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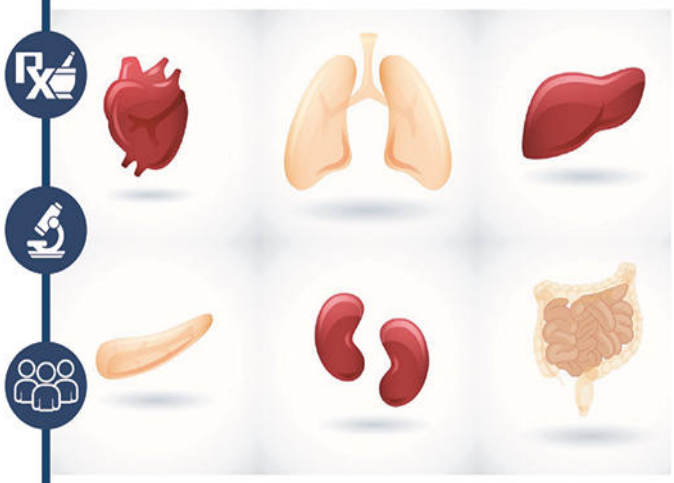

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DR. EVALDO FAVI (Orcid ID : 0000-0001-6465-428X)

Article type : Original Article

Outcomes and surgical complications following living-donor renal transplantation using kidneys retrieved with trans-peritoneal or retro-peritoneal hand-assisted laparoscopic nephrectomy.

Evaldo Favi[1,2], Samuele Iesari[3,4], Nivia Catarsini[5], Rajesh Sivaprakasam[6], Eugenio Cucinotta[5], Tommaso Manzia[7], Carmelo Puliatti[8], Roberto Cacciola[4]

[1] Renal Transplantation, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[2] Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

[3] Pôle de Chirurgie Expérimentale et Transplantation, Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, Brussels, Belgium

[4] Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

[5] General Surgery, Azienda Ospedaliera Universitaria Policlinico G. Martino, Messina, Italy

[6] Renal Transplantation, Barts Health NHS Trust, Royal London Hospital, London, UK

[7] HPB Surgery and Transplantation, Fondazione PTV, Rome, Italy

[8] Organ Transplantation, Parma University Hospital, Parma, Italy

Running head: Trans- vs retro-peritoneal donor nephrectomy

Evaldo Favi Ph.D., M.D.
Renal Transplantation, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
Via della Commenda n. 15, 20122 Milan, Italy
Telephone: +39 02 55035603
Fax: +39 02 55035650
E-mail: evaldofavi@gmail.com

Favi E, Iesari S, Catarsini N, Sivaprakasam R, Cucinotta E, Manzia T, Puliatti C, Cacciola R. Outcomes and surgical complications following living-donor renal transplantation using kidneys retrieved with trans-peritoneal or retro-peritoneal hand-assisted laparoscopic nephrectomy. Clin Transplant

Abstract

The best minimally-invasive procedure for living-donor kidney retrieval remains debated. Our objective was to assess trans-peritoneal (TP) and retro-peritoneal (RP) hand-assisted laparoscopic donor nephrectomy (HALDN). In this single-centre retrospective study, we analysed results from 317 living-donor renal transplants (RT) performed between 2008 and 2016. Donor and recipient outcomes were compared between TP-HALDN (n=235) and RP-HALDN (n=82). Conversion to open nephrectomy (0.4% vs 0%; P=1.000), intra-operative complications (1.7% vs 1.2%; P=1.000), and 1-year overall post-operative complications (11.9% vs 17.1%; P=0.258) rates were similar in TP-HALDN and RP-HALDN. Overall surgical site infections were higher in RP-HALDN (6.1% vs 1.7%; P=0.053) whereas incisional hernias were only recorded following TP-HALDN (3.4% vs 0%; P=0.118). The duration of the procedure was 11-minute shorter for TP-HALDN than RP-HALDN (P<0.001) but extraction time was equivalent (2, IQR 1.5-2.5 minutes; P=1.000). RT following TP-HALDN and RP-HALDN showed comparable one-year death-censored allograft survival (97% vs 98.8%; P=0.685), primary non-function (0.4% vs 0%; P=0.290), delayed graft function (1.3% vs 4.9%; P=0.077), and urological complications (2.6% vs 4.9%; P=0.290) rates. In our series, donor and recipient outcomes were not substantially affected by the approach used for donor nephrectomy. TP-HALDN and RP-HALDN were both safe and effective.

Key words: organ donation; minimally-invasive surgery; hand-assisted laparoscopic nephrectomy; kidney transplantation; complications; outcomes; ureteric leakage; ureteric stenosis; warm ischemia time; surgical training

Evaldo Favi Ph.D., M.D.

Renal Transplantation, Ospedale Maggiore Policlinico, Via della Commenda n. 15, 20122 Milan, Italy.

