Surgical aspects of renal transplantation
Minnee, R.C.

Citation for published version (APA):
There is an ongoing discussion in living renal transplantation whether the right or the left donor nephrectomy is to be preferred if both kidneys are equal, due to the lack of prospective studies. A prospective single-center randomized trial was conducted from April 2002 to September 2006, in which 60 eligible consecutive donors were randomized to either left-sided or right-sided hand-assisted laparoscopic donor nephrectomy (HALDN). Primary endpoint was operation time. Secondary endpoints were donor morbidity, warm ischemia time, delayed graft function, urological complications, quality of life, and graft survival. Median operating time for left-sided HALDN (180 min) was significantly longer compared with right-sided HALDN (150 min; P=0.021). There were no conversions in both groups. There were no major intra- or postoperative complications. One-year graft survival rate was 96% in the left group versus 93% in the right group (P=0.625, log rank). Operating time of HALDN of the right kidney is significantly shorter than HALDN of the left kidney. No differences were detected in complication rates and graft survival between left and right-sided donor nephrectomy.
INTRODUCTION

The number of living donor transplantations has increased during the past 20 years due to the shortage of deceased kidney donors and an increased number of patients on the waiting list for renal transplantation. Living donor kidney transplantation is superior to deceased donor kidney transplantation because of the better patient and graft survival rates, better cost-effectiveness, and improved quality of life (QoL) of the recipient. Traditional open living donor nephrectomy through flank incision is associated with disincentives including long hospital stay, prolonged postoperative pain, cosmetic problems, and slow convalescence. These disincentives might be a drawback for potential donors to donate a kidney. With the advent of laparoscopic living donor nephrectomy, a reduction in hospital stay, less postoperative analgesic requirements, improved cosmetics, and an earlier return to normal daily activities have been reported.

There is an ongoing discussion whether the right or the left kidney donor nephrectomy is to be preferred. Most centers prefer to use the left kidney for live kidney donation because of the longer renal vein, which is advantageous during the implantation. However, some surgeons prefer the right kidney because it is easier to recover than the left kidney and the risk of spleen laceration is decreased. A recent study demonstrated the negative effect of longstanding pneumoperitoneum on kidney function. Reduction of operation time with maintenance of the beneficial effect of the minimal invasive aspect of the laparoscopic donor nephrectomy is essential. There are no prospective studies comparing the outcome of left-sided versus right-sided laparoscopic donor nephrectomy in terms of operating time. Therefore, a prospective single-center randomized trial was conducted performing either a left- or a right-sided hand-assisted laparoscopic donor nephrectomy.

PATIENTS AND METHODS

Sixty consecutive patients were included in the study from April 2002 to September 2006. The trial flow diagram was shown in Figure 1. The median follow-up period was 12 months. Specific preoperative donor evaluation included blood and urine examination, angiography, pyelography, and renal scintigraphy.

Nephrologists enrolled the donors. Inclusion criteria were donors with age greater than 18 years, an identical kidney with regard to renal vascular anatomy, renal function, urinary tract, and written informed consent. Surgeons assigned the donor for randomization if both kidneys had symmetrical function and anatomy and were feasible for transplantation. Unilateral multiple arteries were excluded. Cases of bilateral multiple arteries were only included in the study if both kidneys were judged transplantable by the surgeon.
All procedures were done by two surgeons (W.A.B. and/or M.M.I.). The randomization was not stratified by surgeon. Both surgeons had done at least 20 hand-assisted donor nephrectomies of the left as well as of the right kidney.

After completing preoperative QoL questionnaires, patients were allocated to one of the two groups using sealed opaque envelope randomization. Randomization was done by an independent research fellow. There was no sequence of randomization because the envelopes were picked randomly and had no numbers on the outside. The surgeon was informed about the randomization outcome 1 hour before the operation. The study was approved by the Medical Ethical Committee in the Academic Medical Center Amsterdam.

**Donor Surgical technique**

The hand-assisted laparoscopic donor nephrectomy (HALDN) was done transperitoneally. After open dissection of the distal ureter and gonadal vein through a 7–8 cm Pfannenstiel
incision, the nondominant operators’ hand was introduced through a handport (Omniport, Tyco Healthcare, Hampshire, UK) and two 10- to 12-mm trocars were placed. The insufflation pressure was maximally 12 mmHg. The right or left colon was then mobilized. After transecting the ureter distally, the renal artery was transected with metal clips, while an endoscopic stapler (Endopath ETS Compact Linear Cutter, Johnson & Johnson, Dilbeek, Belgium) was used to transect the renal vein. The kidney was extracted through the Pfannenstiel incision and cold flushed and preserved with University of Wisconsin solution.

