

ORIGINAL ARTICLE

Hand-assisted retroperitoneoscopic donor nephrectomy offers more liberal use of right kidneys: lessons learned from 565 cases – a retrospective single-center study

Emin Baris Akin¹ , İlhami Soykan Barlas¹ & Murat Dayangac²

¹ Department of General Surgery, Division of Transplantation, Demiroglu Bilim University, Istanbul, Turkey

² Center for Organ Transplantation, Medipol University, Istanbul, Turkey

Correspondence

Emin Baris Akin, Sisli Florence Nightingale Hospital, Sisli Merkez, Abide-i Hürriyet Street No:164, 34387 Sisli, Istanbul, Turkey.
Tel.: +905334151051.
E-mail: ebakin@hotmail.com

ABSTRACT

The introduction of laparoscopic donor nephrectomy caused a shift toward, left donor nephrectomy. Some centers report a significantly low rate of endoscopic right donor nephrectomy. Hand-assisted retroperitoneoscopic donor nephrectomy (HARP-DN) was introduced as a novel surgical technique, which aims to avoid intra-abdominal complications. It was also reported to provide technical advantages for right-sided DN. In this retrospective single-center study, we evaluated the impact of HARP-DN technique on utilization of right-sided DNs. After the implementation of HARP-DN on February 2009, a total of 565 DNs were performed until December 2015. The introduction of HARP-DN technique resulted in an immediate increase in the utilization of right kidneys from 6.1% to an average of 19.6% annually. The donors' outcome was similar to the left-sided and right-sided DN groups, excluding the increased incidence of incisional hernias in left kidney donors. None of the donors developed intra-abdominal complications. In conclusion, the implementation of HARP technique significantly increased the use of right-sided DNs, which enables a more liberal use of donors in LDKT.

Transplant International 2021; 34: 445–454

Key words

donor nephrectomy, kidney transplantation, hand-assisted retroperitoneoscopic donor nephrectomy

Received: 26 May 2020; Revision requested: 8 June 2020; Accepted: 15 December 2020

Introduction

In the golden age of minimally invasive surgery, laparoscopic donor nephrectomy (LDN) has become the standard of care in living donor kidney transplantation (LDKT) [1]. Early experience from right LDN was marked by technical challenges and surgical complications [2,3]. Therefore, the global transition from open to minimally invasive donor surgery triggered a trend toward the left donor nephrectomy (DN). Based on

data reported to the United Network for Organ Sharing (UNOS) Renal Transplant Registry, from 1988 to 1998, the annual rate of right-sided kidney transplants ranged between 24.7% and 38.3% with a mean of 27.6%. With the introduction of LDN, right donor nephrectomies decreased significantly to the range of 10.96% and 13.54% between 2005 and 2015 [4]. A similar trend was witnessed in Europe as well [5,6]. Eventually, the utilization rate of right living donor kidneys dropped under 1% in some large LDN series [7]. Not to

mention, University of Minnesota focused on higher probability of left kidney procurement in LDN among other techniques in their series of more than 4000 donors [8].

Currently, there is an ongoing discussion about sub-standard outcomes of transplanting right kidneys due to the technical challenges of right DN and transplanting a kidney with shorter right renal vein. A recent paired Organ Procurement and Transplantation Network analysis revealed a notably higher delayed graft function (DGF) and graft loss within the first 6 months after right-sided DDKT [9]. Analysis of Australia and New Zealand Dialysis and Transplant registry revealed 46% higher adjusted odds for DGF, and 72% higher adjusted risk for graft failure during the first year of right-sided DDKT [10]. A US National cohort study found a modest association for transplantation of deceased donor right kidneys with delayed graft function and graft loss within the first six months but no deleterious associations with long-term patient or graft survival [11]. On the other hand, deceased donor right kidneys offered similar patient and graft outcome compared to left side in different countries [12,13]. In regard to living donor kidney transplantation, some studies reported a possible association between venous thrombosis through the use of right living donor kidneys [3,9,14], whereas other studies did not confirm this [15-18]. A retrospective US national registry on living donors found statistical difference in graft thrombosis as a cause of graft failure and inferior graft survival for right DN [19]. Currently, right-sided DN is routinely performed by larger centers while smaller ones remain less active due to technical challenges with the procedure and the poorer outcomes, which is cited in literature. Accordingly, the choice of laterality should be based on the surgeon. In addition, the tendency toward left LDN is rational; however, the balance should be well tailored to avoid the contradiction of the principle that the better kidney should always stay with the donor. One of the potential drawbacks of left-sided DN is unnecessary elimination of some donor candidates and denial of right kidney donors from the benefits associated with minimally invasive surgery, which can cause psychosocial problems and minimize the living donor pool [20].

