allow transplantation to continue this trajectory.

President-elect Luciano Potena said that with innovation, sustainability and equity, change was possible and ESOT was the organisation to push this agenda.

From the outset, COVID-19 was front of mind. Potena described how until June, the MiCo Convention Centre in Milan, where the in-person element of the meeting was being held, was being used as a temporary COVID hospital. “There is no glamour – we want to recognise the time and gravity of this period,” Potena, who is also Scientific Programme Committee co-chair, explained.

An emotive video showed the dramatic toll of COVID-19 on health workers, through pictures from leading photographer Alberto Giuliani and numbers revealing the reduction in transplant activity.

The three talks that followed were gritty in subject matter. Congress co-Chair, Maria Rosa Costanzo, a cardiologist at Midwest Cardiovascular Institute in Naperville, US, introduced the first speaker Hannah Valantine and paid tribute to their long-standing relationship as the “early women of heart transplantation”.

UK-born Valantine, who went to work at Stanford University as a young doctor in 1986 and is now Professor of Medicine, gave the keynote address, ‘Genetic diversities as a paradigm of inequality management’. During an insightful talk, Valantine, a former NIH Chief Scientific Officer for Scientific Workforce Diversity, covered racial inequalities in post-transplant outcomes and racial differences in risk factors for poor outcomes.

African Americans in the US have higher rates of graft loss, diabetes, a longer time on waiting lists and have fewer living donors than their white counterparts. However, it’s not just an issue of access – even in countries where there is a universal healthcare system, such as the UK, she said we see these disparities as well. UK research has shown that graft survival is inferior with all non-white kidney donors, independent of the recipient’s ethnicity, and that has played out across other organ transplants. “It’s really a complicated and somewhat nuanced situation,” she described.

Valantine then examined the role of HLA heterogeneity and mitochondrial DNA mismatch before calling for a new future paradigm in organ transplants using tailored, precision medicine. The ultimate aim is equity in biomedicine, integrating the social, environmental and biological determinants of health.

“It’s really a complicated and somewhat nuanced situation”



Valantine concluded that while the phrase “great minds think alike” may be common, in actual fact accepting that “great minds think differently” is the key to helping address racial inequality in transplantation.

Sir Michael Marmot, Professor of Epidemiology at University College London, and Director of the UCL Institute of Health Equity, then delivered a fascinating presentation on social justice and health equity.

Author of the influential *Marmot Review and Build Back Fairer* (a report on the impact of COVID-19 in the UK), Marmot described how inequality, deprivation and life expectancy in England had worsened in the last 10 years, a trend which has been accelerated even further by the pandemic.

In stand-out statistics from his own recent research, he explained how during the first half of 2020, life expectancy in Greater Manchester in the UK went down by 1.6 years for men and 1.2 years for women. England had the worst excess mortality of all rich nations during the pandemic, he added.

Sir Michael Marmot blamed these reductions on poor governance and political culture, a rise in social and economic inequality, a reduction in public spending, and the fact England was unhealthy coming into the pandemic. Health, he said, was a measure of societal success. “I would say to governments everywhere, put a fair distribution of health and wellbeing at the heart of all Government policy.” The Guardian newspaper described Sir Michael Marmot’s report as “jaw-dropping”.

‘Perspectives of managing inequities in transplantation’ concluded the session, where Cillo and Potena discussed the profound impact of the pandemic. Whilst the speed of vaccine development was unprecedented, it had not been matched by the roll out globally, leading to an apartheid of sorts. In a wide-ranging approach, Cillo said we need a more holistic and global view, and covered climate change and One Health – the ambition to attain optimal health for people, animals, and our environment.

He said, “In the last 18 months we have learned that we cannot achieve health in single countries if we do not interface even with the farthest country. We cannot achieve human health if we don’t approach the connection among environmental, animal and human health.”

Cillo said pre-pandemic factors that influence inequalities in access to the transplant waiting lists include older age, lower socioeconomic status and health literacy. He explained that in 2008 the EU set in place an action plan to improve self-sufficiency in solid organ transplantation across Europe. Although the plan resulted in meaningful increases in transplants in several countries, there were reductions in others, highlighting the diversity in response and the need for a unified approach.

Machine perfusion, he added, is the response of innovation to the problem of organ supply, which the Congress will examine in detail. However, to be effective on a large scale, this approach needs to be widely available and affordable.

Potena added that promoting value-based care defined around the patient was key, including developing transplant programmes in low-income countries to reduce costly long-term dialysis which can be unaffordable for many.

A new, future, vision is needed to tackle all these issues, with Potena and Cillo then mapping out a 6-point plan:

- Face inequalities in high-income countries
- Reach self-sufficiency in Solid Organ Transplantation (SOT)
- Improve sustainability
- Improve research & development
- Encourage definition and achievement of value
- Promote programme development in low-income countries



Potena said this was not “Utopia” or an “intellectual exercise” but a time for real change. “This is a call for action. We believe ESOT is the place for such an action.

We invite you to get involved with us, to breathe new values of innovation, sustainability and equity in transplantation and to get involved with our society.”

Rethinking What Success Looks Like

A ‘quiet revolution’ in transplantation means that metrics such as patient and graft survival are increasingly becoming obsolete and new endpoints are needed, Monday’s Plenary Session heard.

The session, called *‘The end of Kaplan-Meier: New endpoints in transplantation’*, was told that with the emergence of precision medicine and the importance of demonstrating value, the time is right to completely rethink what success looks like for transplantation in the 21st century.

Speaker Maarten Naesens said that graft failure rates in the 10 years post-transplant have dropped from 45% in 1966, to 15% in 2015, so new endpoints were needed, which should be a “point of pride”.

Naesens, Clinical Director of the Nephrology and Renal Transplantation unit of the University Hospitals Leuven, asked: “We are seeing a revolution. Why are we so pessimistic?” He added the challenge was how to further the revolution in the coming years.

An ESOT working group had met with the European Medicines Agency (EMA) to discuss this issue of alternative endpoints for clinical trials, submitting a 100-page document to them and held further online discussion meetings over acceptable and non-acceptable endpoints.

This group learned that the EMA supported the use of Patient Reported Outcome Measures (PROMs) – not as secondary but as primary endpoints. As a result, Naesens said it was crucial to include patients in conferences and workshops and “in everything we do”.

In his talk, *‘Novel endpoints for tailoring therapeutic interventions’*, he concluded: “In the past medical advancements were really made by the doctor. In the future, the advancements will be made by the patient. And we will put the patient at the centre.” He paid tribute to the people involved in the working group which he said must be expanded, including patients and caregivers.



The emphasis on the patient was reinstated by Canadian Jillianne Code, a Professor of Learning who has had two heart transplants after being diagnosed with heart failure in her 20s. Despite being a virtual presenter, she demonstrated in an emotional discussion on why life should be measured, not death.

In her talk, called *‘An education of [real] survival analysis: Learning it’s about life, not failure’*, she questioned the use of Kaplan-Meier’s. She described her life as challenging but beautiful, with an uncertain existence as “a clinical trial of one... I am a clinical trial.”

She explained how she has set up the Heartlife Foundation to support and empower patients and help them understand that survival is not a helpful way for them to think about their illness.

Code said “I am a qualitative researcher by training, I do understand Kaplan-Meier’s is meant to measure survivability. I often wonder ‘what does that mean for me?’ I have so much treatment and you can see all the meds I take. With everything else that my body has gone through, what does my risk look like?”

She went on to say that survival for people with heart transplants has gone up and is now at 12 years but she again questioned the meaning. “Trying to calculate my own survivability makes me scratch my head. It doesn’t make a lot of sense.” She said the risk assessments say there’s 50:50 survival after 10 years for heart transplant patients. “Doesn’t everyone roll a dice waking up every day?”

WATCH THE OPENING PLENARY VIDEO

She ended “As somebody who’s lived through this, the real learning and education about heart transplant patients is that it’s about life, not failure.”

Earlier, Dr Euan Ashley, Professor of Cardiology and Genetics at Stanford University, and an expert on digital genomic medicine, began with an anecdote about a patient whose tachycardia was diagnosed after his Smart Watch told he was in fat-burning mode – while he was on the coach eating pizza. If this can happen, he asked, what about other uses in healthcare?

His talk on ‘*Big data analysis in definition of medical endpoints*’ demonstrated the effectiveness of digital and wearable devices and electronic health records in providing a rich, real-time window into patient trajectories and activity.

