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Early and Late Graft Function after Laparoscopic Hand-Assisted Donor Nephrectomy for Living Kidney Transplantation: Comparison with Open Donor Nephrectomy

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Key Words
Donor nephrectomy · Graft function · Kidney transplantation · Laparoscopy · Live donation

Abstract
Background and Purpose: Laparoscopic donor nephrectomy has become the procedure of choice for living kidney transplantation in many centers. We report on our experience with laparoscopic hand-assisted donor nephrectomy, in particular concerning graft function compared with open donor nephrectomy. ***Materials and Methods:*** Between 1995 and March 2007, 72 patients with end-stage renal disease have received kidney transplantation from living donors. Open living donor nephrectomy (ODN) was performed in 35 donors, whereas 37 donors had undergone laparoscopic hand-assisted nephrectomy (HALDN). Immediate graft function, serum creatinine and serum cystatin C 1 year after the transplantation were evaluated. ***Results:*** Median operative time was 138 min (113–180 min) in the HALDN group and 112 min (91–162 min) in the ODN group ($p < 0.05$). Warm ischemia time was 87 s (63–150 s) in the HALDN and 81 s (56–123 s) in the ODN groups, respectively ($p = 0.13$). Both the rate of primary graft function as well as kidney graft function parameters serum creatinine and serum cystatin C 1 year after transplantation showed no statistically significant difference between the two groups of patients. ***Conclusions:*** Laparoscopic hand-assisted donor nephrectomy is safe and has no negative impact on the transplanted graft function when compared with open donor nephrectomy.

Introduction

Since its initial application 50 years ago, living kidney donation is considered an established practice in transplantation medicine. Its clinical and social significance has increased in recent years as the gap between needed and available donor organs has continuously been growing due to a decline in the number of cadaveric kidney donations [1]. The living kidney donation helps not only to reduce the number of patients waiting for an organ donation, but it also has – regarding the graft function – decisive advantages over the cadaveric kidney grafts [2, 3]. Reasons for this include the reduction of waiting time for a donor organ resulting in decrease of morbidity in patients on waiting list, the comparatively short cold isch-

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Table 1. Characteristics of patient's population

	HALDN	ODN	p
Number of patients	35	37	NA
Age, years (mean ± SD)	40 ± 14	44 ± 13	NS
Ratio male/female	2.9	1.3	<0.01
Immunosuppression regimen			
Triple	26/35	26/37	NS
Triple + 1	9/35	11/37	
Operative time, min (median)	138 (113–180)	112 (91–162)	<0.05
Warm ischemia time, s	87 (63–150)	81 (56–123)	0.13
Hospitalization period, days	5–7	10–12	<0.05

emia time, and due to the predictability of the operation, optimal immunosuppression of the recipient prior to transplantation [3, 4].

The method of live kidney donation itself has experienced a further development along with the introduction of laparoscopic surgical techniques. Thus, in many transplant centers laparoscopic donor nephrectomy (LDN) has become the preferred method of choice in the live kidney donation [5]. The reason for this is the superior benefits of minimally invasiveness nature of laparoscopic techniques [6]. However, there is some controversial discussion about the adverse effect of possible longer warm ischemia time during the laparoscopic donor nephrectomy on recipients graft function [7]. In addition, the possible influence of pneumoperitoneum with its potential risk of compression of the great vessels has also been discussed as disadvantages of laparoscopy [8, 9]. Therefore, hand-assisted laparoscopic donor nephrectomy (HALDN) was introduced to address certain disadvantages of LDN [10]. The use of the hand-assisted approach permits the surgical team to use the necessary extraction incision to their advantage throughout the procedure. Potential advantages of hand-assisted donor nephrectomy include shorter operative time, a shorter learning curve related to the presence of robust tactile feedback, the ability to manually assist in dissection, prevention of torsion of the kidney after the lateral attachments have been dissected, and ease of obtaining hemostasis by manual compression of bleeding vessels [11].

At our center, the HALDN has been the method of choice for donor nephrectomy since December 2003. The purpose of the present study was to investigate whether laparoscopic hand-assisted donor nephrectomy results in negative changes in transplanted graft compared to open donor nephrectomy, in particular concerning primary and late graft function.