Laparoscopic donor nephrectomy, even though it is rare, has been associated with risks of intra-abdominal organ injuries and intestinal obstruction [21-23]. Although a meta-analysis by Kortram et al. [24] comparing the currently used minimally invasive DN techniques reported comparable short-term complication rates, only the transperitoneal approach has been

associated with risks of intra-abdominal organ injuries. In a randomized controlled trial, Dols et al. verified the safety of HARP-DN and its exceedance of standard LDN in left-sided DN [25]. A recent meta-analysis by Özdemir-van Brunschot et al. revealed that when the complications of the retroperitoneal approach were compared to those of the transperitoneal approach, the retroperitoneoscopic approach was associated with significantly less complications and all intra-abdominal injuries occurred in the transperitoneal DN group [26]. Hand-assisted retroperitoneoscopic donor nephrectomy (HARP-DN) combines the advantages of minimally invasive technique and manual control with the benefits of retroperitoneal access, as well as direct and quicker approach to the vessels in the renal hilum [27-30]. The initial reports associated with left HARP-DN have been comparable in success to other minimally invasive DN techniques [31-34]. The subsequent prospective studies further explored its potential technical benefits in right-sided DN procedure [35,36].

In our LDKT program, the initial minimally invasive DN technique was hand-assisted LDN (HAL-DN), however, after 3 years of experience, we have subsequently switched to HARP-DN technique. In this retrospective cohort study, we reviewed our single-center experience with the HARP-DN technique with special emphasis on the utilization of right-sided DN.

Material and methods

We performed HAL-DN technique on 71 living donors between February 2006 and September 2009. In February 2009, we implemented HARP-DN technique within a transition period of eight months. We retrospectively reviewed the records of 565 LDKT cases with HARP-DN procedure, which were performed between February 2009 and December 2015. All potential donors were discussed in the multidisciplinary kidney transplant meeting, which included transplant surgeons, nephrologists, cardiologists, radiologists, and nurse practitioners. The anatomy of the kidneys was assessed by contrast-enhanced computed tomography (CT) angiography. Donor selection criteria included not only the kidney function and morphology, but also a psychosocial assessment and a thorough evaluation of any past or present medical condition that could impact the safety of the donor. Any donor with a revised cardiac risk index score > 1 underwent additional cardiac testing (for example, nuclear stress testing and coronary angiography) according to American College of Cardiology/American Heart Association guidelines [37].

All operative procedures were either performed or supervised by the same surgeon (EBA). The renal grafts were placed preperitoneal into the iliac fossa. Recipients received a calcineurin inhibitor-based immunosuppressive regimen, which included steroids with either mycophenolate or m-Tor inhibitor. The charts of all donors and their recipients were reviewed retrospectively. Fourteen donors were lost-to-follow-up and a total of 4 donors died (Car accident in 7 years ($n = 1$), Lung cancer in 20 months ($n = 1$), Cardiac related death in 17 months and 3 years, respectively ($n = 2$). All other donors were contacted by telephone. 190 donors (33.6%) accepted to come for physical examination.

Statistical analyses

Patient characteristics were expressed through mean and standard deviation (SD) in continuous variables, as well as number and percentage for categorical variables. Differences between the groups were compared using the chi-square test for categorical variables and Student *t* test for continuous variables. A 2-tailed *P* value less than 0.05 was considered significant. Survival analysis was performed using Kaplan–Meier curve and compared with the log-rank test. All statistical analyses were performed using SPSS Statistics for Windows, Version 17.0. (Chicago: SPSS Inc.).