He said as well as his team, many others were studying this too and the patient take up was huge. In the Apple Heart study, 150,000 people signed up, allowing a scale not previously seen. He furthered that researchers had been worried that they would see lots of young people going to the Emergency department concerned about Atrial Fibrillation, but that did not happen.

He explained how the ability to look at digital phenotypes – inferring individual behaviour through digital data – was better than patient surveys. Rather than asking how many steps they took last Thursday they could measure in real time through an accelerometer.

Professor Alexandre Loupy, Head of the Paris Translational Research Centre for Organ Transplantation, explored the importance of fine-tuning endpoints to improve both efficiency and patient outcomes in specific transplantation settings. He said: “Now in the 21 century we have tons of data, genomics, biomarkers – how do we predict? We need to better process this data.”



Alexandre Loupy



He gave the example of the need to enhance allograft allocation through AI based simulation tools and virtual systems. Loupy concluded by highlighting that “fine tuning end points involves fine tuning ourselves as clinicians.”

The lively Q&A was led by co-chairs Anna Forsberg, Clinical Professor in Caring Sciences specialising in organ transplantation at Lund University, and Transplant International editor and ESOT Past President Thierry Berney.

Nephrologist Raj Thuraisingham, ESOT Education Committee Chair, commented “We all die eventually – it’s premature death we need to measure.” Maarten Naesens described the question as crucial but asked – what do you compare it with? The Congress subject matter was divided into domains and tracks and the panel was asked whether patients should have their own track within the meeting. But Marten Naesens answered firmly: “Don’t silo patients with their own track, they must be involved in all we do.”

Thierry Berney concluded: “This was a very inspiring and stimulating session on novel endpoints covering high tech, and emotional aspects.”



Raj Thuraisingham

From Crisis to Opportunity

Transplantation in Europe suffered a “real crisis”, with the number of transplants reduced by more than 25% in the UK and France in 2020 compared with 2019, the Plenary Session on Tuesday heard.

Organ donations were affected too, with 24.5% fewer in the UK and 21.4% in France. Italy fared better, with a drop of 9.8% in transplants and 12.8% in donations, while Germany had 6.6% fewer transplants and only a 2% reduction in donations.

The figures were announced by the session co-chair, Massimo Cardillo, Director General of the Italian National Transplant Centre, on the same day as a major publication in the journal *Lancet Public Health* of a study of kidney, liver, lung and heart transplant data from 22 countries across four continents, written by members of the ESOT TLJ working group on COVID-19.

The study, which made headlines across the world, found that the overall drop was almost 16% by the end of 2020, with more than 11,200 fewer transplants carried out and 48,239 patient life-years lost.

Cardillo said the experience in Italy had led to important lessons in reforming services and redeploying of resources, such as the need to invest in technology and digitalisation, and training for staff in these mediums. Understanding about COVID-19 and transplantation had rapidly advanced and it had been shown that it was possible to use donated organs from infected people. He said more than 20 had been done in Italy, with no cases of transmission. International collaboration and organ sharing had also improved as well as better communications generally, providing information with impact.



The session ‘*Re-deploying resources in the era of SARS-CoV-2*’, co-chaired by Vassilios Papalois, discussed how transplant activities continue at a time

when healthcare systems are pushed to their limits. It heard from four speakers who argued that, while the pandemic had been extremely challenging, it had pushed boundaries in a beneficial way.

Dorry Segev, Professor of Surgery and Epidemiology and the founder and Director of the Epidemiology Research Group in Organ Transplantation (ERGOT) at Johns Hopkins University in Baltimore, described an innovative observational study “of 8,000 people we had never met in person”, which showed remote trials of recipients are possible and effective.

He and his team began a study of the safety and efficacy of vaccination in terms of antibody status on transplant patients and other immunocompromised people in December as soon as vaccines became available in the US. As this was at the height of the third wave of COVID, it was dangerous for immunosuppressed patients to leave homes let alone come to hospitals for the trial, so it was organised remotely. More than 1,000 patients enrolled in first week.

Home visits were made to test vaccine reactogenicity and remote collection was organised with a special capillary blood collection device to test immunogenicity at baseline, 1 month and 3 months following the Pfizer or the Moderna vaccination, which trialists posted back.

By April, they were able to publish safety data on 740 patients who had received two doses. “Very early, we knew that this was safe, and we were able to encourage transplant patients to get vaccinated,” he said.



They also found that antibodies were detectable in less than 20% of transplant patients after one dose, in stark contrast to 100% of immunocompetent

people who participated in the randomised trial. Later, when looking at two doses, they were able to separate out transplant patients into non-responders (43%), weak responders (39%) and positive responders (18%), but these may be converted into stronger responses with boosters.

The researchers are now looking at the efficacy of antibody response after doses three and four and the trial called COVID-19 Protection After Transplantation has been described by Anthony Fauci, director of the NIAID in the US as “novel and ambitious.”

1. Vassilios Papalois
2. Dorry Segev



Segev said, “We can run research studies of 1000s of people who never leave their homes, who we never have to meet in person. This has really important implications not just for research, but for clinical care.”

He said it may impact researchers’ ability to study higher risk patients, find early markers of rejection and early markers of disease development. “I can tell you, for me personally, it has completely changed the way I view how we’re going to do science moving forward.”

Massimo Puoti presented a case study of a 1,067-bed Niguarda hospital in Milan which he said was “hijacked” with COVID, with 3,675 cases including 501 in ICU. Transplant activity was reduced by 32% (heart) and 7% (liver).

He said, however, that the hospital was flexible and able to build in a rapid response to caring for infected patients and use increased telehealth to reinforce a chronic care model, as well as innovate by improving the opportunities for screening, such as introducing point of care testing for Hepatitis C at COVID vaccination sites.

In fact, there was an element of COVID as a disruptive innovation, with “turbo-chaotic” COVID-19 research, leading to more than 6,000 clinical trials and rapid publication which should be maintained for other disease areas. Finally, he emphasised that care must be taken to support the mental health of the workforce.

In his talk, *‘Facing crisis: The need for a modelling approach’*, Glenn Bonney, a liver, pancreas, and transplant surgeon at the National University Hospital in Singapore, first looked at the reduction of organ transplants during pandemic, with the UK and the Netherlands experiencing a 50-90% reduction in donations.

Bonney showed how the use of extended criteria livers – those which have certain risk factors and were not previously used – had decreased wait time for liver transplantation without adverse impacting post-transplant survival. From a model that he and his team developed, Bonney revealed the significant impact the pandemic had on waitlist mortality rates.

In the last talk, Stefaan van der Spiegel, Head of Sector, Health Innovation and Substances of Human Origin from DG Sante at the European Commission, discussed what the EU can do in building resilience into health systems in Europe – and what it can’t do.

In *‘EU centrality in reshaping and relaunching the health system’*, he explored the role of the EU in transplantation policy, highlighting that there are no plans to change the 2010 EU Organs Directive. However, he said there are “ongoing, active” revisions to a number of EU directives on blood, tissues and cells, which would be finalised by the end of the year.

“For a society like ESOT, these are important things to keep an eye on because if we come to a revision of the EU Organs Directive in a couple of years, I think what will be decided here on in the blood, cells and tissue transplantation field will be very important.”

Van der Spiegel then looked at the EU policy objectives around transplantation, revealing 10 priority actions and presented several useful tools available, including the €5.3bn budget available as part of EU4Health programme.

He ended on the positive note that it was clear there were possible new funding opportunities for the field of organ transplantation. “I think the sector has views on what is needed, and I think there’s now opportunities coming... so it’s a good moment to explore that.”

Closing Plenary: Rocket Science Needs More Fuel

The Congress ended on a triumphant note with praise for the tremendous achievements in transplantation so far, excitement over the possibilities for the future, combined with passionate calls for increases in funding and diversity.

The speakers said the first hybrid Congress, while a logistical challenge, was a resounding success. Outgoing President Papalois said it was “nothing short of a miracle”, while conference co-chair Cillo said it was “unprecedented and unforgettable”.

But far from being complacent, the Closing Plenary highlighted some of the ongoing challenges that ESOT and the wider transplant community are tackling. In a riveting talk, nephrologist and biomedical engineer William Fissell outlined his pioneering research in artificial kidneys, with the goal to create a part biological, part synthetic hybrid universal donor organ. This would not be rejected by the recipient, releasing them from years of immune suppression medication, and the



entire device would be under the skin, with no catheters to remove fluid. With it, his team would like to make kidney dialysis “a museum oddity, like iron lungs.”