Patients and Methods

Patients

This study was a retrospective, nonrandomized single-center analysis. Patients' characteristics are summarized in table 1. From 1995 to March 2007, 72 kidneys from live donors (relatives, partners) were transplanted at our center. Of these, 35 kidneys had been removed conventionally in open technique mostly operated on between 1995 and November 2003. After the introduction of HALDN as the method of choice for donor nephrectomy in our clinic in December 2003, a total of 37 living donors had undergone laparoscopic hand-assisted donor nephrectomy. During this time period, open nephrectomy has been offered to donors only if serious contraindications to laparoscopic technique were existent, i.e. previous multiple abdominal surgery or patients request for open technique.

The immunosuppression protocol was standardized in all recipients consisting of a triple combination (tacrolimus, methylprednisolone and mycofenolate-mofetil). Patients with a particular immunological risk received an additional therapy with antithymocyte globulin (ATG) or IL-2R inhibitor basiliximab as induction therapy.

Preoperative Management

Our living donor work-up is standardized. Briefly, potential donors are thoroughly screened by medical history, physical examination, an array of tests (hematology, coagulation, blood chemistry, and urine analysis), kidney and chest imaging, infectious disease including viral studies, immunologic studies to determine donor-recipient match, and EKG. All donors also undergo a psychological evaluation by a clinical psychologist. This clinical psychologist determines the psychological and social suitability of donors, fully evaluating them for motivation and willingness to donate, hardships that might be incurred, and social support. Further, all donations were screened for exclusion of organ trade according to the German law.

Operative Technique

While the open procedure was performed by multiple surgeons, all HALDN operations were done by one single surgeon (P.F.). The technique of open donor nephrectomy has been described in detail by multiple authors and is now considered as standardized. For the HALDN procedure, after extensive expla-

Table 2. Primary and late graft function and biochemical markers of glomerular filtration rate 1 year posttransplantation

	HALDN	ODN	p
Number of patients	35	37	NA
Graft function, %			
Primary graft function	97.1	97.3	0.21
One-year posttransplant graft function	94.1	91.6	0.05
Biochemical marker of GFR, mean ± SD			
S-Crea, 1 year posttransplant, μmol/l	154 ± 55.4	147 ± 45.9	0.08
S-Cyst C, 1 year posttransplant, mg/l	1.91 ± 0.74	1.56 ± 0.49	0.06

S-Crea = Serum creatinine; S-Cyst C = serum cystatin C.

nation of the operative risks and preparation of the patients and after inquiries to Eurotransplant regarding potential kidneys becoming available for the recipient, both donor and recipient are taken into the operating theatre. The donor is placed in the right or left flank position, supported by adequate padding. The abdominal cavity is explored using a five-port transperitoneal approach (an 11-mm umbilical port for the laparoscope, one 5-mm port for liver retraction, and two 5-mm trocars and one 10-mm trocar as working ports). After creation of the pneumoperitoneum by insertion of a Veress needle through an incision above the umbilicus, a 10-mm trocar is placed for camera insertion. Thereafter, four additional working trocars are introduced. The insufflation pressure is maximally 12 mm Hg. Depending on the side from which the kidney is to be removed, the peritoneum is opened laterocolically and the colon mobilized medially. This maneuver is followed by inspection and subsequent depiction of the psoas muscle and the ureter. Preparation follows along the ureter and the adnexal vessels to the renal hilum, where the vessels were identified. After complete exposure of the kidney and vessels with ligation of the side branches of the renal vein, the vena cava and the abdominal aorta are isolated. Thereafter, the hand port (Omniport®; Advanced Surgical Concepts Ltd., Dublin, Ireland) is placed via a lower abdominal median laparotomy. The vessels are further prepared under digital control, and after intravenous administration of heparin, the ureter is cut between two clips at the transition to the pelvis minor. The renal artery is double ligated with 'hem-o-lok' clips, and cut, with two clips set proximal to the aorta. The vein is closed by a row of Endo-TA staples. Immediately after extirpation of the kidney, perfusion with HTK solution is carried out. The recipient was being prepared simultaneously in the neighboring operating theatre. This results in a reduction of the cold ischemia time to less than 30 min.