Recipients
Implantation of the kidney was done directly after the donor nephrectomy via the extraperitoneal approach in the iliac fossa. After successful transplantation, all recipients were followed for at least 1 year. After 1 year follow-up, patients were transferred to the referral center. Standard immunosuppression consisted of prednisone, a calcineurin inhibitor, mycophenolate mofetil, and prophylactic anti-CD25 monoclonal antibody (basiliximab). First episodes of acute rejection were treated with pulse doses of methylprednisolone; second episodes with thymoglobulin. Delayed graft function was defined as the need for dialysis within the first postoperative week.

Postoperative care
Postoperatively, all patients were treated equally with regard to feeding, pain regulation, mobilization, and postoperative care. The donor and a study-independent physician determined timing of discharge. Donors were seen at our outpatient department at 6 weeks, 3 months, and 1 year after donation.

Primary and secondary endpoints
The hypothesis was that donors who underwent a right-sided HALDN would have a shorter operation time. Operation time served as primary endpoint. Secondary endpoints were donor morbidity, warm ischemia time, delayed graft function, urological complications, and graft survival. Various questionnaires were also set as secondary endpoints. Postoperative QoL was measured with the Short-Form 36 Health Survey (SF-36)\(^7\), the Gastro-Intestinal Quality of Life index (GIQLI)\(^8\) and the Multidimensional Fatigue Inventory-20 (MFI-20)\(^9\). The SF-36 is a generic QoL measurement that assesses eight health concepts: physical function, role physical, bodily pain, general health perceptions, vitality, social functioning, role emotional and mental health. The GIQLI is a gastrointestinal specific questionnaire. To measure fatigue, the MFI-20 was used. Furthermore, a 0 to 10 visual analogue scale (VAS) measure of pain in rest/motion and nausea was analyzed. Acute rejections were recorded and analyzed.
**Data collection**
Operative time was defined as time elapsed from skin incision to placement of the final skin suture. Warm ischemic time was defined as time elapsed from clamping of the renal artery to initiation of cold perfusion with University of Wisconsin solution. Urinary tract infections, wound infections, lymphoceles, and pulmonary infections were considered minor complications. Bleeding with transfusion of packed red blood cells, reoperation, graft failure, and prolonged ileus (>5 days) were considered major complications. Hospital stay was counted in days from the operating day to the day of discharge. The manuscript was written with the Consort Statement as guidance.

**Statistical analysis and power analysis**
Patients were analyzed according to the intention to treat principle. A power analysis ($\alpha = 0.05$, $\beta = 0.1$) was based on operation time. A difference in operating time of 30 minutes (150 minutes ± 30 minutes for the right group and 180 minutes ± 30 minutes for the left group) between the two groups was considered as a clinical significant difference related to the total operation time. This difference revealed that a sample size of 25 donors had to be included in each arm. A drop-out of 20% was anticipated and therefore a group size of 2 x 30 patients was included. Both groups were compared using chi-square test (discrete data) or Mann-Whitney $U$ test (continuous data) as indicated and 90% ranges are used. Differences in quality of life were compared by repeated measurement analysis of variance. Survival analysis was performed by the Kaplan–Meier technique and the log-rank test. A $p$-value of $< 0.05$ was considered statistically significant. For statistical analyses the SPSS software package (SPSS, Chicago, Illinois, USA) was used.

**RESULTS**

Characteristics, surgical outcomes and postoperative outcomes of donors and recipients were shown in Table 1.