Despite being told they would never be able to achieve preclinical haemofilter implantation, after 16 years they were able to announce its success. However, he revealed his frustration that the next step was being held up for lack of funding because the work falls between two stalls – not new or transformative to gain basic science funding, but too early to gain industry support.

Fissell, from Vanderbilt University Medical Centre in Nashville, Tennessee, called on funders to come forward to enable him to advance the work which he said was around two years before clinical trials. He pleaded “I would like to become, someday, part of the history of transplantation. Our project needs funding. One of you somewhere knows someone who can support us.”



Later in his first address as President, in another call for reform of the status quo, Potena called on more women to get involved within ESOT at an Executive level. He said progress had been made but “fresh faces” and further diversity was needed. He explained “Three years ago we had only 28% of women; with the new elected



council we have 44% of women, but we are still five white dudes, running the society as an Executive Committee.” He said he hoped that in the future, female colleagues would have the courage to push forward and to stand for election to the committee.

The substantive session was dedicated to the past, present and future, entitled *‘From candlelight to rocket science: The journey of transplantation’*. Session co-chair Stefan Schneeberger said while transplantation had been thriving for a decade on the achievements of the early days, there was now an “avalanche” of new technologies resulting in palpable advances to patient care.

At the outset, Maria Rosa Costanzo gave a talk on scientific achievements including developments in organ donation awareness amongst minorities, improvements in paediatric organ transplantation, normothermic regional perfusion and the significant advances in personalised medicine in heart transplantation.

She paid tribute to her heroes, particularly Dr Sharon Hunt, “the mother of transplant, cardiology”, and Dr Eric Rose from Columbia who, she said, taught her how to speak freely and not to be afraid to disagree “because only a free exchange of ideas can lead to progress”.

For the present, Cillo described how the congress had been planned over 700 days, with 100 teleconferences, many over Zoom, often with children, pets and partners’ cooking joining in the meetings. He caused laughs by remembering how of the 12,000 emails sent about the Congress, Cillos’s were on average 15 words long while Potena’s were 150.

1. Vassilios Papalois & Luciano Potena

2. Luciano Potena

3. Stefan Schneeberger

On a more serious note, he explained how, when the Congress was first being planned in late 2019 it was prophetic that the word connect was chosen to be central, along with interplay and interface – one that has become overused due to the pandemic.

Despite the challenges, it had been possible to organise 14 pre-Congress webinars, host delegates from 74 countries, publish more than 1,000 abstracts, set up a live studio and attract international press coverage – much of this down to the ESOT Congress all-female organising team, led by Devi Mey.

Then the session turned to the future. After Fissell’s talk on artificial kidneys, another exciting aspect highlighted surrounded organoids, artificially grown mass of cells that resemble an organ.

In Hans Clevers’ presentation ‘Organoids to model human disease’, he explained the details of his research and findings and demonstrated the long-term survival of transplanted colon organoids grown from a single stem cell. From this, Hans showed an example of how this approach could be used as a personalised medicine for restoring CFTR function and gene correction. He also revealed how it could be used to develop hepatocyte (liver cell) organoids.



Devi Mey

At the very end of the Congress, Papalois paid tribute to the new President, and said Potena had spent his career being committed “to work, to do, and to serve.” His hallmark, he said, as a clinician and a scientist, was his ability to bring teams together, to select the right people, secure the right resources, help them to develop and lead them to success.

In response, Potena admitted with a smile that his address would take “slightly longer than 150 words.” He praised Papalois as an outstanding example of being a President, not just of ESOT but also UEMS, at the same time as being a member of multiple advisory boards and editor in chief of a journal and meanwhile performing more than 2,000 organ transplants.

He went on to share his Presidential vision, saying their profession was founded on the gift of donation, which can heal and save lives, and their work needed to be looked at through this lens. He added “Without that [gift] we would not be here, we would not have the advancements in science, we would not have developed anything... we have to add value to this gift not just prolonging life, but a whole series of things we need to do.”

He spelled out how he wants to encourage the multi-disciplinary nature of the Society. “We cannot do anything alone,” he said. “This is the vision that I hope to bring to the society in the next two years, to promote sustainable and scientific advancement to multidisciplinary communities to give value to our sections and communities.”

“...to work, to do, and to serve”



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esot.org #ESOTTLJ

STATE-OF-THE-ART HIGHLIGHTS

Measuring the value of organ donation programmes

With a focus on the value of organ donation programmes, Paolo Muiesan and Ugo Boggi co-chaired a State-of-the-Art session with the aim of discussing how healthcare systems need to be able to set their priorities plus monitor and measure their outcomes to demonstrate value, with the rising global cost of healthcare. These themes were led by key representatives of healthcare organisations in Europe and shared with delegates at the Congress.

Beatriz Dominguez-Gill opened the session by telling the group about the performance in Spanish donation programmes. She discussed how Spain has been able to reach high levels of transplantation due to their system, going into detail about the Spanish Quality Assurance Program specifically - as this has allowed them to assess performance in the deceased donation process to identify areas of improvement. Dominguez-Gill shared results of audits from the past 20 years which have proved to represent important learning opportunities, before diving into the actions that have been taken, due to the program, to improve the donation process. To conclude her talk, Dominguez-Gill reminded the group that even with an apparent good performance in deceased donation, there is still room for improvement in the Spanish programmes.

The next speaker, Mirela Busic, followed up by informing the group about the key performance indicators in donation programmes in Croatia. She began by discussing Croatia's policies and presented key insights into the country's activity in organ donation. Busic presented a flowchart which served as a basic tool for assessing hospital performance and then proceeded to go through the donation pathway; from possible donor identification, to transplantation, stressing that any non-conformity in the process is reported, analysed, and corrected with close collaboration between teams. Busic looked to close the meeting as she discussed how the system has effectively contributed to a transplant program approaching self-sufficiency. She left the group with a key message in that the guiding ethical principles laid down by the WHO should be mirrored and promoted in every national donation policy to gain and preserve public trust in this sensitive field.



Carl Jorns next spoke about the Swedish approach to donation performance evaluation- the Swedish Quality Assurance Program. He first gave a brief overview of Sweden's transplant activity- with centre-orientated donation and organ allocation. Jorns highlighted three milestones of the last 10 years: the introduction of the National DCD project, STEP- Scandiatransplant Kidney Exchange Program, and the Swedish Organ Donation Quality System. Jorns then went into the key quality indicators involved in the donation pathway and how the Swedish Intensive Care Registry are responsible for registering and operating them. A short clip was played showing how data regarding the indicators in Sweden can be extracted via the registry, before considering its limitations. He then proceeded to talk about Sweden's approach to living organ donation and donation after death (DCD), with the introduction of the national DCD project- brought about more recently to formulate and introduce a national protocol for controlled DCD across ICU's. He finally gave an overview of the ScandiaTransplant Kidney Exchange Program - constructed to increase the possible matches for donation, before closing.

The final speaker, Marta López Fraga, closed the session by talking about what is being done on a European level (a unified perspective) to support countries with the improvement and harmonisation of the donation process. Fraga went into detail about the activities the Council of Europe (CoE) get involved with to help assess the efficiency of donation programmes, such as the publication of the Newsletter Transplant and Technical Guide- useful to monitor activity over the years and provide practical support for those working in transplantation, and to improve clinical outcomes. To expand the system, Fraga discussed how initiatives, such as Accord, analyse regular practises during end-of-life care by implementing improvement measures based on observations- leading to a greater availability of organs for donation. Lastly, she discussed the importance of harmonised registries to facilitate international data sharing, which not only provides transparency of practises, but also provides crucial information to generate evidence to in-turn improve quality of care, as well as evaluating the success of other programmes.

Breaking scepticism in AI-aided clinical management

Over recent years, AI-aided clinical management has become a hot topic. This State-of-the-Art session was chaired by Olivier Thauvat and Oriol Bestard with the aim of discussing the key ethical issues surrounding AI- based systems in healthcare and how machine learning classifiers can be effectively applied for more accurate clinical predication and data management.



Patrick Aloy opened talks by telling the group about formatting biological 'Big Data' to enable personalised systems Pharmacology. He began by discussing the basics of chemoinformatics and how thanks to the big data era, the knowledge available has expanded massively. Aloy used bioactivity fingerprints as an example and provided insights on how they could be used in machine learning. He also spoke about how this idea blends biology and chemistry together to enable systems pharmacology- identifying drug modulators which moderate the global behaviour of a cell/ whole system- before going into some present examples of the potential applications of the bio-fingerprints with the group. Afterwards, he moved on to discuss the future towards personalised systems pharmacology; the idea being to design new specific molecules for each specific patient profile rather than identifying the best drugs from the repertoire already available. Aloy then went on to summarise his talk whilst diving into an example that he has recently been working on.