Introduction

Living-donor renal transplantation (LDRT) is an established practice in many countries.[1-3] The consolidation of living-donation programs worldwide has been associated with an increasing number of minimally-invasive donor nephrectomy (MIDN) techniques.[3-6] Available data suggest that the various procedures described in the literature offer similar donor outcomes.[5,6] However, only few studies used

also recipient-related endpoints to fully evaluate the benefits of different MIDN approaches.[7-9] The advantages and disadvantages of trans-peritoneal (TP) vs retro-peritoneal (RP) access remain debated, particularly in the context of challenging anatomy such as multiple vessels and right kidneys.[4,5,7,8,10]

In our Institution, the technique of choice is the hand-assisted laparoscopic donor nephrectomy (HALDN). This was performed with TP access by the first senior author starting from June 2008. The RP approach was then introduced by the second senior author in July 2011, following adequate exposure and mentoring. The choice between the two procedures was indicated only by the surgeon's preference. Since then, we did not perform any open donor nephrectomy.

This study was prompted by a meta-analysis published in 2015 suggesting some specific advantages of the RP over the TP access because of possible lower intra- and post-operative complication rates.[9] The perceived benefits of the RP approach are represented by reduced risk of unintentional intra-abdominal organs damage (in particular to spleen and bowel), shorter kidney extraction time, and less peri-operative blood transfusions.

We analysed donor outcomes and linked recipient outcomes to the specific technique used for MIDN.

Materials and methods

Study design

This single-centre retrospective study included 317 LDRT performed at the Royal London Hospital between June 2008 and March 2016. Donors and recipients were divided into two groups according to the MIDN approach: TP-HALDN (235 patients) or RP-HALDN (82 patients). All the procedures were carried out by consultant surgeons or under their supervision. Pre-operative assessment and post-operative follow-up of donors and recipients were performed following the Kidney Disease Improving Global Outcomes and the British Transplantation Society and Renal Association guidelines.[11,12]

Data were recorded on a central database by dedicated staff, as per standard practice in our Institution. The outcomes were reviewed by the entire Transplant team as a part of our Transplant Centre Clinical Governance practice. We reported the outcomes of the first year of follow-up as focusing on surgical aspects of the donation. Furthermore, we extended the follow-up of the recipients to three years, in order to capture late complications, particularly urological ones.

Patients were all consented at the time of activation on the National Kidney Transplant Waiting List. Based on the retrospective nature of the study and that no experimental interventions were performed, the research project was discussed during our regular Multidisciplinary Research Meeting and consensus was that further review by our Ethical Committee was not necessary. The study was conducted according to the World Medical Association Declaration of Helsinki and applicable regulatory requirements.[13]

Endpoints

The primary donor-related endpoint was one-year post-operative complications rate. Secondary donor-related endpoints were intra-operative surgical complications, conversion to open surgery, kidney extraction time (time from stapling of the renal artery to cold perfusion of the kidney), duration of the procedure, length of hospital stay, re-admissions, and re-operations.

The primary recipient-related endpoint was three-year post-operative surgical complications rate. Vascular and urological complications were also separately analysed. Secondary recipient-related endpoints were one-year death-censored graft survival (DCGS), primary non-function (PNF), and delayed graft function (DGF). PNF and DGF were defined as graft function unable to prevent continuative dialysis when other causes of transplant failure were excluded and the need for dialysis during the first post-operative week, respectively.

Description of HALDN

The donor is always positioned in a lateral decubitus with minimal angulation of the operating table at the hip level. In the TP-HALDN, the hand-port (GelPort Laparoscopic System™, Applied Medical, Rancho Santa Margarita, CA, USA) is placed through an 8-cm transverse incision, midway between the pubis and umbilicus; in case of left-sided nephrectomies carried out in donors with long trunk, in order to facilitate an easier dissection of the upper pole of the kidney with minimal handling of the spleen, a midline 8-cm longitudinal incision above the umbilicus is preferred. In our series of RP-HALDN, two incisions were performed for the hand-port. Initially, the hand-port was placed through a Pfannenstiel. Subsequently, the same transverse incision adopted for TP-HALDN was used. In both TP and RP approach, the fascia of the recti muscles is dissected from the muscular plane. The recti muscles are never divided. The access to the peritoneal cavity is achieved through the linea alba, following careful splitting of the recti muscles. In the RP-HALDN, a blunt hand dissection, extending to the lower pole of the kidney, allows the creation of the RP space. The 10-mm camera-port is placed in the iliac fossa and the pneumo-peritoneum or retro-pneumo-peritoneum is achieved with pressure between 12 and 14 mmHg. The second 12-mm working-port is placed under direct vision. Further blunt hand dissection is generally required before inserting the second 12-mm working-port in the RP approach. In the TP-HALDN, the colon is mobilised in order to gain access to the kidney. The insertion of a further 5-mm working-port is often required for right-sided procedures to introduce a laparoscopic liver retractor. Once the colon is mobilised in the TP-HALDN and the retro-pneumo-peritoneum is established in the RP-HALDN, the procedures are virtually identical. The renal vessels are dissected and controlled with the combination of the harmonic scalpel (Ultracision™,

Ethicon, Somerville, NJ, USA) and the vessel-sealing device (Ligasure™, Medtronic, Dublin, Ireland). The gonadal and adrenal veins are routinely divided. The dissection of the vessels is extended to the aorta aiming to reveal the origin of the renal artery. The ureter is dissected with a generous cuff of peri-ureteral tissue including the gonadal vein. Three clips (Ligaclip™, Ethicon, Somerville, NJ, USA) are applied to the distal ureter before being divided with laparoscopic scissors. Following careful dissection and control of the peri-aortic lymphatics, the renal artery and vein are divided with the vascular stapler (Endo GIA™, Covidien, Dublin, Ireland). The kidney is removed through the hand-port incision, always received by the implanting surgeon, and immediately flushed with 1 L of cold perfusion fluid (Soltran™, Baxter, Berkshire, UK).