Parameters

Primary and late function of the transplant grafts were evaluated by reviewing the patient's clinical records. Primary graft function was those cases classified, where after the transplantation no dialysis was required, this meaning an absence of delayed graft function (DGF) on postoperative days 1 through 7. To determine the late function 12 months after the transplantation, we evaluated whether and how many transplant grafts have lost their function within this year. The renal parameters serum creatinine (S-Crea) and serum cystatin C (S-Cyst C) of both groups at 12 months postoperatively were compared. S-Crea was measured using the Jaffe method (Beckmann Coulter), and S-Cyst C was measured using immunonephelometric technique (Dade, Behring, G). As a more specific biochemical marker for assessing the GFR, we chose the serum cystatin C. It is a low-molecular-weight protein (13 kDa) produced by nearly all eukaryotic cells. Its synthesis occurs on a constant rate which makes it quite suitable for assessment of GFR even in the so-called 'creatinine-blind' range [25].

Statistical Analysis

The data are presented as mean (± SD). Statistical analysis was performed using Graphpad Instat 3 (GraphPad Software Inc., Calif., USA). Comparisons between the groups was performed using the unpaired t test (Mann-Whitney, CI = 95%). In all calculations, $p < 0.05$ was considered significant.

Results

The demographic data of patients of both groups are listed in table 1. Patients of both groups were comparable regarding the number, age, and immunosuppression regimen.

Primary Graft Function

When comparing the rate of primary graft function, no significant difference was observed between the recipients of the open-surgical and laparoscopic hand-assisted harvested live-donated organs (table 2).

Late Graft Function

In the open donor nephrectomy group, data of 36 transplant graft recipients were analyzed. Of these, 33 transplants functioned well at the end of the first year. Of the remaining 3 recipients, 1 transplant has lost function because of recurrent rejections, 1 patient died within the 1st year after transplantation, and 1 graft had to be removed shortly after the transplantation due to acute rejection. In

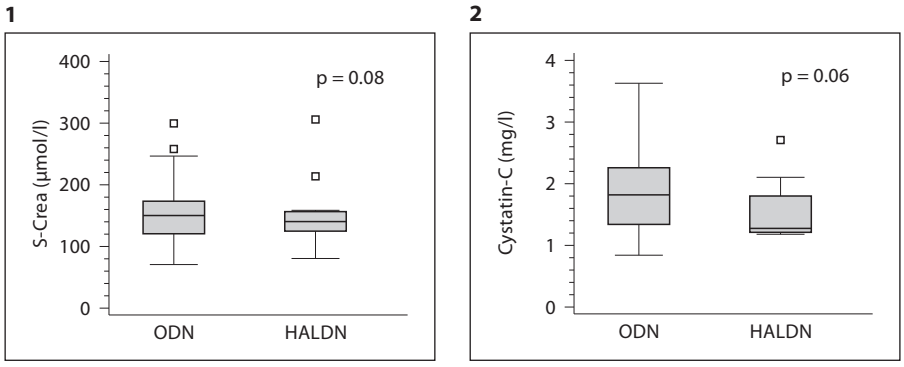

Fig. 1. Serum creatinine (S-Crea) 1 year after transplantation in recipients of ODN and HALDN.

Fig. 2. Serum cystatin-C 1 year after transplantation in recipients of ODN and HALDN.

the laparoscopic donor nephrectomy group, data of 34 transplant graft recipients were analyzed 1 year after the transplantation. However, during the same period of 1 year 1 graft has lost its function due to chronic rejection, whereas 1 patient died during this period (table 2). Furthermore, both parameters of the glomerular filtration rate for the characterization of renal function, S-Crea and S-Cyst C showed no statistically significant difference between the groups 1 year after transplantation (table 2; fig. 1, 2).

Discussion

Renal transplantation is lifesaving for patients with end-stage renal failure. One method to address the growing shortage of organs for kidney transplantation is the use of living kidney donors. Although open-donor nephrectomy can be performed safely in selected candidates, lengthy hospital stay, convalescence, postoperative pain, and poor cosmesis face the donor [12]. In Europe, living donor transplantation accounts for 15–30% of all kidney transplantations [13]. In the United States, living kidney donors outnumber cadaveric kidney donors [14]. Nevertheless, living donor nephrectomy is a unique surgical challenge, since the surgery is performed on a healthy individual.