Tommy Ivanics followed up by talking about the application of artificial intelligence (AI) techniques for donor-recipient matching. He first touched on the imbalance between donors and recipients before discussing how it could be mitigated, specifically by optimising the allocation system. He went into how there are so many factors involved in deciding allocation and the limitations to the current models used in the process. He mentioned how AI has the potential to bridge the gap between the number of variables and having good predictive performance of the models. Ivanics went into detail about AI machine learning and how it can take both historical data and outcomes to make predictions, considering far more variables

than traditional statistical models, and its ability to adapt once more data is added to be more refined. He gave examples of the models used in donor-recipient matching, the classification tree and Artificial Neural Networks and highlighted their 'multidimensional complex nature'. Ivanics moved onto looking at some studies surrounding the use of AI as an innovative donor-recipient matching model for use in liver transplantation. He then shared a study that looked at the limitations vs traditional statistical methods. To conclude, Ivanics weighed up the positives and negatives of the machine learning technology before taking an optimistic look at the future.

The next speaker, Alexandre Loupy, discussed the use of AI for diagnostics in transplantation. He began by talking about AI-based prediction models and the issues of poor data sets that need to be overcome. He highlighted how AI may not always be necessary. After, he went into how it could be improved by building a solid reference set to be worked from, namely the "D6 approach". He highlighted that Banff is stepping into AI positively. With the unmet needs defined, he talked about how they can proceed with the identification of genes, building an operating molecular platform, generating a high-quality reference set and in turn, make the relevant statistical models a reality. He ended the talk by going over the final step of delivering the AI driven integrated molecular report to hospitals and centres, which provides the diagnostic probabilities. To conclude, Loupy highlighted the change in paradigm and the future.

To close the session, Simon Knight told the group about personalised survival predictions. He firstly discussed why survival following transplantation is predicted on both an individual and a population level. He briefly discussed how it is done in current practise with existing prediction models- which rely on traditional statistical modelling and are not very individualised. Leading on from this, Knight moved onto discussing how we could use AI to better predict supervised machine learning and he went through the process. He compared the benefits and challenges of machine learning vs statistical modelling, highlighting how AI is less limited, but more difficult to interpret. He went into the literature surrounding the use of machine learning for survival prediction in kidney and liver transplantation specifically. Finally, Knight discussed the challenges surrounding machine learning, what needs to be improved and the need for more acceptability in the healthcare world.

Transplant organs of the future

This session was co-chaired by Sandra Lindstedt and Martin Hoogduijn with the aim of discussing the ongoing development of biological and engineering techniques that will lead to the availability of novel types of organs for transplantation. In this session, four potential State-of-the-Art organ transplants were presented by three different speakers.

Julia Radan opened the session by conducting a talk on genetically multi-modified pigs as donors of cells, tissues, and organs for xenotransplantation. With the supply of organs for transplantation far lower than the needed supply of human organs, Radan stressed how an alternative source is necessary and the long-term survival of xenotransplantation is of great interest to people all over the world. Radan then presented various findings from published literature. Using her expertise in the cardiac field, Radan summarised her talk by demonstrating that consistent long-term survival (>3 months) after orthotopic cardiac xenotransplantation is possible and that its clinical use is within reach. In the not-so-distant future, porcine donor hearts will become more readily available and abolish any waiting lists; the same can be said for renal and islet transplantation, and this is something we should all be incredibly excited about.

The next speaker, Hiromitsu Nakauchi, began his talk on interspecies organ generation using cell competitive niche. Nakauchi spoke about the future goal – generating human organs in livestock animals and demonstrated various bits of research that has helped science take steps forward to achieve this goal. He spoke about interspecies compatibility and the xenogenic barrier, time course analysis of embryonic chimerism, Igf1 and how its deletion can create cell competitive niche and how this all links together. Nakauchi summarised his talk by confirming that Igf1r-null mouse embryos provide a cell competitive niche which augments donor chimerism in multiple organs but only from mid- to late- developmental stages. The talk ended by highlighting the fact that understanding the manipulation of the xenobarrier may be key to the generation of human organs in livestock animals and that he hopes that more scientists will want to research and be a part of this breakthrough field.



The third and final speaker, Nuria Montserrat, concluded the session by giving a presentation on organoids. Montserrat began talking about the importance of cell differentiation potential and how key that topic of understanding is to generate tissues in the laboratory. She explained how over time, cell differentiation and cell biology has evolved and been misunderstood. Due to scientific advances, we have been able to get to a place in which we can produce organoids from human pluripotent stem cells. Montserrat highlighted that these are multiple organ-specific cell types that can recapitulate some specific organ functions, and this will play a vital part in the future of organ transplantation.

Following on from this, Montserrat dived into specifics and explained the methodology behind the generation of specific organoids. She went on to explain the assessments needed in vitro as well as some of the key steps that need to take place for successful organoid engineering in vivo. Montserrat briefly discussed one of her latest collaborations where her team in Barcelona looked at generating kidney organoids to inhibit SARS-CoV-2 infections. To conclude her talk, Montserrat explained how researchers and clinicians need to collaborate better in order to advance organoid technology to deliver important results to the organ transplant community.

SCIENTIFIC HIGHLIGHTS

Transplants fall by a third worldwide during first wave of COVID-19

The number of solid organ transplants performed during the first wave of COVID-19 in 2020 plunged by 31% compared to the previous year, according to a new global study presented at the Congress and published in The Lancet Public Health.

The research leveraged international data from 22 countries across four continents and revealed major variations in the response of transplant programmes to the COVID-19 pandemic, with transplant activity dropping by more than 90 per cent in some countries. Kidney transplantation showed the largest reduction across nearly all countries during 2020 compared to 2019, with the study finding a decrease in living donor kidney (-40 per cent) and liver (-33 per cent) transplants. For deceased donor transplants, there was a reduction in kidney (-12 per cent), liver (-9 per cent), lung (-17 per cent) and heart (-5 per cent) transplants.

According to modelling calculations, the slowdown in transplants resulted in more than 48,000 years of patient life loss. The estimated numbers of life-years lost were 37,664 years for patients waitlisted for a kidney, 7,370 for a liver, 1,799 years for a lung, and 1,406 for a heart.

The research highlighted how some countries managed to sustain the rate of transplant procedures whilst others experienced serious reductions in the number of transplants compared to the previous year and, in some areas, living donor kidney and liver transplantation ceased completely. Overall, there was a strong temporal association between increased COVID-19 infection rate and reductions in deceased and living solid organ transplants.

Olivier Aubert, Assistant Professor at the Paris Translational Research Centre for Organ Transplantation and lead author of the study, commented, “The first wave of COVID-19 had a devastating impact on the number of transplants across many countries, affecting patient waiting lists and regrettably leading to a substantial loss of life.”



Alexandre Loupy, Head of the Paris Translational Research Centre for Organ Transplantation and last author of the study, furthered, “Living donor transplantation, which reduced more substantially, requires significant resources and planning compared to deceased donor transplantation. This is extremely difficult during a pandemic when resources are stretched and staff redeployed.

There are also major ethical concerns for the wellbeing and safety of the donor. It’s clear that there are many indirect deaths associated with COVID-19 and our study confirms that the pandemic has far-reaching consequences on many medical specialties.”

Aubert added, “Beyond the near universal reduction in transplant activity, certain countries and regions managed to carry-out procedures despite major challenges presented by the pandemic. These findings warrant further analysis on a regional, national and global level to understand why reductions did or did not occur. Understanding how different countries and healthcare systems responded to COVID-19-related challenges can facilitate improved pandemic preparedness and how to safely maintain transplant programmes to provide life-saving procedures for patients.”

To facilitate understanding of the temporal trends and consequences of the pandemic on worldwide, national, and regional solid organ transplant activities for researchers, clinicians, and public health authorities, the authors created an open-access dashboard that presents data interactively for solid organ transplant activities and COVID-19 cases.

Asian donor and black recipient kidney grafts more likely to fail sooner compared with white counterparts

Black transplant recipients and patients who received kidneys from Asian donors had a significantly higher risk of kidney graft failure within seven years. The study of 20,304 kidney organs transplanted between January 2001 and December 2015 from the United Kingdom NHS Transplant Registry, found Asian donor and black recipient ethnicities were associated with inferior long-term outcomes, when compared with white counterparts.