Donor peri-operative care

Donors are treated following the same peri-operative care protocol, regardless of the surgical technique. The antibiotic prophylaxis was a single shot of intravenous amoxicillin/clavulanic acid or meropenem (since 2014), administered 30 minutes before the operation. A 14-Fr urinary catheter is inserted after induction of the general anaesthesia and removed on post-operative day 1. Pain control is achieved using intravenous fentanyl-based patient-controlled analgesia during the first 24 hours and by administration of oral analgesia (paracetamol, non-steroidal anti-inflammatory drugs or opiates according to the World Health Organization scale) thereafter. Fluid and solid food oral intake is resumed within 12 and 24 hours of the operation, respectively. Patients are mobilised as soon as possible (on first post-operative day). Deep vein thrombosis prophylaxis consists of graduated compression stocking and subcutaneous low-molecular weight heparin for 14 days.

Statistical analysis

Categorical and numerical variables were described using proportions or medians (1st-3rd interquartile range, IQR) and were compared using Fisher's exact test, Chi-square test or Mann-Whitney U test as appropriate. Outcome-related statistically significant differences between TP-HALDN and RP-HALDN were further investigated using logistic regression models. The crude odds ratio (OR), 95% confidence interval (CI), and P-value were reported for the predictors. The predictive ability was omitted in those cases in which there were no events in one arm as the assumptions required for logistic regressions could not be fully met. R and Pseudo-R square values were included to provide information about the percentage of variance explained by the predictors, in all the regressions. DCGS was analysed using the Kaplan-Meier method. Survival curves were compared with log-rank. The significance of statistical tests was taken at a P-value of <0.05. Analyses were performed using SPSS (version 23.0; IBM Corp., Armonk, NY, USA).

Results

Donor and recipient characteristics

From June 2008 to March 2016, we performed 321 consecutive HALDN and LDRT. Four donors and four recipients were excluded from the study as they were part of the paired kidney exchange scheme run by NHS Blood and Transplant; therefore, we could not obtain all the information required. Overall, data from 317 donors and 317 recipients were analysed.

Of the donors, 235/317 (74.1%) underwent TP-HALDN whereas 82/317 (25.9%) underwent RP-HALDN. Donor characteristics in the two groups were similar (Table 1). Namely, ethnicity, gender distribution, age (TP-HALDN: 46, IQR 37-54 vs RP-HALDN: 44, IQR 36-54 years; P=0.511), BMI (TP-HALDN: 25.98, IQR 23.99-27.97 vs RP-HALDN: 26.35, IQR 24.63-28.08 kg/m^2; P=0.203), proportion of right-sided nephrectomy (TP-HALDN: 80/235, 34.0% vs RP-HALDN: 33/82, 40.2%; P=0.349), and proportion of nephrectomy performed on patients with multiple renal vessels (TP-HALDN: 65/235, 27.7% vs RP-HALDN: 23/82, 28.0%; P=1.000) were not significantly different.

Recipient characteristics are detailed in Table 1. Except for a small difference in age (TP-HALDN: 42, IQR 32-51 vs RP-HALDN: 49, IQR 37-54 years; P=0.023) and gender distribution (56.2% males in TP-HALDN vs 69.5% in RP-HALDN; P=0.037), the two groups were comparable.

Donor outcomes

There were no deaths among the donors.

Overall, conversion rate to open surgery was 0.3% (1/317). The conversion occurred during a left-sided TP-HALDN because of bleeding from the renal artery stump, immediately after stapling. The haemorrhage was controlled easily with digital pressure and following conversion, the artery stump was over-sewn manually. The donor did not require any blood transfusion and the kidney was successfully transplanted.

Intra-operative complications rates of TP-HALDN and RP-HALDN were 1.7% (4/235) and 1.2% (1/82), respectively (P=1.000). Specifically, during TP-HALDN we observed two intra-operative bleedings (one requiring conversion described above and one from a large left lumbar vein requiring peri-operative blood transfusion) and two superficial jejunal thermal injuries (both performing a left-sided nephrectomy) whereas during RP-HALDN we recorded one superficial right colon thermal injury. In all cases of bowel injury, there was no evidence of intestinal leakage. All injuries were immediately repaired laparoscopically (extra-mucosal suture). There were no sequelae consisting of bowel perforation or obstruction; although one patient required a second-look laparoscopy for abdominal pain that revealed no abnormalities. No episodes of unintentional damage to spleen, liver, adrenal gland, pancreas or bladder were observed.

The median duration of the procedure was shorter in the TP-HALDN group than RP-HALDN: 96 (IQR 75-127) vs 107 (IQR 93-145) minutes, respectively (P<0.001). Linear regression analysis confirmed that RP-HALDN was associated with an average 11.5-minute longer operative time than TP-HALDN (95%CI 8.1-14.9; P<0.001). The median extraction time was 2 (IQR 1.5-2.5) minutes with both the techniques (P=1.000). We never observed cases of entrapment of the kidney during extraction.