Historic background and surgical technique

After having considerable experience in HAL-DN procedure (261 cases) during fellowship training (2001–2004) at Ohio State University in the United States, the same technique was adopted in our transplant program [22]. We experienced extensive intra-abdominal adhesions during incisional hernia repair of a donor one year after DN. With concerns about intra-abdominal adhesions due to the leakage of all fat and debris into the abdomen, we decided to switch from the transperitoneal to retroperitoneal DN technique. A donor with a history of gastric surgery was the first patient to undergo DN via the retroperitoneal approach. After this successful debut, we used HARP-DN selectively in 35 cases between February and September 2009. We performed 14 HAL-DN procedures in the same period which was preferred particularly in donors with low BMI and kidneys with multiple arteries. There were 3 right HAL-DN cases at the initial half of this transition period, and during the second half we performed 7 right HARP-DN procedures. We implemented HARP-

DN as the adopted technique of DN after this transition period.

The surgical technique

The whole procedure remained unchanged from our original HAL technique including both surgeons positioning at the abdominal side of the donor, using two 12 mm trocars and the surgeon's right hand placing intra-abdominally on left-sided DN and vice versa. The main difference in the HARP-DN technique is the creation of a retroperitoneal space by blunt manual dissection in the beginning of the procedure. Initially, the median hand port incision was switched to a paramedian incision for easier access to the retroperitoneum, which was changed to a Pfannenstiel incision for cosmetic concerns later in time ($n = 31$, 5.4%). After the creation of retroperitoneal space, the first trocar was introduced 2 cm inferior to the costal margin at the anterior axillary line under manual control (Picture 1a). The hand port placement and insufflation facilitated retroperitoneal dissection toward the Psoas muscle posteriorly and the abdominal wall anteriorly. Extending the retroperitoneal dissection up to the sub-xiphoid area allowed the introduction of the second trocar for camera. Then, the kidney was visualized with the incision of Gerota's fascia. The initial mobilization of the kidney and the pull-down maneuver helped prevent extensive mobilization of the diaphragmatic peritoneum. The ureter and the vascular structures were dissected by hook cautery in assistance with a sealing device (Liga-Sure™ (Medtronic, Minneapolis, USA)). On the left side, the gonadal and the adrenal vein were routinely divided to preserve the full length of the left renal vein. At the time of kidney retrieval, we switched the camera and the instruments between the trocars to provide a perpendicular angle for the stapling device (Picture 1b). After cutting the ureter, the arteries and veins were stapled (Ethicon linear stapler) and divided with endoscopic scissors consequently. Then, the kidney was extracted manually. In the HARP approach, the extra 5-mm trocar used for liver retractor during right-sided DN was avoided.

The hand-assisted laparoscopic donor nephrectomy era

We performed 71 HAL-DN procedures between June 2006 and November 2009. The male to female ratio was 32/39. The mean age of donors was 42.7 ± 13.6 . Mean body weight was 74.8 ± 11.0 kg. In the HAL-DN era,

only five patients (6.1%) underwent right-sided DN where a liver retractor was used in all cases. The mean dissection time (the time between the first incision and completion of renal hilar dissection) was 114.07 ± 34.9 min. There was only one donor with multiple arteries in the right HAL group. One donor had massive postoperative bleeding due to the displacement of hem-o-lock clip at the renal artery stump after left-sided HAL-DN, which needed emergency laparotomy. One right kidney donor had minor liver injury secondary to liver retractor. As for another right kidney donor, one of the accessory arteries had to be sacrificed due to intraoperative injury which required blood transfusion during the surgery. One donor developed incisional hernia in the HAL-DN group.

Selection criteria for right hand-assisted retroperitoneoscopic donor nephrectomy