Unadjusted survival analysis demonstrated significantly poorer long-term allograft (donor kidney) outcomes associated with Asian and black donors, compared to white donors. The 7-year graft survival was 71.9% from Asian donors, 74.0% from black donors and 80.5% from white donors.

When Cox Regression Analysis (a statistical technique) was used to account for other factors and give more insight into the true nature of the associations with outcomes, the hazard ratio was 1.37 for Asian donors (a 37% increased risk of the donor organ failing compared to white donors), and 1.21 for black recipients (a 21% increased risk of organ graft failure compared to white recipients).

The research team, led by Abdul Rahman Hakeem, a Consultant Hepatobiliary and Transplant Surgeon at St James's University Hospital NHS Trust, Leeds, United Kingdom, found better Human Leukocyte Antigens (HLA) tissue matches when the donor and recipient pairs were the same ethnicity.

At seven years, 81% of white donor/recipient pairs still had a successful graft compared to 70.6% of Asian and 69.2% of black pairs. Interestingly, further analysis revealed graft survival outcomes were worse for black recipients who received kidneys from black donors (a hazard ratio of 1.92, so a 92% increased risk of the donor organ failing compared to a white donor-white recipient pair).

The other pairs with significantly worse outcomes were when an Asian donor kidney was transplanted into a white recipient and when a white donor kidney was transplanted into a black recipient with 56% and 22% increased risk of the donor organ failing compared to a white donor-white recipient pair, respectively.

“For a start, ethnic minority patients face significant disadvantage in access to the renal transplant waiting lists in the UK and may wait twice as long as white recipients for a deceased donor renal transplant, spending longer time on dialysis, so their health may have deteriorated more,” explained Hakeem.

“The longer wait for a donor kidney is due to a shortage of grafts from ethnic minority patients – in our study, Asian people make up 12.4% of deceased donor recipients and black people 6.7% of recipients, yet Asian people account for 1.6% of all donors and black people 1.2% of donors.”

Hakeem added “despite efforts to improve education about transplant and organ donation amongst ethnic minority groups, awareness and donation rates remain low, when compared to white people.” In the UK, for example, organ allocation policy for donation after brain death (DBD) donors changed in 2006, with an emphasis on equity of access, in addition to HLA matching. This policy appears to have improved access to kidney transplantation among ethnic minorities; however, advantages have been limited by an increase in the number of patients on the transplant waiting list.

Immune response in kidney transplant recipients after COVID infection and mRNA vaccination

Kidney transplant recipients (KTR) appear to have a lower immune response after contracting COVID compared with healthy volunteers, preliminary results of a study show. The researchers are now recruiting KTRs who are being given the mRNA COVID vaccination to see if there is a similar response.

Renal transplant patients are at very high risk of severe disease and mortality following SARS-Cov2 infection, so they have been defined as a priority population to receive RNA-based vaccination. However, they were excluded from the pivotal studies evaluating these new vaccines. Due to therapeutic immunosuppression, the short and long-term efficiency of anti-SARS-Cov2 vaccination in KTR population are undetermined.

In the study, anti-SARS-Cov2 immune responses will be monitored in KTR after clinically symptomatic infection (n=67, COVID KTR) or RNA vaccination (n=100, Vacc KTR). Results of these two cohorts will be compared between them and with 2 cohorts of matched healthy volunteers (HV).

In preliminary results, both COVID KTR and HV all developed early anti-SARS-Cov2 IgM. However, while all COVID HV also developed high titers of anti-SARS-Cov2 IgG – blood tests to check for antibodies - only 66% of KTR did the same. Of the remaining COVID KTR, 25% developed low titers (10 to 20 less) and 10% had no detectable IgG response.

The researchers, led by Xavier Charmetant in Lyon, France, suspected a defective germinal centre response in KTR. This was confirmed by in vitro functional assay. Cytotoxic T cell responses in both COVID KTR and HV cohorts are currently under investigation. These data will be studied with patients' clinical pictures to establish protective correlates (signs of immunity).

Charmetant said the vaccination campaign of KTR has already started in their transplantation centre and they have already been authorised to enrol 100 KTR and 30 HV. He added: “In a few months, we expect to be able to provide a precise estimation of the efficiency of mRNA vaccination in KTR. Identification of the variable associated with the response to vaccine will be helpful to clinicians to select the appropriate care for each patient.”

Challenging the gold-standard: The expression of peripheral blood pro-inflammatory cytokines is increased in kidney transplant patients, even in the absence of histological lesions

Cytokines and chemokines have a complex regulatory influence on inflammation and play a critical role in the pathophysiology of allograft rejection. However, the relationship between peripheral blood cytokine expression profiles and clinical kidney transplant rejection is insufficiently investigated. Here, Van Loon and colleagues demonstrate that the expression of pro-inflammatory cytokines is increased in peripheral blood of kidney transplant patients with circulating HLA-DSA, even in the absence of histopathology of rejection.

The researchers, led by Van Loon set out to assess and evaluate the levels of 28 cytokines, chemokines and growth factors using multiplexed Luminex magnetic bead testing in 293 peripheral blood samples. Blood samples were collected over a four-year period (between 2012 and 2016), when undergoing a kidney allograft biopsy for graft dysfunction within the first year after transplantation. This methodology was carried out in a cohort of 192 consecutive transplants at a single kidney transplant centre.

Results from the principal component analysis and hierarchical clustering uncovered two clusters, distinct in their pro-inflammatory cytokine levels. Patients in Cluster I (N=20) had higher pro-inflammatory protein expression vs patients in Cluster 2 (N=172). Cluster I was hallmarked by a higher prevalence of donor-specific anti-HLA antibodies (HLA-DSA) (75%) as well as a higher incidence of histopathological rejection (70%) compared to Cluster II (HLA-DSA in 1.7% and rejection in 33.7%). In 30% of biopsies in Cluster I, there was no histological evidence of rejection. Cluster I had a worse graft survival independent of clinical confounders and histological evidence of ongoing rejection (adjusted hazard ratio 3.31, 95% CI 1.09 -10.03, p=0.03).

Other elements, such as serum C-reactive protein and polyomavirus and/or CMV viremia did not differ between the two clusters. In silico analysis of publicly available single-cell RNAseq data from kidney transplant biopsies demonstrated expression of the observed cytokines in endothelia cells, monocytes and NK cells.

These results challenge the vision that kidney transplant histology is the gold standard for identification of ongoing allo-immune processes.



A precious expansion of the cirrhotic patients donor pool has been demonstrated by allocating 5 SARS-CoV-2 RNA positive donors to 5 IgG-positive recipients

In more ways than one, healthcare itself as well as the availability of liver donors has been threatened due to the COVID-19 pandemic. During this time, the Italian National Transplant Centre allowed liver transplantation (LT) from patients who tested positive for SARS-CoV-2 to patients with severe liver disease who were SARS-CoV-2 positive or with a previous history of COVID-19. This screening programme resulted in a precious expansion of the donor pool by allocating 5 SARS-CoV-2 RNA positive donors to 5 IgG-positive recipients.

The researchers, led by Margherita Saracco set out to assess the prevalence of neutralising antibodies against SARS-CoV-2 in all the cirrhotic patients on LT waiting list to increase the chances of donor-recipient match.

Starting on the 25th of November 2020 for approximately 10 weeks, every patient on the LT waiting list was tested for SARS-CoV-2 neutralising antibodies using a LIAISON® SARS-CoV-2 S1/S2 IgG test. COVID-19 asymptomatic patients with positive IgG test underwent immediate SARS-CoV-2 molecular testing using nasopharyngeal swab (NPS, with Simplexa® COVID-19 Direct, DiaSorin Molecular). All patients with IgG antibodies were retested within 2 months after the first evaluation.

At the start and end of the enrolment period, 61 and 75 patients respectively, were actively on the LT waiting list. During the study period, 27 first adult LTs were performed in our Centre. 98 patients underwent SARS-CoV-2 IgG test, and 22 (22.4%) of them tested positive. 8/22 (36.4%) had a previous documented history of COVID-19; the remaining 14 (63.6%) were asymptomatic and tested negative at NPS. 5 out of those 22 IgG positive cirrhotics (22.7%) received a graft from a positive SARS-CoV-2 RNA donor. After a median post-LT follow-up of 8.5 weeks no SARS-CoV-2-related complications occurred. Only 1 patient showed intermittent NPS positivity without clinical or radiological sign of disease.