Hospital stay was also equivalent (3, IQR 2-4 days; P=0.852).

After one-year follow-up, the proportion of patients experiencing post-operative complications was 11.9% (28/235) in TP-HALDN and 17.1% (14/82) in RP-HALDN (P=0.258). The Comprehensive Complication Index[14] and the Clavien-Dindo Classification[15] did not show any statistically significant difference between the two techniques (Table 2 and Table 3). The rate of patients with severe post-operative abdominal pain (symptoms requiring specific diagnostic work up or further procedures) was similar (TP-HALDN: 1/235, 0.4% vs RP-HALDN: 1/82, 1.2%; P=0.451). Also, the incidence of paralytic ileus (inability to restore oral intake by post-operative day 2) was equivalent (TP-HALDN: 6/235, 2.6% vs RP-HALDN: 2/82, 2.4%; P=1.000). We did observe that overall (5/82, 6.1% vs 4/235, 1.7%; P=0.053), superficial (4/82, 4.9% vs 3/235, 1.3%; P=0.077), and deep (1/82, 1.2% vs 1/235, 0.4%; P=0.451) surgical site infections (SSI) were higher in RP-HALDN than TP-HALDN. Incisional hernia was only recorded among donors undergoing TP-HALDN (TP-HALDN: 8/235, 3.4% vs RP-HALDN: 0/82, 0%; P=0.118).

Thirteen/235 (5.5%) of the donors in TP-HALDN and 3/82 (3.7%) of the donors in RP-HALDN required further surgical treatment (P=0.769). Re-operations were divided in three sub-groups: urgent (within 72 hours of diagnosis), semi-elective (within four weeks of diagnosis), and elective (thereafter). Urgent re-operations were recorded only after TP-HALDN (TP-HALDN: 2/235, 0.9% vs RP-HALDN: 0/82, 0%; P=1.000); two patients required a second look laparoscopy for abdominal pain (both the explorations proved to be negative for bowel leak or obstruction). There were two semi-elective re-operations in each group (TP-HALDN: 2/235, 0.9% vs RP-HALDN: 2/82, 2.4%; P=0.276). The semi-elective procedures performed following TP-HALDN were for wound debridement and percutaneous drainage of abdominal collection whereas those carried out after RP-HALDN were both for wound debridement. The proportion of donors undergoing elective surgery was 3.8% (9/235) in TP-HALDN and 1.2% (1/82) in RP-HALDN (P=0.463). The elective re-operations in the first group were a laparoscopic clipping of para-aortic lymphatic vessels causing chylous ascites and eight incisional hernia repairs. The only elective procedure in RP-HALDN was a US-guided percutaneous drainage of hydrocele.

Sub-analysis of right-sided vs left-sided or single-vessel vs multiple-vessel nephrectomies could not demonstrate any statistically significant difference between the two MIDN techniques in terms of

conversion to open surgery, intra-operative complications, extraction time, and post-operative complications (Table 4 and Table 5).

Recipient outcomes

RT from TP-HALDN or RP-HALDN showed similar 1-year DCGS rates (97% vs 98.8%; P=0.685).

We observed one episode (1/235, 0.4%) of PNF in TP-HALDN and none (0/82, 0%) in the RP-HALDN group (P=1.000). The incidence of DGF after TP-HALDN and RP-HALDN was 1.3% (3/235) and 4.9% (4/82), respectively (P=0.077).

Three-year overall post-operative complication rates were comparable (TP-HALDN: 31/235, 13.2% vs RP-HALDN: 11/82, 13.4%; P=1.000). Post-operative vascular and urological complications were also analysed separately. We recorded five (5/235, 2.1%) vascular complications in TP-HALDN and one (1/82, 1.2%) in RP-HALDN (P=1.000). Vascular complications after TP-HALDN were renal vein thrombosis (n=2), renal vein haemorrhage (n=1), renal artery thrombosis (n=1), and renal artery stenosis (n=1). In the RP-HALDN we recorded a single episode of renal vein thrombosis. All vascular complications were observed during the first post-transplant year. Overall, there were six (6/235, 2.6%) urological complications in TP-HALDN and four (4/82, 4.9%) in RP-HALDN (P=0.289). Urological complications were divided in three categories: immediate (within seven days of transplant), early (between the second post-transplant week and the third month of follow-up), and late (thereafter). We observed one immediate (ureteric leak), eight early (ureteric stenosis), and one late urological complication (ureteric stenosis). All urological complications were recorded during the first post-transplant year and required surgical treatment in the form of re-implantation of the ureter. There were no recurrences. As shown in Table 6, transplant-related outcomes in the two groups were comparable.

Sub-analysis of RT performed using right vs left or single-vessel vs multiple-vessel kidneys did not demonstrate any statistically significant difference between TP-HALDN and RP-HALDN in terms of DCGS, PNF, DGF, and post-operative surgical complications rates (Table 4 and Table 5).

Discussion

Since the beginning of the 21st century, the overall activity of LDRT has more than quadruplicated worldwide.[2,5] The Global Observatory of Donation and Transplantation reports that during 2018, 31.767 LDRT were performed while in the year 2000, 7.676.[16] In our Institution, we have directly witnessed this remarkable increase, especially between 2008 and 2016, when MIDN was introduced. Many different surgical techniques have been proposed over the years.[3-6] However, solid evidence supporting one specific approach over the other ones is lacking. In this study, we have comprehensively reviewed our

experience with HALDN linking donor and recipient outcomes to the access used for nephrectomy (TP-HALDN vs RP-HALDN); specifically including a number of variables that are seldom reported.