We performed 111 (19.6%) right HARP-DN out of 565 cases in our series. The annual rate of right DN increased significantly right after switching from HAL to HARP technique (Fig. 1). The three major reasons for preferring the right side are kidney stones, cysts, and achieving single artery (Fig. 2). We preferred to remove the kidney that had any cyst including the ones classified as Bosniak. Small cysts with a diameter of 1–2 mm were considered as well. In cases where there were minor cysts in both kidneys, we beared in mind the Bosniak classification and number of cysts. Multiple arteries on the left side and single artery on the right side were two of the most frequent reasons in our

series. Early branching at the left side ($n = 4$) was included in this group as well. Existence of a lower pole artery was an important factor in cases with multiple arteries in both kidneys. We utilize living donor kidneys which consist millimetric stones after metabolic screening of urine if stones are unilateral. Sometimes there can be a tissue calcification resembling kidney stones at CT angiography. These suspicious calcifications are considered an imperfect side in our protocol. There were three cases with multiple lesions of cysts, single artery, and millimetric stones. We prefer to take the kidney with renal artery vascular lesions if the other kidney is free of vascular lesions after reevaluation with conventional angiography. Small size and lower glomerular filtration rate, double ureter, and rotational abnormalities are other reasons to prefer right DN. We preferred the right side to prevent trauma during DN in one case with minor splenic artery aneurysm and one with liver hemangioma on the left lobe.

RESULTS

The data including the demographics, operative variables, and the outcome of 565 donors with left and right-sided HARP-DN is shown in the Table 1. There was no difference in donor demographics between the two groups. The ratio of cases with multiple arteries and the dissection time were also similar. From 2009 to 2014, there was a continuous trend toward a shortened dissection time, which showed a statistically significant difference between the years ($P < 0.001$) (Fig. 3).