In the cohort assessed by Saracco and colleagues, 22.4% of cirrhotic patients on the LT waiting list tested positive for SARS-CoV-2 neutralizing antibodies and 63.6% of them did not show a history of COVID-19.

A dynamic, integrative prediction system has been generated to predict long-term kidney-graft survival using artificial intelligence

A dynamic, integrative prediction system that accurately predicts the risk of long-term graft failure has been developed that outperforms any current prediction models in kidney transplantation based on traditional approaches.

The researchers, led by Marc Raynaud set out to develop and provide kidney recipients with a risk-assessment of their graft survival to combat an existing unmet need. Existing models revealed that a kidney recipients' immunological profile, graft scarring, allograft inflammation, and repeated measurements of eGFR and proteinuria were risk factors of graft survival. Their key aim was to develop a dynamic system that generates continuously refined predictions, updated by evolving clinical data.

An international study of deep cohorts of kidney recipients utilised data from 8 transplant centres from Europe, the US and South-America across 6 randomised controlled trials (RCT). Recipients underwent assessment of clinical, functional, histological, and immunological parameters, alongside measures of eGFR and proteinuria.

A total of 13,608 patients were included in the international study (3,774 patients in the derivation cohort, 834 in the external validation cohorts), and 416,510 eGFR and proteinuria measurements were evaluated over the study duration. The median follow-up post-transplantation was 6.56 years (IQR 4.27-9.54).

The final dynamic, integrative prediction system demonstrated very accurate calibration and discrimination in the derivation cohort (AUC=0.857). The performances were further confirmed utilising data from the 14 validation cohorts from Europe (overall AUC=0.845), the USA (overall AUC=0.820), South-America (overall AUC=0.868), and the RCTs (overall AUC=0.857).

Raynaud and his fellow researchers successfully a system that accurately predicts the risk of long-term graft failure and believe that this system may be successfully in helping to refine the prognostic judgements of clinicians in everyday practice.

Regular activity post-kidney transplant prevents diabetes and offers better glucose tolerance and smaller waistline

Regular physical activity after a kidney transplant provides significant prevention against the development of pre-diabetic conditions and post-transplant diabetes mellitus (PTDM), a new study from Slovakia has found.

Researchers compared two groups of post kidney transplant patients, one of which did 150 minutes of moderate intensity physical exertion per week. At 6 months follow up, the active group were more likely to have normal oral glucose tolerance and lower waist circumference, and less likely to have diabetes.

PTDM is significant risk factor for the survival of graft recipients and occurs in 10-30% of patients after kidney transplant. The condition is associated with premature cardiovascular morbidity and mortality. Weight gain, obesity and dyslipidemia are strong predictors of PTDM but by modifying them with active lifestyle, it is possible to reduce incidence of the condition and improve the long-term survival of patients and grafts.

As part of the study, 22 participants post-KT performed aerobic workouts including a sub-group which did more intensive combined aerobic plus strength sports activity. Monitoring was provided by a sports tracker called Xiaomi Mi Band 4, compatible with Mi Fit mobile app. A control group consisted of 22 stable patients after KT. Both groups had the same immunosuppressive protocol.

The patients were tested for oral glucose tolerance (oGTT) at 6 month follow-up and it was found there were significantly fewer patients with normal oGTT in the control group compared with the study group (P < 0.0001). In the control group, there were significantly more patients diagnosed with PTDM (P = 0.0212) and with pre-diabetic condition (impaired plasma glucose, impaired glucose tolerance) at 6 months (P = 0.0078). The study group had significantly lower waist circumference at 3 and 6 months (P = 0.0437, P = 0.0372) and low-density lipoprotein at 6 months (P = 0.0444).

Further, the subgroup performing intensive training achieved a significant additional effect on the reduction of waist circumference (P = 0.0173). Patients practicing aerobic activity only achieved significant decrease in triglycerides, compared with those practicing combined activity (P = 0.046).

The researchers, led by Karol Graák, from the University Hospital Martin, Jessenius Medical Faculty of Comenius University, Department of Surgery and Transplantation Centre, Martin, Slovakia, concluded that regular physical activity after KT provides significant prevention against development of pre-diabetic conditions and PTDM.



DOMAIN IN FOCUS:
PRECISION MEDICINE

Tailored treatment and diagnosis
for transplant patients

In the world of oncology, tailored treatment and care based on the patient’s individual genetics is common and often expected. Not so in transplantation. However, precision medicine – the ability to consider a patient’s individual characteristics and tailor care accordingly – is becoming an increasing possibility, and in some areas is even happening.

At the forefront is Maria Rosa Costanzo, a world-renowned cardiologist based at Mid West Cardiovascular Institute in Illinois and Medical Director of the US organisation Heart Failure Research. Costanzo co-chaired the ESOT Congress with Umberto Cillo and spoke on the final day on the achievements of transplantation, including on precision medicine.

She defines the term as tailoring a number of activities to the transplant recipient, such as the monitoring of their clinical status, the assessment of their immune status, drug dosage, and the type of medication, and even the prophylaxis against the opportunistic infections that immunocompromised patients are at risk of.

Costanzo said there are many areas of transplantation in which precision medicine can play a very important role, based on four pillars:

- Pharmacogenomics
- Immune monitoring
- Diagnosis of rejection
- Prophylaxis for infection

“Now it is almost unheard of, that patients get heart biopsies after one to two years after transplantation”

Reducing the need
for organ biopsies

Of these, the one pillar that is most advanced clinically, and perhaps the most important, is a non-invasive test to establish the risk of organ rejection and therefore reducing the need for invasive biopsies in recipients.

This new test, called AlloMap, is increasingly being used for heart transplant patients. It doesn’t diagnose rejection per se, but it can predict when there is a very low chance of rejection by analysing the expression of different genes which happens when the transplanted organ is showing signs of rejection. It can give a negative predictive value for rejection of almost 95 to 99%. Costanzo is currently using this test in her practice with heart transplant recipients and says in the US most transplant centres have adopted the LM map.

“This is a test that will not diagnose rejection, but it’s very good at telling you that the likelihood of rejection is very, very low. Now it is almost unheard of, that patients get heart biopsies after one to two years after transplantation”, she explains.

This makes an ‘enormous’ difference to patients, reducing the risk of complications that can be caused by repeated biopsies such as tricuspid regurgitation – leaking of the tricuspid valve, or the creation of coronary fistulas, as well as the need for the patient to travel to attend hospital and wait for pathology results.

Tailoring doses of
anti-rejection drugs

Post-transplant, immunosuppressive medications are monitored by blood tests and based on the results, standard doses are prescribed. But the increased understanding of the human genome and pharmacogenomics means that we now know that certain patients have genetic mutations which means their enzymes metabolise drugs differently.

For example, 65% of patients with African ancestry have a mutation affecting the enzyme that processes tacrolimus, so in clinical practice doctors are beginning to recommend that they should receive one and a half to twice the dose given to other patients.

This has a dual outcome – reducing rejection and eliminating diversity and inequities in heart transplantation.

Another example is mycophenolate which many patients cannot tolerate due to Gastro-intestinal side effects. Costanzo says: “We now know that there is a genetic predisposition to the development of the side effects. So the concept would be to make sure that the patients do not have this predisposition, before the medication is used.”

Lower levels of immune
suppression for certain patients

Traditionally immune suppression has been standardised but it is now known that some patients have less active immune responses so may require less treatment.

This is based on a test which quantifies Adenosine triphosphate (ATP), which is released by activated lymphocytes, and gives the patient an immune score. If the lymphocytes are less activated, it means that they have a lesser ability to mount an immune response.

Personalising prophylaxis against
opportunistic infections

After transplant, patients are given blanket CMV prophylaxis to prevent this infection, but doctors are now beginning to identify those who are at very low risk who maybe only need six months to a year of antiviral drugs.

Costanzo says: “We have ways to monitor them, so that if we see that the viral load begins to increase we can treat them. So, In other words, prophylactic versus a pre-emptive approach.” She says this is ‘extremely important’ because these medications have significant effects, particularly for the kidneys, which are already vulnerable due to the use of calcium-channel inhibitors.”



Maria Rosa Costanzo

DOMAIN IN FOCUS:
EMERGING APPROACHES & TECHNOLOGIES

Buzz over perfusion
finally coming of age

A host of exciting new techniques and developments, including artificial organs and robotic surgery, were discussed at the Congress, as well as significant new approaches in existing technologies. The field is changing rapidly, delegates were told, with major impacts on the future of transplantation.