The main outcomes of our donors are comparable with those reported in other series evaluating MIDN.[5,9,17-19] Having recorded only one conversion to open procedure (0.3%) represents one of the most rewarding aspect of our experience; particularly because an overall conversion rate of 1.1% has been estimated by a recent meta-analysis.[5] Intra-operative (1.6%) and post-operative (13%) complication rates were also in line with current trends.[5]

The legitimately perceived advantages of RP-HALDN are related to the preservation of the intra-peritoneal organs. However, such logical interpretation is currently not supported by clear evidence; as most of the available studies comparing TP and RP techniques for MIDN offer different results.[7,20-23] The reported benefits of the RP approach were actually presented in studies comparing RP-HALDN vs pure-laparoscopic donor nephrectomy rather than TP-HALDN.[9] Importantly, recent series and a meta-analysis performed on a combined dataset of 1470 procedures have demonstrated that main donor outcomes were not significantly influenced by the surgical approach chosen for the operation.[5,24,25] Our experience suggests that TP-HALDN and RP-HALDN have similar intra- and post-operative surgical complication rates. In particular, we could not confirm the perceived advantages of the RP approach in terms of intra-operative organs damage, peri-operative bleeding, and post-operative abdominal pain or ileus because no episodes of unintentional splenectomy, liver injury, bowel perforation or bowel obstruction were observed, neither in the TP or in the RP group. Also, the incidence of haemorrhagic complications (0.6%), severe abdominal pain (0.6%) or ileus (2.5%) were constantly within the reported average.

SSI may represent a debilitating complication deserving detailed analysis. Our overall SSI infection rate was 2.8%. Although it is slightly above the reported average of 1.6%[5], we have presented both superficial and deep SSI as a composite outcome. Furthermore, we considered all infections recorded during the follow-up; including those requiring intravenous antibiotic administration, re-admission or re-operation. Comparison with other series remains difficult, because detailed information regarding post-operative infections have been rarely reported and the criteria used to define infectious complications appear inconsistent.[5] We observed higher SSI rates after RP-HALDN than TP-HALDN (6.1% vs 1.7%). Such a difference was mainly due to superficial SSI (4.9% vs 1.3%). We believe that the reason behind this discrepancy is that the Pfannenstiel incision initially used in the RP-HALDN required a more laborious dissection to allow access to the muscular plane and the RP space. Also, supra-pubic skin folds often observed post-operatively, might have contributed.[26] Following the adoption of the same incision described for the TP-HALDN, infection rate decreased remarkably and the technique remained unchanged.

The incidence of incisional hernia was higher after TP-HALDN than RP-HALDN (3.4% vs 0%).[27,28] We do not believe that such difference may be related to donor characteristics, length of the procedures or post-operative infections because gender distribution, age, and BMI were equivalent; furthermore, the duration of the operation and SSI were lower in the TP-HALDN group. A plausible explanation is that the incision of the peritoneum combined with the hand-port placement on the midline, required for the TP technique may favor the development of incisional hernia as it represents a tension point of the abdominal wall.[27-29]

As previously observed by Buell and colleagues,[30] we noted that the vast majority of surgical complications including SSI and incisional hernia occurred in the early stages of our experience with both techniques; incisional hernia between 2009 and 2012 and SSI between 2011 and 2014. The opportunity of regular departmental audit and immediate feedback on the occurrence of such complications has allowed the implementation of relevant corrections and improvements in the surgical setting as well as donor peri-operative antibiotic prophylaxis and wound care protocols. In the subsequent years, the observations of incisional hernia and SSI became increasingly sporadic.

We found that the length of the procedure was longer for RP-HALDN than TP-HALDN. However, a difference of about 11 minutes does not represent in our opinion a substantial advantage of TP-HALDN. Remarkably, the extraction time was identical with no episodes of kidney entrapment in both groups. Furthermore, neither technique generally took more than two hours while most of the studies on pure-laparoscopic or robotic donor nephrectomy report longer operating times as well as extraction times.[5,19,31]

Median donor hospital stay was three days and substantially equivalent in TP-HALDN and RP-HALDN. The reduced length of hospitalization is a recognised advantage of MIDN.[6,32] The relatively wide variability of the safe discharge observed in this series probably reflects the social circumstances of our patients. We had a large number of donors coming from other UK regions or abroad. Limitations of discharging donors to temporary residences rather than directly to their homes have undoubtedly impacted on hospitalisation.