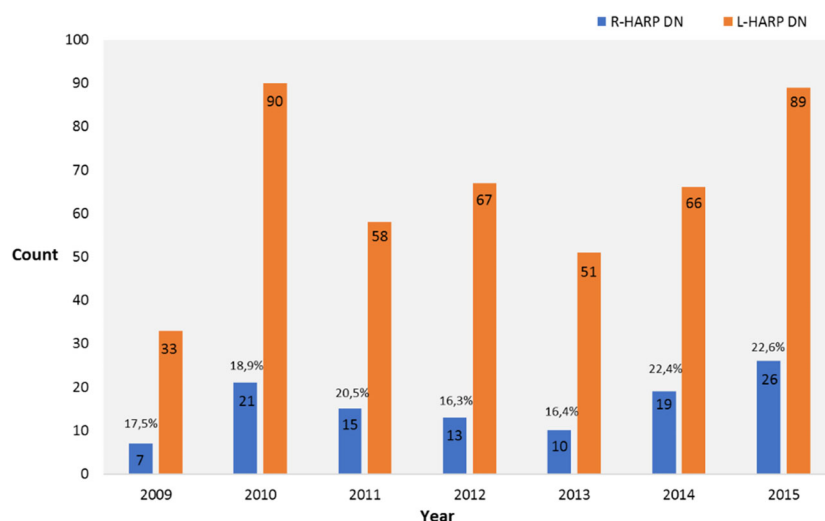


Figure 1 Annual rate of right- / left-sided kidney transplantation

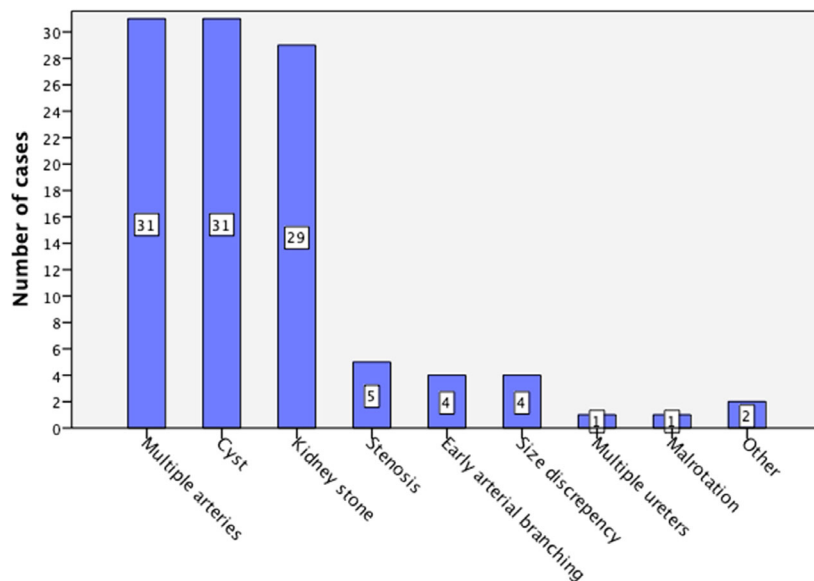


Figure 2 The indication to use the right kidney

Table 1. Demographics and operative data of the donors

	Right-sided HARP-DN N = 111 (19.6%)	Left-sided HARP-DN N = 454 (80.4%)	P value
Age (year)	45.9 ± 12.2	43.9 ± 12.2	0.1
Body mass index(kg/m ²)	27.2 ± 4.19	27.5 ± 51.4	0.5
Dissection time(minute)	100.4 ± 38.5	101.3 ± 27.3	0.7
Multiple arteries	19/111 (18.0%)	77/454 (17.0%)	0.7
Major peritoneal opening	14.4% (16/111)	6.8% (31/454)	0.02
Transition to open	0	0	

Donor outcome

There was no perioperative donor mortality. None of the cases were switched to open procedure. None of the donors had blood loss more than 500 cc or required blood transfusion. Three cases had an estimated blood loss of more than 150 cc. There was no major intraoperative complication except one renal artery injury during a left HARP-DN. The kidney was mobilized and removed quickly with HARP approach in this case and the kidney had immediate graft function after transplantation. The most frequent intraoperative complication was major peritoneal opening (more than 4 cm), which was notably higher in the right HARP-DN group (14.4% vs. 6.8%, $P = 0.02$). There were 17 donors (3 %) with incisional hernia in the left HARP-DN with paramedian incision. The mean body mass index (BMI) of these donors (30.04) was higher than the average BMI.

There was no incisional hernia in patients with Pfannenstiel incision or in the right HARP-DN group. Fourteen patients (2.47 %) had surgical site infection (9 left, 5 right) requiring wound care and antibiotic treatment; one donor with left HARP-DN had extensive subcutaneous cellulitis requiring surgical treatment.

Recipient outcome

There was one surgical complication causing loss of transplanted kidney where the transplanted left kidney was thrombosed because of renal artery occlusion secondary to intimal flap at recipient's iliac artery. There was no significant difference between the right and left kidney recipients regarding graft and patient survival (Fig. 4a,b). There were 6 patients with ureter stenosis (5 left/1 right), all of which had surgical treatment except one treated with endoscopic dilatation.

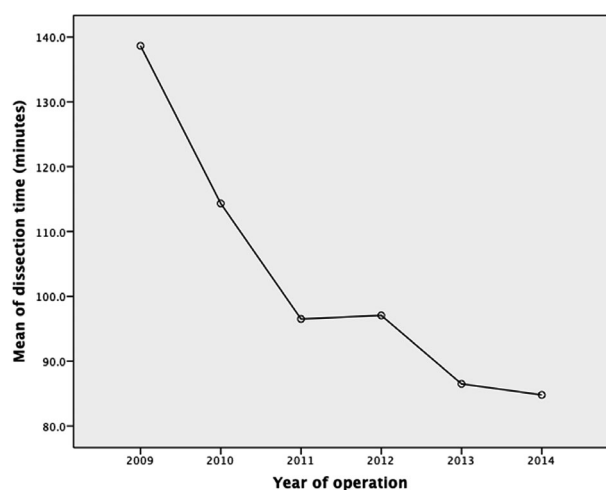


Figure 3 The evolution of dissection time in HARP-DN technique

Discussion

This was a retrospective review of a single-center experience about transition from HAL to HARP-DN. The primary motivation for switching to HARP-DN was to prevent intra-abdominal adhesions. However, we were totally surprised when we realized that the rate of right DN significantly increased after switching to the HARP-DN approach. Five of the initial 15 cases were right-sided DNs and the rate of right DN increased from 6% to 17.5% within the first year. Meanwhile, several articles were published demonstrating HARP technique as safe and advantageous for right DN [34,35]. We believe the reflection of this similar experience was increased utilization of right DN in our series.

In their cumulative summation learning curve analysis, Serrano et al. reported that transplant surgery fellows exhibit a tipping point in LDN performance by 24–28 cases and proficiency by 35–38 cases [38]. It is obvious that our experience during the implementation of HARP technique was far beyond required learning curve for DN due to extended clinical fellowship training (261 cases) and further experience of adoption of HAL-DN procedure (71 cases) in our program. Another important point is the immediate effect of retroperitoneal access on the reduction of mean dissection time. Figure 3 shows how the implementation of HARP-DN significantly decreased the dissection time for right-sided DNs from the beginning.