A major breakthrough has been the development of artificial organs, both purely artificial and also a hybrid mix of human cells and artificial elements. Clinical trials are close in artificial kidneys – synthetic miniaturised grafts which are powered by a battery.

Robotic surgery, while still considered pioneering in the field of transplantation, is also developing rapidly. The congress heard from Ugo Boggi, Professor of Surgery at the University of Pisa and a leading expert in robotic surgery and pancreatic, liver and kidney transplantation.

Kidney removal and implantation is possible robotically, he said, and as well as pancreas transplantation. As well as in Italy, one or two centres are doing this in Belgium.

Another emerging technique is living liver donation. Historically this has been done more frequently in the Far East than the US or Europe. The meeting heard from specialists from the University of Colorado, US, who perform nearly 100 liver transplants annually, including live donations – their centre carries out the highest number in the US, despite having a well-established organ donation. In Europe the field is less developed, with Turkey having one of the highest rates.

Other exciting developments include the use of CRISPR technology, known for its use in gene editing, in the diagnostic testing of kidney transplant patients, and Artificial Intelligence (AI)

But the biggest buzz was around organ perfusion, the technique where a machine keeps donated organs warm by continuously pumping blood through them. Traditionally, donated organs are placed on ice until they are transplanted into a recipient.

Instead, normothermic perfusion significantly reduces “cold ischemic time” without blood flow, which is better for the organ, and gives transplant experts the opportunity to better assess its quality and function before it is transplanted into a patient.

It also extends the operating window of time, allowing organs to survive longer outside the body, making immediate transplant less urgent.

It has been used since the 1960s and after being introduced technicians found ice cheaper and easier to transport. However, in the last 10 years, with developments in the machinery and technology, it has become increasingly popular, particularly in the last four or five years.

This was reflected by the topic being discussed widely throughout the Congress, with one session detailing how to start a programme, what can go wrong and how to fix it.



Gabriel Oniscu, Secretary of ESOT and incoming President-elect, said: “We have seen this transfer from being used by enthusiasts to routine clinical practice.

We now need to tackle how to make it more sustainable and hands on.

“It could change practice in a number of ways, but most importantly by producing better quality organs.

“Everyone is talking about it and trying to do it in some form or other, now it’s about defining the right machines and the right techniques for the right organs.”

He said combined with regenerative medicine and stem cell technology, there was the potential to repair and recondition organs, improving quality for patients. “With organ perfusion we are no longer in flux – we are in transition.”

1. Gabriel Oniscu



ESOT Hands-On



Alessandra Bertacco

ESOT CONGRESS 2021 AWARDS

ESOT Leonardo Da Vinci Transplant Research Innovation Award

The Leonardo Da Vinci Transplant Research Innovation Award is the most prestigious scientific award at the ESOT Congress, stimulating an unprecedented and innovative approach to research. There are two winners of this award; one for clinical research and one for basic or translational science.

Prior to the congress, eight outstanding contributions were selected from all of the scientific abstracts submitted to the meeting; four of which represented to clinical research and four dedicated to basic or translational science. The lead authors of all eight submissions received free registration to the congress.

After the abstract presentations, held on Monday during the LVD ESOT Leonardo Da Vinci Trasplant Research Innovation Award Session, winners of the award were selected after joint votes of a jury and delegate voting via the app.

ESOT would like to congratulate Marc Raynaud for winning the clinical science award and Nicola De Stefano for picking up the basic science prize! Both prizes were presented during the Closing Plenary Session.

Marc Raynaud's research focused on 'Dynamic prediction of kidney-graft survival with artificial intelligence: An international study of deep cohorts of kidney recipients', whilst Nicola De Stefano presented the study: 'Extracellular vesicles from human liver stem cells reduce injury in a model of normothermic perfusion of rat ischemic livers'. Both awardees will be rewarded with a €10,000 prize and an invitation to submit a peer reviewed article in Transplant International.



It was a pleasure to see all 8 abstracts striving to win the coveted award and we would like to extend a sincere thank you and pay tribute to all the speakers and their presentations:

- **Kevin louis**
Il-21 driven expansion and reprogramming of t-bet expressing b cells during antibody-mediated rejection of kidney transplants
- **Sergi Betriu Ménde**
Specific elimination of anti-hla antibody-producing b cells in an in vivo mouse model by using chimeric hla antibody receptor (char) t cells
- **Claire Albert**
Enhanced delivery of nanomedicine to kidney graft endothelial cells during ex vivo perfusion
- **Nicola De Stefano**
Extracellular vesicles from human liver stem cells reduce injury in a model of normothermic perfusion of rat ischemic livers
- **Elisabet van Loon**
Peripheral blood inflammatory chemokines uncover allo-immune inflammation in the absence of histological lesions
- **Margherita Saracco**
Screening for sars-cov-2 neutralizing antibodies in cirrhotic patients waiting for liver transplantation: impact on donor pool expansion
- **Marc Raynaud**
Dynamic prediction of kidney-graft survival with artificial intelligence: an international study of deep cohorts of kidney recipients
- **Karol Graňák**
Regular physical activity in the prevention of post-transplant diabetes mellitus and associated metabolic conditions in kidney transplant recipients



Stronger Together PRO Award

The Stronger Together PRO Award is presented to the group of abstracts submitted by a single organisation with the best average score (minimum of five abstracts submitted by the institution). ESOT would like to congratulate the Paris Transplant Research Centre for Organ Transplantation for winning the Stronger Together PRO Award for 2021!

During a Live Studio session, ESOT President Vassilios Papalois explained, "The award not only rewards the quality of science, but also the quality of teamwork within a transplant group."

Alexandre Loupy and Carmen Lefaucheur joined Vassilios Papalois in the Studio on behalf of the group. "We are really honoured and proud to receive this award", explained Alexandre Loupy. "As a team, we are all looking into the same direction in trying to improve patient outcomes".

This is the third time the Paris Transplant Research Centre for Organ Transplantation has won this prestigious award – who will be awarded a €5,000 prize.



Marius Renard Paediatric Transplant Award

The Marius Renard Paediatric Transplant Award is a Joint ESOT and IPTA Award for the best abstract submitted to the Congress within the field of paediatric transplantation. The abstract can be either on clinical innovation or the advancement of scientific research and must be of original work.

Congratulations to Reshma Rana Magar for winning this year's award, for their abstract titled 'Pre-emptive kidney transplantation versus non-pre-emptive kidney transplantation in children: a systematic review and meta-analysis'.

Reshma received a certificate of achievement and a €500 prize, as well as an invitation to submit their work to Transplant International.

Extracorporeal Photopheresis (ECP) Immunomodulation Award in Solid Organ Transplantation

Supported by Mallinckrodt, this award offers a €50,000 educational grant to recognise and support the institution of individuals who are making a difference in advancing the knowledge around ECP Immunomodulation in Solid Organ Transplantation. The award offers a unique opportunity for transplantation professionals by supporting their development, fostering knowledge exchange, and encouraging collaborations within the field.

Four applicants were shortlisted and invited to the Congress to present their project during special Science Slam Symposium:

- **Cristiano Amarelli**
Immunologic and functional predictors of ECP response in heart transplantation
- **Johanne Hjort Baatrup**
ECP treatment of chronic humoral rejection in cardiac transplantation: exploring immunomodulation by exosomes
- **Johannes Goekler**
The influence of ECP induction therapy on circulating and tissue biomarkers after heart transplantation
- **Michael Perch**
Scandinavian registry for extra corporal photopheresis in lung transplantation

Following a tough decision from the judging panel, ESOT and Mallinckrodt would like to congratulate Johanne Hjort Baatrup for winning this award!



SECTIONS & COMMITTEES ROUND-UP

Throughout the morning of day one at the ESOT Congress 2021 we were treated to specialty update symposia from all the ESOT Sections & Committees, which covered a variety of topics.

The BSC and ECTORS explored the interesting idea of organ regeneration especially with regard to the liver and kidney. ECTTA featured an interesting debate on the pros and cons of hypothermic non-ischaemic machine perfusion versus normothermic machine perfusion. EDTCO highlighted the latest thinking around brain death and optimising donor organs especially regarding Intensive Care for Organ Donation (ICOD) facilities.

An update on the Banff criteria and the use of this powerful system of classifying rejection in clinical practice played centre stage at the EKITA session. The topic of marginal organs and marginal recipients was the main trust for ELITA, and we were challenged around what were thought to be contraindications to liver transplantation.