Our 1-year DCGS rate was 97.5% (97% after TP-HALDN and 98.8% following RP-HALDN), substantially comparable with the national (UK) average[33] and with the outcomes recently reported by other groups.[34] Considering that our study population included more than 20% of high-risk recipients and medically-complex donors, these results further demonstrate that HALDN can offer excellent transplant-related outcomes, regardless of the specific approach chosen.[5,7,24]

Overall PNF (0.3%) and DGF (2.2%) rates observed in the present study are similar to the best results described in the literature[35] and reflect the short extraction time achieved with HALDN. Consistently maintaining cold ischemia time (CIT) below three hours has also undoubtedly played a role[35-37] but we do

believe that other non-measurable factors might have been beneficial. Specifically, during both TP-HALDN and RP-HALDN we have always allowed adequate time for the kidney to "rest" before stapling, ensuring optimal mean arterial pressure being established. Furthermore, we have consistently ensured the attendance of two senior consultants during the most crucial parts of the procedure thus allowing the surgeon to remain focused on the critical steps of the operation. This practice is shared by many transplant centers and reduces the inevitable stress on the mentored surgeon while maintaining the highest quality of the service without the effects of multiple learning curves.[30,38] Reported incidence of DGF after LDRT varies from 4% to 10%, depending on the series[35]. We noticed that DGF rate was higher after RP-HALDN than TP-HALDN (4.9% vs 1.3%). The reason behind this difference is difficult to explain because donor age, extraction time, CIT, proportions of right-sided or multiple-vessel MIDN, and main recipient characteristics were equivalent in the two groups. Comparison between patients with vs without DGF also failed to detect any significant difference (data not shown) and given the small number of events (n=4), multivariate regression analysis could not be performed. Reviewing the medical records of the patients experiencing this complication in the RP-HALDN group, we observed that they were all at high risk of DGF due to dialysis vintage, previous transplantation, and sensitization. On the contrary, no specific donor-related (female gender, advanced age, obesity, hypertension) risk factors could be identified.[35] Properly designed studies with larger populations and randomization are probably needed to definitely address this issue.

Analysis of recipient post-operative surgical complications also demonstrated similar results with TP-HALDN and RP-HALDN. We focused on urological complications. This aspect of clinical practice cannot be emphasised enough. Especially in medium-sized centers like ours, it is easy suffering the perception of increased complications anytime we observed one. It certainly reflects the experience of a unit that can cope and adapt to rapidly increased case volumes with the inevitable, resultant numbers of complications.[30,38] Nevertheless, we found that urological complications rate remained low throughout the study period and comparable to other published series.[39,40] Apart from a single episode of urinary leak, all urological complications were recorded after stent removal. Such observation is not surprising as ureteric stenosis usually remains silent whilst the stent is in place.[41] We believe that the small difference in urological complications between TP-HALDN (2.6%) and RP-HALDN (4.9%) is probably due to some cases when efficient pneumo-retro-peritoneum was particularly difficult to establish, leading to more laborious ureteric dissection and unintentional skeletonization of the ureter.

For many years, left kidneys have widely represented the first option when evaluating a potential donor for nephrectomy, regardless of the surgical approach chosen. More difficult dissection of the kidney and shorter renal vein have been the main factors behind this policy but longer donor operating time, more

challenging vascular anastomosis in the recipient, and increased risk of DGF after transplantation have been also considered valid reasons for avoiding the right side.[4,35] Even though, several reports have suggested that in medium- to high-volume centers with properly trained surgeons, both right-sided and multiple-vessel donor nephrectomies can be safely performed with a MIDN technique,[5,7,8,10,30,38] many Transplant units remain concerned regarding right-sided MIDN. Our data support the use of TP-HALDN and RP-HALDN for right-sided and multiple-vessel kidneys because no differences in donor- or recipient-related outcomes could be detected. In our experience, the use of RP-HALDN has facilitated obtaining longer allograft arteries. We observed such benefit particularly in cases of early retro-caval bifurcation, allowing easier transplantation of the right kidney.

We recognise the limitations of this study such as the relatively small sample size and the lack of randomization. However, the groups included were fully representative of the actual living-donor and recipient pool. Moreover, matching donor and recipient outcomes allowed us to offer a thorough evaluation of both the techniques. Importantly, right-sided and multiple-vessel MIDN were equally represented.

In our experience, both TP-HALDN and RP-HALDN can be performed safely with excellent donor and recipient outcomes. In the modern era of LDRT, minimally-invasive techniques have greatly diminished the role of traditional open nephrectomy which should now be considered an obsolete technique. In the course of the years, we strengthened the belief that having more than one technique available in the unit is a major advantage for the service and patient care. We also witnessed that constructive governance paired with consolidated mentoring process allow a rewarding growth of the LDRT program.

EF: data analysis/interpretation, drafting, critical revision, final approval; SI: data analysis/ interpretation, drafting, final approval; NC: data acquisition/analysis, final approval; RS: data acquisition/analysis, critical revision, final approval; EC: data interpretation, critical revision, final approval; TM: data interpretation, critical revision, final approval; CP: data interpretation, critical revision, final approval; RC: study design, drafting, critical revision, final approval.

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Table 1. Donor and recipient baseline characteristics.