The use of the dominant hand for intra-abdominal assistance is an important advantage in hand-assisted surgery. Most of the minimally invasive DN techniques require switching the assisting hand which is left hand for the right HARP-DN in our technique. The

assumption that the right-sided DN is comparably challenging arises not only from the deeper intra-abdominal anatomy and the involvement of the liver on right side, but also from the use of nondominant arm. The retroperitoneal approach offers the benefit of direct access to hilum of the kidney and ureter, while avoiding the requirement for liver retractors. The avoidance of intraperitoneal organs eliminates the risk of intra-abdominal organ injury while enhancing the surgeon's focus on DN. Therefore, the retroperitoneal access eases the use of nondominant left hand for hand assistance, which contributes to the acquisition of technical confidence in a short period of time. As our right-sided HARP-DN technique requires the left hand being within the abdomen and the dominant right hand being free to operate for the right nephrectomy, surgeons who does not like the dominant hand inside the abdomen for a left nephrectomy would be more enthusiastic for right side. Another important benefit of the HARP technique is the symmetrical operative field on both sides, providing a reciprocal surgical approach, which improves surgical orientation.

Intra-abdominal complications are reported exceedingly rare in LDN but may cause significant morbidity once they occur. A recent meta-analysis has reported that retroperitoneoscopic DN was associated with significantly fewer intra-abdominal complications than the transperitoneal approach [26]. Most of the other studies show that there is no effect of surgical technique on donor or recipient outcome [24,25]. On the other hand, severe morbidity including intra-abdominal complications are mainly reported by experienced centers, while centers with low volume of living donor surgery are generally unnoticed in literature. According to our experience, some donor derived problems like irritable bowel syndrome cause an exceedingly rare complication of extensive intra-abdominal adhesions after HAL-DN and trigger the technical switch to HARP. No matter what the reason for this rare experience was, we were successful to avoid intra-abdominal organ injuries, early or late intestinal obstruction or intra-abdominal bleeding involving liver and spleen in our HARP series.

Herein, we present one of the largest series comparing the outcomes of right and left-sided HARP-DNs in literature. There was no significant difference regarding technical aspects and surgical outcomes and both intra-operative and postoperative complications were comparable. We also presented a similar experience for multiple artery donor nephrectomies before [39]. The most frequent complication was having a peritoneal opening which occurred almost always near the midline