**Donors**
Median operating time for left HALDN was significantly longer (180 min, range 117–266) compared with right HALDN (150 min, range 92–219, 95% confidence interval [CI] 3.93–46.38, P=0.021; Figure 2). The mean difference of operating time was 25 min (95% CI 4–46). There were no conversions in both groups. Intraoperative complications occurred in three patients (10%) during left HALDN: bleeding in two and one lesion of a polar artery. Four intraoperative complications (13%) occurred during right HALDN: two serosal lesions of the colon, bleeding in one, and one lesion of a polar artery. None of the patients with intraoperative bleeding needed intra- or postoperative blood transfusion. However, it was
necessary to introduce an extra 5-mm trocar during the operation to assist in controlling the bleeding. None of the patients with a serosal lesion of the colon needed a colonic repair. All polar artery lesions were repaired successfully before implantation. Minor postoperative complications after left HALDN were a swollen testicle and a supraventricular tachycardia. Both were treated conservatively. No minor postoperative complications occurred in the right HALDN group. No major postoperative complications occurred in either group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Left (N = 29)</th>
<th>Right (N = 31)</th>
<th>p¹,²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Donor and Recipient Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Donor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, median years (range)</td>
<td>50 (23-74)</td>
<td>46 (21-62)</td>
<td>0.328</td>
</tr>
<tr>
<td>Male/female</td>
<td>15/14</td>
<td>13/18</td>
<td>0.617</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.2 (21-34)</td>
<td>24.9 (19-34)</td>
<td>0.367</td>
</tr>
<tr>
<td>Prior abdominal operation (%)</td>
<td>9 (31)</td>
<td>12 (39)</td>
<td>0.725</td>
</tr>
<tr>
<td>Multiple arteries (%)</td>
<td>1 (3)</td>
<td>4 (13)</td>
<td>0.392</td>
</tr>
<tr>
<td>Multiple veins (%)</td>
<td>4 (14)</td>
<td>0 (0)</td>
<td>0.105</td>
</tr>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, median years (range)</td>
<td>47 (17-68)</td>
<td>48 (15-72)</td>
<td>0.473</td>
</tr>
<tr>
<td>male/female</td>
<td>20/9</td>
<td>20/11</td>
<td>0.927</td>
</tr>
<tr>
<td>Renal transplantation (%)</td>
<td>4 (14)</td>
<td>1 (3)</td>
<td>0.311</td>
</tr>
<tr>
<td><strong>Surgical and Postoperative Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Donor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conversion to open donor nephrectomy</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Operating time median minutes (range)</td>
<td>180 (117-266)</td>
<td>150 (92-219)</td>
<td>0.021</td>
</tr>
<tr>
<td>Warm ischemic time median minutes (range)</td>
<td>3 (2-5)</td>
<td>3 (1-4)</td>
<td>0.853</td>
</tr>
<tr>
<td>Blood loss median ml (range)</td>
<td>60 (10-1000)</td>
<td>55 (25-1200)</td>
<td>0.718</td>
</tr>
<tr>
<td>Intraoperative complications (%)</td>
<td>3 (10)</td>
<td>4 (13)</td>
<td>1.000</td>
</tr>
<tr>
<td>Postoperative complications (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>minor</td>
<td>2 (7)</td>
<td>0 (0)</td>
<td>0.443</td>
</tr>
<tr>
<td>major</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Hospital stay median days (range)</td>
<td>4 (2-7)</td>
<td>4 (2-7)</td>
<td>0.322</td>
</tr>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operating time median minutes (range)</td>
<td>138 (99-229)</td>
<td>148 (107-267)</td>
<td>0.379</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>3 (10)</td>
<td>6 (19)</td>
<td>0.539</td>
</tr>
<tr>
<td>Ureteral complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percutaneous nephrostomy catheter</td>
<td>3 (10)</td>
<td>2 (7)</td>
<td>0.938</td>
</tr>
<tr>
<td>Surgical re-intervention</td>
<td>2 (7)</td>
<td>1 (3)</td>
<td>0.953</td>
</tr>
<tr>
<td>One-year graft survival³</td>
<td>1/22 96%</td>
<td>2/22 93%</td>
<td>0.631</td>
</tr>
</tbody>
</table>

¹ χ² test; ² Mann-Whitney U Test; ³ log rank;
Left or right donor nephrectomy

Recipient
Median operating time for transplantation was 138 min (range 99–229) in the left group and 148 min (range 107–267) in the right group (P=0.379). No grafts were used for vascular reconstruction. A total of 58 kidneys were transplanted to the right iliac fossa and two into the left fossa. Four renal grafts required arterial reconstruction due to two renal arteries. In all cases, a common ostium was performed. There was no statistically significant difference between both groups in the number of patients with a urological complication. No graft thrombosis occurred in both groups. Delayed graft function occurred in two patients: one in the left group and the other in the right group. One-year graft survival rate was 96% in the left group versus 93% in the right group (P=0.625, log rank). Three grafts were lost during follow-up (one left and two right kidneys), all caused by histological proven humoral rejection, resistant against immunosuppressive drug therapy and plasmapheresis. They were lost at 26, 27, and 112 days after the operation.

Quality of life
At 3 to 6 months after surgery, all patients had a similar QOL equal to the situation before surgery. There were no significant differences between both HALDN groups in pain VAS scores at rest, while moving/coughing, or nausea (Fig. 3) at any moment during follow-up. There were no significant differences between both HALDN groups in all of the eight dimensions of the SF-36, in total GIQLI score, or in the MFI-20 at any moment during follow-up (Figs. 4 and 5)
DISCUSSION

We demonstrated that right-sided HALDN is associated with a significantly shorter operating time of a median of 30 min. The shorter operation time for the right HALDN is probably the result of the lower position of the right kidney, less extensive colonic dissection needed for right-sided HALDN, and no side-branches of the right renal vein. Many surgeons prefer the left kidney for a donor nephrectomy because of the longer renal vein, which makes implantation less demanding\textsuperscript{10,11}. However, drawbacks of the left-sided HALDN are higher chance of lacerating the spleen during laparoscopic mobilization of the splenic flexure of the colon and handling of the lumbar and supra-adrenal side branches of the left renal vein. A major drawback for using the right kidney is the shorter length of the renal vein. Transection of the renal vein with a laparoscopic vascular stapler leads to additional loss of available length necessary for implantation. Additional drawbacks are the need for liver displacement, potentially caval vein bleeding and the increased incidence of vascular thrombosis as reported in some studies\textsuperscript{12}. In our study, no renal vein thrombosis occurred and we did not have to use any additional venous reconstruction to extend the right renal vein.