	TP-HALDN (n=235)	RP-HALDN (n=82)	
Variables	**Median (IQR) or n (%)**		**P**
Donor Afro-Caribbean	29 (12.3)	10 (12.2)	1.000
Donor male gender	113 (48.1)	42 (51.2)	0.701
Donor age (years)	46 (37-54)	44 (36-54)	0.511
Donor age ≥ 60 years	32 (13.6)	10 (12.2)	0.851
Donor BMI (kg/m^2)	25.98 (23.99-27.97)	26.35 (24.63-28.08)	0.203
Right-sided nephrectomy	80 (34.0)	33 (40.2)	0.349
Multiple-vessel nephrectomy	65 (27.7)	23 (28.0)	1.000
Recipient Afro-Caribbean	40 (17.0)	14 (17.1)	1.000
Recipient male gender	132 (56.2)	57 (69.5)	0.037
Recipient age (years)	42 (32-51)	49 (37-54)	0.023
Recipient age ≥ 60 years	25 (10.6)	9 (11.0)	1.000
Recipient BMI (kg/m^2)	24.47 (22.74-26.21)	24.95 (23.23-26.68)	0.074
Primary kidney transplant	200 (85.1)	69 (84.1)	0.858
CNI-based immunosuppression	235 (100)	82 (100)	1.000

TP-HALDN, trans-peritoneal hand-assisted laparoscopic donor nephrectomy; RP-HALDN, retro-peritoneal hand-assisted laparoscopic donor nephrectomy; IQR, interquartile range; BMI, body mass index; CNI, calcineurin inhibitor.

Table 2. Donor outcomes after TP-HALDN vs RP-HALDN.

	TP-HALDN (n=235)	RP-HALDN (n=82)	P*	Regressions	P
Variables	**Median (IQR) or n (%)**			**Coefficient or OR (95%CI)**	
Conversion	1 (0.4)	0 (0.0)	1.000	-	-
IO complication	4 (1.7)	1 (1.2)	1.000	-	-
- Bleeding	2 (0.9)	0 (0.0)	1.000	-	-
- Bowel injury	2 (0.9)	1 (1.2)	1.000	-	-
Operation length (min)	96 (75-127)	107 (93-145)	<0.001	11.523 (8.118-14.929)†	<0.001
1-year PO complication	28 (11.9)	14 (17.1)	0.258	-	-
- Ileus	6 (2.6)	2 (2.4)	1.000	-	-
- Blood transfusion	0 (0)	0 (0)	1.000	-	-
- SSI	4 (1.7)	5 (6.1)	0.053	-	-
- Incisional hernia	8 (3.4)	0 (0)	0.118	§	-
CCI	0 (0.0-0.0)	0 (0.0-0.0)	-	-	-
Hospital stay (day)	3 (2-4)	3 (2-4)	0.852	-	-
1-year re-operation	13 (5.5)	3 (3.7)	0.303	-	-
- Urgent	2 (0.9)	0 (0)	1.000	-	-
- Semi-elective	2 (0.9)	2 (2.4)	0.276	-	-
- Elective	9 (3.8)	1 (1.2)	0.463	-	-

1-year re-admission	20 (8.5)	9 (11)	0.509	-	-

* Distributions were compared with Mann-Whitney's U test while proportions with Fisher's exact test or Chi-square test. All tests are two-sided.

† Linear regression coefficient (95%CI), R^2=0.123.

§ The effect size is not measurable due to the singularity of the phenomenon.

TP-HALDN, trans-peritoneal hand-assisted laparoscopic donor nephrectomy; RP-HALDN, retro-peritoneal hand-assisted laparoscopic donor nephrectomy; IQR, interquartile range; IO, intra-operative; PO, post-operative; SSI, surgical site infection; CCI, Comprehensive Complication Index.

Table 3. Clavien-Dindo classification of post-operative donor complications after TP-HALDN vs RP-HALDN.

	TP-HALDN (n=235)	RP-HALDN (n=82)	P
Variables	**Median (IQR) or n (%)**		
Clavien-Dindo I	10 (4.3)	6 (7.3)	0.378
- Abdominal pain	0 (0.0)	1 (1.2)	0.259
- Abnormal liver function tests	1 (0.4)	0 (0.0)	1.000
- Acute urinary retention	2 (0.9)	0 (0.0)	1.000
- Fever of unknown origin	0 (0.0)	1 (1.2)	0.259
- Hydrocele	0 (0.0)	1 (1.2)	0.259
- Ileus	5 (2.1)	2 (2.4)	1.000
- Intra-abdominal collection	0 (0.0)	1 (1.2)	0.259
- Scrotal hematoma	1 (0.4)	0 (0.0)	1.000
- Subcutaneous hematoma	0 (0.0)	1 (1.2)	0.259
Clavien-Dindo II	7 (3)	6 (7.3)	0.107
- Surgical site infection	4 (1.7)	4 (4.9)	0.212
- Urinary tract infection	4 (1.7)	2 (2.4)	0.651
Clavien-Dindo IIIa	0 (0.0)	0 (0.0)	-
Clavien-Dindo IIIb	15 (6.4)	1 (1.2)	0.079
- Abdominal pain	1 (0.4)	0 (0.0)	1.000
- Chylous ascites	1 (0.4)	0 (0.0)	1.000
- Surgical site infection	0 (0.0)	1 (1.2)	0.259
- Ileus	1 (0.4)	0 (0.0)	1.000
- Incisional hernia	8 (3.4)	0 (0.0)	0.118

Clavien-Dindo IV	0 (0.0)	0 (0.0)	-
Clavien-Dindo V	0 (0.0)	0 (0.0)	-

TP-HALDN, trans-peritoneal hand-assisted laparoscopic donor nephrectomy; RP-HALDN, retro-peritoneal hand-assisted laparoscopic donor nephrectomy; IQR, interquartile range.