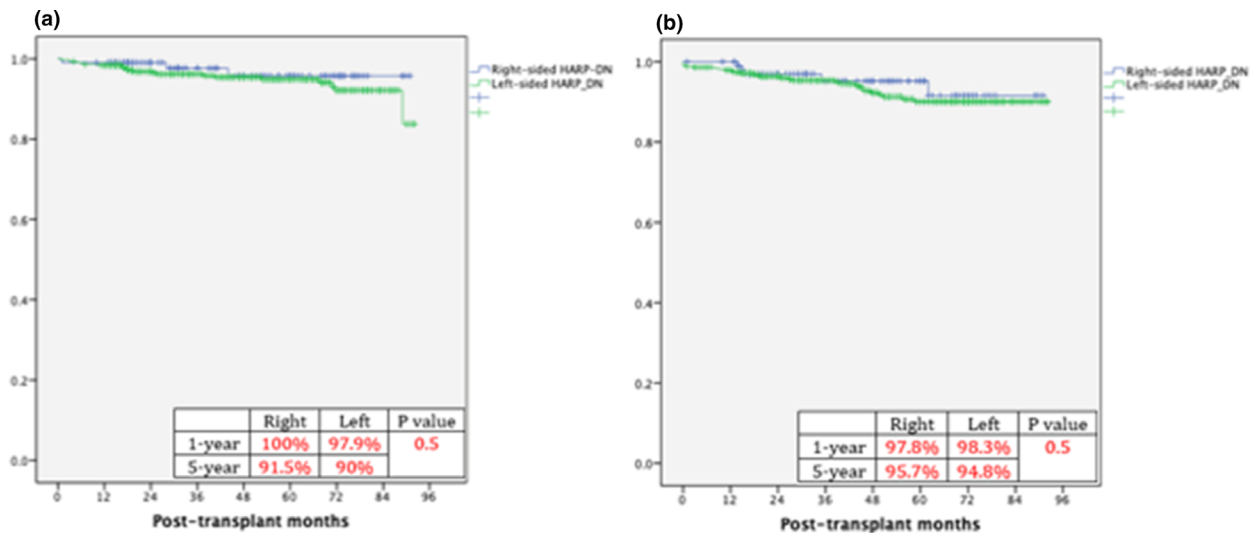
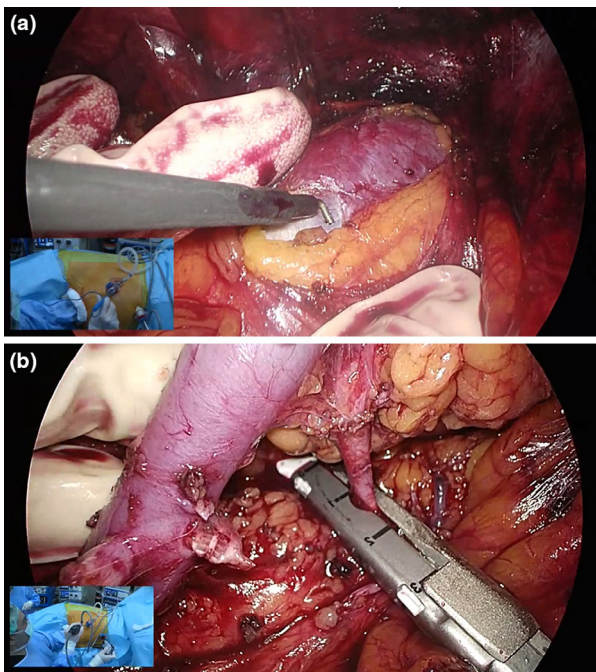


Figure 4 (a) Patient survival in right vs. left-sided kidney recipients, (b) Death-censored graft survival in right vs. left-sided kidney recipients



1. (a) Right Donor nephrectomy; Both surgeons stand at the abdominal side of the patient who is lying in lateral decubitus position. The primary surgeon had left assisting through the hand port at Pfannenstiel incision. Using lap instruments through subcostal trocar. The assisting surgeon holds the camera through the subxyphoid trocar. (b) At the time of stapling renal artery and vein, the trocars are switched so that subxyphoid trocar enables better angle for the stapler

where the peritoneum becomes thin and inseparable from the anterior abdominal wall. Repairing peritoneal tears at the end of the procedure were not required

unless they were near the hand port incision. Even a major detachment of peritoneum at the anterior abdominal wall still served for the benefit of separating the retroperitoneal compartment from intra-abdominal organs and preventing spillage of debris into the abdomen. Eventually, we concluded that peritoneal tear was a frequent incident rather than a complication.

The major morbidities like conversion to open surgery, major bleeding and blood transfusion, surgical reoperation, or readmission were documented accurately. We did not evaluate ml estimation for blood loss believing that it is going to be inaccurate. None of the donors had more than 500 ml of bleeding or requirement for blood transfusion in our series. We believe that the avoidance of intra-abdominal solid organ injury contributed to the prevention of major bleeding. The only major complication (Clavien-Dindo grade 3) which required laparotomy was a deep surgical site infection. Except for the incisional hernia surgeries, there was no donor readmission after discharge. The hand-assisted DN has been previously shown to cause incisional hernia more frequently compared to pure laparoscopic DN [40]. The reported incidence of incisional hernia in HARP-DN series ranges between 0.7% to 3.8% [40,41]. Our rate of incisional hernia from the hand port site was 3%. They were all left-sided HARP-DN cases with paramedian incision. Our rate of incisional hernia in the hand port site was 3%, which exclusively occurred in the left-sided paramedian incisions. As a matter of fact, one of our previous studies showed that the Pfannenstiel incision enabled better body image satisfaction than that of paramedian incision [42]. Therefore, we have eventually switched to Pfannenstiel incision for the hand port.