The use of laparoscopy was one of the most important steps in the progress of medicine in the 20th century. Laparoscopic radical nephrectomy is now considered as the new gold standard surgical treatment for benign renal masses as well as localized renal cell carcinoma [15, 16]. Laparoscopic donor nephrectomy (LDN), first described by Ratner et al. [17], offers less postoperative pain, a quicker convalescence, and a better cosmetic result than open nephrectomy (ODN), thus, possibly increasing the number of renal donors [17, 18]. Although retrospective studies comparing laparoscopic donor nephrectomy (LDN) to conventional nephrectomy suggest similar graft function 1 year after transplantation, it has been shown that recipients of laparoscopically procured kidneys have higher creatinine levels and a greater need for dialysis in the first weeks posttransplantation [19]. Mechanical injury of the graft due to atraumatic handling, longer warm ischemia time caused by more time-consuming extraction, and renal ischemia due to pneumoperitoneum have been suggested to cause early graft dysfunction. Clinical and experimental studies have shown that during laparoscopic procedures, increased intra-abdominal pressure can cause transient renal dysfunction (oliguria) due to impaired renal blood flow, caused by compression of both renal parenchyma and renal vessels [20].

Many lessons have thus been learned from the initial experiences with LDN, which has resulted in the introduction of technical modifications of the original procedure with the sole purpose of making the procedure safer. For instance, HALDN was introduced in 1998 by Wolf et al. [10] to minimize the disadvantages of LDN, including a steep learning curve of this advanced laparoscopic procedure, longer warm ischemia time, and an increased operative time. A shorter learning curve seems to arise from the return of tactile feedback [22]. Even though HALDN has additional costs related to the sleeve, we think the presence of the surgeon's hand in the abdomen contributed to our 0% conversion rate. Third, warm ischemia times as reported for HALDN are significantly shorter than for the completely laparoscopic technique. In our series, the warm ischemia time was 87 s (63–150 s), which is quite low compared to the reported warm ischemia times for the conventional laparoscopic technique.

A commonly cited disincentive to offering donors the option of laparoscopic kidney procurement is – as already mentioned – concern about the graft quality. In this report, we compared early renal function (as determined by recipient serum creatinine and urine output) between

our HALDN and open donor groups, and found them to be similar. This differs from results reported by others for kidneys that were removed completely laparoscopically, whose early renal function (as determined by recipient serum creatinine) was significantly worse during the first week posttransplant than that of kidneys from open nephrectomies [23]. Other studies have noted no difference in the incidence of DGF when comparing the open technique with either HALN or completely laparoscopic techniques, but in those studies, recipient serum creatinine was not critically evaluated [24].

A delayed kidney graft function is a consequence of acute tubular necrosis (ATN) due to prolonged ischemia/reperfusion injury during handling and implantation of donated graft. However, in our series both early and delayed graft functions were comparable in both the ODN and the HALDN groups, suggesting no further aggravation of ischemia/reperfusion injury of the donated organ by the hand-assisted laparoscopic technique. To evaluate renal function parameters, we used serum creatinine and serum cystatin C. The latter reflects more exactly the glomerular filtration rate (GFR), since creatinine is subject to large interindividual variations. In addition, changes in kidney function results in clinically measurable increase in the serum creatinine, if at least 50% of nephron apparatus are damaged. As a more specific biochemical marker for assessing the GFR, we therefore chose the serum cystatin C. In our study, the rate of late graft function as measured by glomerular filtration rate 1 year after transplantation was not significantly different in recipients of open or laparoscopically hand-assisted harvested organs. Further, our data on early and late graft function in HALDN suggest that the clinical impact of the much-discussed possible impairment of kidney function by CO_2 pneumoperitoneum due to an increase in intra-abdominal pressure with reduction of renal blood flow is questionable. A parallel study on the impact of the operation technique, in particular laparoscopically hand-assisted versus open donor nephrectomy, on the function of the donor's remaining kidney at our center has revealed that up to one year after the procedures no significant difference in the glomerular filtration rates between the two groups was shown [4]. However, the present study has some limitations, which need to be kept in mind. First, the retrospective nature of the study, comparing two nonrandomized groups, needs to be mentioned. Second, in both groups, there is a relatively small sample size of the study population, actually due to the fact that we had to match the HALDN patients with a historical group of ODN patients.

Conclusions

Hand-assisted LDN has proven in this series to be as safe and effective as open DN while preserving the benefits of minimally invasive surgery. Major point of criticism against the use of laparoscopic surgical techniques is the fear that extended warm ischemia time and the CO_2 pneumoperitoneum could harm the donor organ with subsequent negative impact on the recipient's primary and late graft function. Consistent with previous reports, no difference in parameters of graft function up to 1 year after the operation could be observed between the open and laparoscopically hand-assisted procured living donor kidneys.

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