Table 4. Donor and recipient outcomes after right- vs left-sided or single- vs multiple-vessel HALDN.

	Left-sided HALDN (n=204)	**Right-sided HALDN (n=113)**	**P**
Variables	**n (%)**		
Conversion to open nephrectomy	1/204 (0.5)	0/113 (0)	1.000
Donor IO complication	4/204 (2)	1/113 (0.9)	0.659
Warm ischemia time > 3 minutes	15/204 (7.4)	10/113 (8.8)	0.667
Donor 1-year PO complication	26/204 (12.7)	16/113 (14.2)	0.732
1-year death-censored graft loss	5/204 (2.5)	3/113 (2.7)	1.000
Primary non-function	1/204 (0.5)	0/113 (0)	1.000
Delayed graft function	3/204 (1.5)	4/113 (3.5)	0.252
Recipient 3-year PO complication	25/204 (12.3)	17/113 (15)	0.493
	Single-vessel HALDN (n=229)	**Multiple-vessel HALDN (n=88)**	**P**
Variables	**n (%)**		
Conversion to open nephrectomy	1/229 (0.4)	0/88 (0)	1.000
Donor IO complication	3/229 (1.3)	2/88 (2.3)	0.620
Warm ischemia time > 3 minutes	15/229 (6.5)	10/88 (11.4)	0.166
Donor 1-year PO complication	29/229 (12.7)	13/88 (14.8)	0.711
1-year death-censored graft loss	5/229 (2.2)	3/88 (3.4)	0.689
Primary non-function	0/229 (0)	1/88 (1.1)	1.000
Delayed graft function	4/229 (1.7)	3/88 (3.4)	0.402
Recipient 3-year PO complication	28/229 (12.2)	14/88 (15.9)	0.459

HALDN, hand-assisted laparoscopic donor nephrectomy; IQR, interquartile range; IO, intra-operative; PO, post-operative.

Table 5. Donor and recipient outcomes after right-sided or multiple-vessel TP-HALDN vs RP-HALDN.

Right-sided nephrectomy			
	TP-HALDN (n=80)	**RP-HALDN (n=33)**	**P**
Variables	**n (%)**		
Conversion to open nephrectomy	0/80 (0)	0/33 (0)	1.000
Donor IO complication	0/80 (0)	1/33 (3)	0.292
Warm ischemia time > 3 minutes	7/80 (8.7)	3/33 (9.1)	1.000
Donor 1-year PO complication	11/80 (13.7)	5/33 (15.2)	1.000
1-year death-censored graft loss	2/80 (2.5)	1/33 (3)	1.000
Primary non-function	0/80 (0)	0/33 (0)	1.000
Delayed graft function	2/80 (2.5)	2/33 (6.1)	0.579
Recipient 3-year PO complication	12/80 (15)	5/33 (15.2)	1.000
Multiple-vessel nephrectomy			
	TP-HALDN (n=65)	**RP-HALDN (n=23)**	**P**
Variables	**n (%)**		
Conversion to open nephrectomy	0/65 (0)	0/23 (0)	1.000
Donor IO complication	2/65 (3.1)	0/23 (0)	1.000
Warm ischemia time > 3 minutes	7/65 (12.3)	3/23 (13)	0.717
Donor 1-year PO complication	9/65 (13.8)	4/23 (17.4)	0.736
1-year death-censored graft loss	3/65 (4.6)	0/23 (0)	0.564
Primary non-function	1/65 (1.5)	0/23 (0)	1.000
Delayed graft function	2/65 (3.1)	1/23 (4.3)	1.000

Recipient 3-year PO complication	11/65 (17)	3/23 (13)	1.000

TP-HALDN, trans-peritoneal hand-assisted laparoscopic donor nephrectomy; RP-HALDN, retro-peritoneal hand-assisted laparoscopic donor nephrectomy; IQR, interquartile range; IO, intra-operative; PO, post-operative.

Table 6. Recipient outcomes after TP-HALDN vs RP-HALDN.

	TP-HALDN (n=235)	RP-HALDN (n=82)	
Variables	**Median (IQR) or n (%)**		**P**
1-year death-censored graft loss	7 (3.0)	1 (1.2)	0.685
Primary non-function	1 (0.4)	0 (0.0)	1.000
Delayed graft function	3 (1.3)	4 (4.9)	0.077
Intra-operative complication	3 (1.3)	0 (0.0)	0.571
3-year post-operative complications	31 (13.2)	11 (13.4)	1.000
Vascular complications	5 (2.1)	1 (1.2)	1.000
- Renal vein thrombosis	2 (0.9)	1 (1.2)	1.000
- Renal vein haemorrhage	1 (0.4)	0 (0.0)	1.000
- Renal artery thrombosis	1 (0.4)	0 (0.0)	1.000
- Renal artery stenosis	1 (0.4)	0 (0.0)	1.000
Urologic complications	6 (2.6)	4 (4.9)	0.290
- Ureteral leakage	1 (0.4)	0 (0.0)	1.000
- Ureteral stenosis	5 (2.1)	4 (4.9)	0.244

TP-HALDN, trans-peritoneal hand-assisted laparoscopic donor nephrectomy; RP-HALDN, retro-peritoneal hand-assisted laparoscopic donor nephrectomy; IQR, interquartile range.