There is wide variation in utilizing right kidneys among the transplant centers. Most significant difference in tendency is to use left kidneys with multiple arteries at the recipient side mainly to avoid challenge of short renal vein on the right kidney. There are some studies which demonstrate the use of multiple arteries; left kidneys can be used safely instead of single artery right kidneys [3]. On the other hand, kidney grafts with multiple renal arteries have been associated with longer warm and cold ischemia times, a higher risk of ureteral complications, and delayed graft function in some series [43,44]. We used to utilize right kidney to achieve single artery in most of the cases during our HAL-DN period. But we preferred utilizing right kidneys without exemption to achieve single artery in our HARP-DN series. We performed adequate traction of kidney during stapling by using single sided vascular stapler instead of cutting staplers to save adequate length at the renal vein stump. We mostly performed mobilization of iliac vein on the recipient's side due to the rare possibility of ligation of internal iliac vein. There are several recommended technical strategies in literature such as using gonadal vein or prosthetic materials as patch to deal with challenging short renal veins as well [18,45]. These strategies enable safe transplantation of right living donor kidneys in experienced centers [35].

One of the most significant impacts of the HARP-DN technique was the transformation of our kidney selection criteria. With confidence in using the right kidneys more liberally, we shifted the focus on minor radiological findings such as simple renal cysts and parenchymal calcifications. Renal cancer was a crucial reason for starting dialysis after donation before documentation. [46]. We concede Bosniak classification as a guide to evaluate malign masses in individuals with dual kidneys rather than a donor who will live with a solitary kidney. Small cysts less than 1.5 cm in size are sometimes hard to evaluate by CT scan [47]. Magnetic resonance imaging can offer better evaluation for small cysts [48]. We were concerned to underestimate 1–2 mm cysts because they are challenging to evaluate with complete accuracy and rule out malignancy by both radiological imaging studies [47]. It should be taken into consideration that utilization of technical advance in radiological imaging can vary depending on the center. Our protocol to remove any kidney with cyst may require debate for medical benefit; however, we believe it is the appropriate solution in light of the psychological benefit the donor will experience by preserving the apt kidney without any cyst. Minor anatomical differences and radiological presumptions were other reasons that increased the utilization of right

kidney during the HARP-DN period. Another limitation of CT scan is the ability to rule out millimetric kidney stones from suspicious parenchymal calcifications and artifacts. We preferred to remove the right kidneys with suspicious calcifications in four donors. Calcified arteries or possible renal artery plaques can be a challenge for consideration as well. Malrotation, pelvic ecstasy or lobulation of kidney, as well as ureter duplications or clinically irrelevant ureteropelvic stenosis are examples for these factors. At times, overuse of living donation in Turkey led our team to consider minor details more than the current recommendations emphasize in the guidelines. With more flexibility to select either kidney in the donor, we updated our criteria to pick the kidney with “any incidental lesion”, including renal artery plaques, parenchymal calcifications, and even millimetric cysts. Obviously, the merit of this “any-benefit” decision-making is up for debate.

We believe that confidence and safety are crucial in deciding the appropriate DN technique for the surgeon. Not to mention, performing the same operation with different techniques is an achievement offering new insight and improving skills for the surgeons. LDN is a standard of care and is a particularly good alternative for low BMI donors as it prevents the challenge to put your hand in a slim donor. Considering hand assistance and full laparoscopy requires completely different operative skills, we believe surgeons who perform laparoscopic hand assistance may benefit greatly from switching to HARP-DN in this regard.

HARP technique not only avoided intra-abdominal complications, but also introduced a dramatic increase to our rate of right donor nephrectomies. We believe that the main reason for this shift is the technical convenience of HARP-DN that promoted the safety and comfort for the right side. The confidence to use right kidneys enables freedom to preserve the better kidney for the donor even in the case of minor reasons. Therefore, HARP-DN might have a contribution for the long-term safety and psychological relief of the donor in our series.

Acknowledgments

No grant and no source of funding.

Conflict of interest

The authors of this manuscript have no conflicts of interest to disclose as described by Transplant International journal.

Authorship

EBA: participated in research design, and in the writing of the paper. ISB: participated in research design. MD: participated in data analysis.

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