There was a very topical discussion in ELPAT around how COVID led to difficult decision and suggested how a “moral balance” framework of thinking helps with the stresses of difficult clinical dilemma. EPITA looked at pluripotential stem cells combined with genetic editing and the possibility that they could be the “surrogate” islet cells of the future.

The use of eHealth platforms featured heavily in the ETAHP session and the potential they have for improving patient outcomes. Finally, hand transplant outcomes in the US and UK along with the state-of-the-art discussion on immunosuppression was the focus of the VCA session.

ESOT would like to extend a sincere thank you to all contributors of these Specialty Update Symposia.

ESOT GRANTS PROGRAMME

ESOT is pleased to share information on the ESOT Grants Programme, which aims to promote the education and career development of transplant professionals in Europe and across the world.

The programme for 2022, launched during the Future Leaders on Stage session, includes: the ESOT Educational Scholarship, the ESOT Study Scholarship, the ESOT Transplant Fellowship and the newly introduced ESOT Global Grants.

Firstly, the ESOT Educational Scholarship provides a brilliant platform for twenty young transplant professionals, allowing recipients to attend ESOT courses and events.

Aimed at European transplant professionals of all disciplines, the ESOT Study Scholarship allows recipients to travel and develop new skills and insights, which can be utilised for their career progression, both in their personal work and in furthering the progress of their institution. The programme duration is between two months and one year and ten scholarships are available.

The ESOT Transplant Fellowship includes both a Basic Science Fellowship and a Clinical Fellowship (one available in each category). These grants, of €55,000 per successful applicant, allow two young professionals to develop knowledge and further their skills by working in a European institution for a year. Projects leading to a doctoral degree or as part of a post-doctoral project are prioritised.

Finally, the ESOT Global Grants are a new initiative launched to support the education and career development of ESOT’s international community. These grants – of which ten are available – are for international members who wish to attend an ESOT course or masterclass, or to visit a European Centre to gain specific knowledge and skills that are vital for their career progression.

Applications for all four categories are now open until 31 October 2021.

[Visit the ESOT website for more information →](#)

New ESOT Councilors

ESOT would like to congratulate a number of people following the 2021 ESOT Council elections:



Ekaterine Berishvili
Councillor (Eastern Europe)



Geir Mjoen
Councillor (Northern Europe)



Chloë Ballesté Delpierre
Councillor (Southern Europe)



Western Europe
Councillor (Frank Dor)



Future Leaders on Stage session

PATIENT INCLUSION ACTIVITIES

Patients at the Heart of the Congress

People with transplants should concentrate on health span, not life span and take up physical activity for its mental, emotional, and social benefits as well as fitness, an online patient symposium heard. A series of speakers said that physical exercise – rather than competitive sport – was helpful and enjoyable, starting off with gentle activity and increasing levels gradually.

And while it may be difficult to contemplate, with fear and worry that exercise may harm the transplanted organ, there is no evidence that this is the case. In fact, the benefits far outweigh the risks, making people happier as well as healthier, speakers said.

The 90-minute Patient Inclusion Initiative event, held the day before the opening of opening of the ESOT Congress 2021 in Milan, was attended by more than 100 people both online and in-person.



Entitled ‘When every small step is a step forward: Being physically active after solid organ transplantation’, the session was chaired by Fiona Loud, Policy

Director for patient support charity Kidney UK, who had a transplant 15 years ago, and Colin White, National Advocacy & Projects Manager with the Irish Kidney Association.

Attendees heard the inspirational stories of two patients, and also from a specialist physiotherapist who reviewed the evidence on exercise in transplant patients and from a physical therapist on how to get started and maintain activity.

In a heart-felt talk, Darren Cawley described how growing up in Ireland he was a Gaelic football player who went on to study Sports and Physical Science at college in England. But he started getting headaches, was diagnosed with kidney disease and was started dialysis almost immediately in his 20s.

After a kidney transplant, he went back to exercise and took part in the World Transplant Games, and while he came third from last he had a mind-set change, seeing the competitors as role models. “I saw other patients seeing themselves as athletes. I was still living as a sick person”, he said.

Sadly he lost the transplant and spent a further nine years in dialysis. When he was transplanted for a second time he did not want to potentially harm the organ with exercise. Eventually he realised that to regain his life he had to stop being a sick person and consider himself a healthy person with health issues.

He said people often overlook the importance of quality of life and fail to make the big distinction between lifespan and health span. “Life span is merely how long you live – but it’s health span – how long you live in good health – that’s important and this is often largely in your control. Be an active participant in your own health and take responsibility.” Doing so has given him more energy and makes him feel better about himself. “That is the goal I set for myself, and I think it’s something that all patients should set for themselves.”

While Crawley acknowledged that he gets a great deal out of competing, this should not be the aim – a view supported by Frank Kuipers from the Netherlands, the co-founder and Vice President of the Dutch Lifestyle and Transplantation Foundation and the founder of the Dutch Transplant Football team.

Kuipers had a triple transplant (liver, pancreas, duodenum) in 2016 at the age of 60 after symptoms of liver disease began in the late 1990s. He began by football training with his young family and advised symposium attendees to stay as fit as possible by getting a walking buddy – in his case his pet dog. After the transplant, he joined the Dutch transplant sport organisation and started cycling for the first time. In 2017, he cycled with Transplantoux and competed at the World Transplant Games in Spain.

However, he was concerned that for the transplant community who did not want to be involved in serious competitive sport, there was no alternative or support. So, he set up a Facebook group ‘bewegen en Transplantie’ to get people active. He set up regular ‘walk and talk’ sessions near his transplant centre – now there are six walking groups.

He admitted there is fear about how much is too much exercise. “You never know what is too much? Riding a horse? Mountain biking?” But the benefits outdo those fears. “Energy levels will rise; people are getting stronger and are able to do more.” He urged others to do the same and set up similar groups throughout Europe.

Sharlene Greenwood, Consultant Physiotherapist and Researcher at King’s College London, and President of the British Renal Association, talked about how to get started and maintain motivation. She runs a renal rehab class in the East Dulwich Community Hospital in London, with specific programmes at the right levels for each patient.

She laid out the common barriers, including fatigue, excess weight due to immunosuppressants, multiple appointments, side effects, fear of damaging the new organ. “It’s a very real challenge.”

Ambivalence or being in two minds is common. She added: “It’s normal to get stuck. If healthcare professionals or family argue for it you push back, it can be difficult to hear someone telling you what to do.”

She gave advice on how healthcare professionals and family could encourage the person:

- Be a good listener, don’t tell people what to do – instead be helpful. Say ‘Lots of people find it difficult, shall I tell you what some of my other patients find useful?’
- Use open questions, ask ‘what might be some of the benefits of sticking to the activity plan? Imagine if you exercised regularly – what would be different? What might happen if you don’t take that first step to physical activity?’
- Ask permission to give advice, be curious about people’s response. Let them ultimately decide. Ask ‘would you mind if I shared some tips, so what do you make of that, what does it mean for you?’

She said it was important before starting to get clearance from the transplant team and look at local or national guidelines. Get a baseline assessment so you can see how much more you are doing subsequently, which will help with motivation; have SMART goals, specific attainable times, such as a walk around the park in the morning twice a week and see where you go from there.

And she encouraged attendees not to worry, as “not taking part is more of a risk than taking part.”

Stefan De Smet, a physiotherapist with an interest in exercise physiology from Belgium, said physical inactivity is linked to worse outcomes in 35 diseases including COVID-19. He suggested that physical exercise should be the initial aim – even just walking to the supermarket – and once that has been achieved then that physical exercise can be attempted within a wider range.

The specific evidence on exercise and transplant patients, shows it increases cardio-respiratory fitness, muscle strength and health-related quality of life. In the later Q&A, he said that there is no data suggesting they can damage their organ if they do too much, but like anyone, the body needs recovery time after exercise.

One interesting study showed that a group of kidney transplant patients doing exercise were more likely to be employed than those not doing exercise training. He said that while more data is needed, there’s growing direct evidence in transplant recipients of the benefits of activity and exercise.

The most important message, he said, was that “It starts today.”

Co-chair Colin White, whose wife has been on dialysis for over 20 years, said promoting physical activity was his passion. He concluded: “It’s fantastic that ESOT are shining a light on this. Sport can turn people off. But physical activity, at a level to suit them, will get a lot more buy in.”



“...not taking part is more of a risk than taking part”

OUR PARTNERS

Industry partnership is a core component of the ESOT Congress and provides a unique platform to work with partners across all sectors of organ transplantation, to support projects and help improve the lives of patients.

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