Lind et al. also reported shorter operation time for the right-sided laparoscopic donor nephrectomy compared to left-sided laparoscopic donor nephrectomy\textsuperscript{4}. However, Husted et al. revealed no difference in operating time between both groups\textsuperscript{13}. An early study of right-sided laparoscopic donor nephrectomy described poor outcomes\textsuperscript{14}. A recent nonrandomized study reported identical results using left-sided laparoscopic donor nephrectomy\textsuperscript{15}.

Our right sided operating time of 150 minutes is comparable with other studies using HALDN\textsuperscript{12,15}. However, our left sided operating time of 180 minutes is shorter compared with other studies\textsuperscript{16,17}. 

![Graph showing postoperative pain as measured with VAS scores (mean ± 2 SEM). The x-axis represents the time after surgery.](image-url)
The operating time for the left donor nephrectomy may be reduced by using a midline incision instead of a Pfannenstiel incision. With this approach, the upper pole of the left kidney may be easier to reach with the nondominant operators’ hand. This may lead to less traction on the vessels and a lower risk of spleen laceration. However, the midline incision is more visibly prominent on the abdomen and is cosmetically inferior to the Pfannenstiel incision.

A recent systematic review stated that there appears to be sufficient evidence to conclude that both renal function and renal blood flow are decreased during pneumoperitoneum. The magnitude of the decrease is dependent on factors, such as preoperative renal func-
tion, level of hydration, level of pneumoperitoneum, patient positioning, and duration of pneumoperitoneum. This review supports the principle to choose the operation with the shortest operation time. The 30-minute difference in our study is a considerable operative time reduction when one relates it to a total operation time of 150 min for a right donor nephrectomy.

Although our study was only powered to detect a significant difference in operation time, we did not detect any significant differences in donor hospital stay, donor intra- and post-operative complication rate, donor quality of life aspects, or renal graft survival between left- or right-sided donor nephrectomy. No grafts were lost due to technical reasons.

There were no conversions in our study. Intraoperative bleeding during the HALDN was easy to control digitally and was resolved without recourse to emergency laparotomy or blood transfusion. Our intraoperative complication rate (13%) is comparable with other HALDN groups 0%-12%\textsuperscript{12,17}. In our study, two patients (3%) had minor complications and no major complications were presented. Major postoperative complication rates vary between 0% and 6%\textsuperscript{12,17}.

Renal vascular anatomy was an important reason for a preferred side and therefore an exclusion criterion. Multiple arteries were used only if they were bilateral and both kidneys were judged transplantable by the surgeon. Recent studies demonstrated the safety of kidney transplantation with multiple arteries\textsuperscript{19,20}.

No significant differences in postoperative quality of life between the left and right group were visible as measures by pain and nausea VAS score, SF-36, GIQLI, and MFI-20. Quality of life decreased significantly immediately after surgery, but was regained within 3 to 6 months after surgery. These results conform to a systematic review, which recorded that most donors experience no change or an improvement in their quality of life after donation\textsuperscript{21}.

The main limitation to this study is the small sample size. The sample size was calculated on a difference in operating time and therefore we cannot make any conclusions about differences in other items than operation time between left- and right-sided HALDN. A donor nephrectomy without complications and successful function in the recipient transplantation are important endpoints. Nowadays many studies in the literature are reporting low complication rates and high graft survival rates. To compare these endpoints between left- and right-sided HALDN, a study with such a larger sample size is needed, but such a study may not be feasible. Because of the negative effect of longstanding pneumoperitoneum on the kidney, reduction in operation time with preservation of the minimal invasive nature of a laparoscopic donor nephrectomy is essential.

In conclusion, operating time of HALDN of the right kidney is significantly shorter than HALDN of the left kidney. There are no differences in morbidity of donor and recipient, hospital stay, or donor QoL.
Acknowledgments

The authors thank Prof. D.A. Legemate, Prof. I.J.M. ten Berge, S.W. Polle and P.J. van Koperen for comments on the draft manuscript and Dr. R.J. Scholten for the statistical analysis.

REFERENCES


