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Efficacy and Safety of Hand-assisted Laparoscopic Nephrectomy in Living-donor Transplantation

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Abstract

Introduction : Recently, some 1,500 living-donor kidney transplantations have been performed per year in Japan. Meanwhile, the number of kidney transplantation cases involving brain-dead donors has increased to approximately 60 cases annually. In addition to eliminating the long waiting period associated with deceased-donor organ transplantation, living-donor organ transplantation prevents ischemia. Laparoscopic nephrectomy is technically more difficult to perform in living than in deceased donors. Hand-assisted laparoscopic donor nephrectomy (HALDN), however, is safe and effective.

Methods : Using healthy donors aged between 20 and 70 years, 100 HALDNs were performed at this institute between July 2003 and December 2011. Patient outcomes in this group were compared with those of 15 open donor nephrectomies (ODNs) performed between January 1995 and June 2003.

Results : Hand-assisted laparoscopic donor nephrectomy was successful in all 100 patients, and no patient required conversion to laparotomy. Estimated blood loss was 43.4 g, which was significantly lower than that with ODN (426.5±247.6 g ; $P<0.001$), and no patient required blood transfusion. Mean operating time was 188.4 and 228.4 min ($P<0.01$) and postoperative hospitalization period 7.9 and 13.0 days ($P<0.001$) with HALDN and ODN, respectively.

Conclusions : These results indicate that HALDN is superior to ODN in terms of operating time, blood loss, postoperative hospitalization, recovery period, and donor satisfaction. However, the procedure is technically demanding and should be performed only by surgeons with advanced laparoscopic skills. Based on the present findings, HALDN may be considered as safe and, hopefully, will increase the living donor pool at our center.

Introduction

Living-donor differs from cadaveric organ transplantation in that it requires consideration of the well-being of the donor in addition to that of the recipient. Laparoscopic living-donor nephrectomy, in particular, requires consideration from the perspective of the donor[1-3]. At the time of writing, more than 1,500 living-donor kidney transplantations are performed annually in Japan. The number of organ transplantation cases involving brain-dead donors has increased to approximately 60 per year, making a total of 331 cases by July 2015, since the law on organ transplantation in Japan was revised in July 2010, allowing brain death to be considered as indicating death. Laparoscopic live-donor nephrectomy, however, is technically more difficult to perform, and requires a steeper learning curve[4].

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Key words : Kidney transplantation, Live-donor nephrectomy, Hand-assisted laparoscopic surgery, Outcome

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Methods

The present study was conducted in accordance with the guidelines of the Declaration of Helsinki. Between July 2003 and December 2011, 100 hand-assisted laparoscopic donor nephrectomies (HALDNs) were performed at the Tokyo Medical University Hachioji Medical Center[4]. In the present retrospective study, patient outcomes were compared between these HALDNs and 15 open nephrectomies (ODNs) performed between 1995 and June 2003. Healthy volunteers aged between 20 and 70 years were selected. The procedures were performed by 3 surgeons. An instructor supervised the first 20 procedures, after which the 3 surgeons performed the procedures independently. The HALDN donors were screened according to the living-donor selection criteria established in Japan, which include the following : a healthy adult who is a relative within 6 degrees ; a spouse or a relative-in-law within 3 degrees of the recipient ; and a glomerular filtration rate higher than 70 mL/(min·1.73 m^2), as determined by a 24-hr creatinine clearance test. Warm ischemia time (WIT) was defined as the time elapsed from clamping the renal arteries of the graft to starting cold reperfusion. Total ischemia time (TIT) was defined as the time elapsed from warm ischemia to starting reperfusion in the recipient's body. Delayed graft function (DGF) was defined as the need for hemodialysis within 1 week after transplantation. Immediate function time was defined as the time from reperfusion to recovery of renal function. The details of the HALDN techniques used in this study were previously described[4-7]. The donor was placed in a flexed, lateral decubitus position. The initial surgical field consisted of two 12-mm laparoscopic ports ; one hand port device was used. A 50-mm midline incision was made in the periumbilical area and the hand port device inserted through the abdominal incision. A 12-mm Hg pneumoperitoneum was established through a 12-mm port. The operating surgeon held the hand port device with his left hand. A flexible endoscope was inserted through the superior port, and the inferior port was used as the operative port. Ultrasonic scissors were used throughout the procedure. The HALDN was commenced with mobilization of the left colon and cutting of Gerota's fascia to the level of the upper pole of the kidney. The pure laparoscopic and HALDN (hybrid) techniques were used ; that is, the hand port device was inserted, after which a 12-mm port was inserted through the hand port for mobilization of kidney vessels. Thereafter, the surgeon switched to the hand-assisted method. The kidney was then shelled out of the envelope of Gerota's fascia. The ureter was separated from the psoas muscle and dissected free from a point below the lower pole of the kidney to the pelvic inlet.

After dissecting the surface of the kidney and separating the ureter, the renal vein was exposed by tracing the gonadal vein in a cephalad direction and completely clearing investing tissue by cutting the lumbar vein. The ureter was divided cephalad to the triple clips. An endostapling device (Multifire Endo GIA™ 30 Universal Stapling System, Covidien, USA) was applied to the renal artery and renal vein. A Multifire Endo TA™ 30 Universal Stapling System (Covidien) was used for multiple arteries.

As a standard procedure, the gonadal, lumbar, and adrenal branches were divided beforehand with clips or ultrasonic scissors. The kidney was removed by hand through the hand port device. After irrigation and inspection for bleeding around the surgical sites, the wounds of the port sites were closed, with all fasciae sutured using a GraNee needle (R-Med Disposable Endoscopic Hand Instruments, USA).

Analyses were performed based on operator, operation duration, and learning curve.

Statistical Analysis

All data are expressed as group means plus standard deviations. The Mann-Whitney U-test was used to compare parametric data. The prevalence of graft survival was evaluated using Kaplan-Meier plots. Values of $P<0.05$ were considered statistically significant.

Results

Hand-assisted laparoscopic donor nephrectomy was successfully performed in all the 100 patients, with no patient requiring conversion to laparotomy. The donors' characteristics are presented in Table 1. The mean donor age was 52.7±11.9 years (range, 24-79 years) in the HALDN group and 50.5±14.5 (range, 20-69) in the ODN group. The mean body mass index (BMI) was 22.8±0.69 kg/m^2 (range, 15.5-35.8 kg/m^2) in the HALDN group and 23.1±2.8 kg/m^2 (range 15.5-35.8 kg/m^2) in the ODN group. Among the patients in the HALDN and ODN groups, 28 (28%) and 3 (20%), respectively, had a BMI of higher than 25 kg/m^2. A total of 3 (3%) nephrectomies were right-sided. The primary preoperative indications for right nephrectomy were significantly different from those for left nephrectomy. Multiple renal arteries were detected in 17 grafts (17%). In 3 donors, an exit wound was made on the site of a previous abdominal incision. The preoperative mean serum creatinine (s-Cr) level of the donors was 0.72±0.16 mg/dl (0.4-1.2), while the serum creatinine clearance was 102.4±20.3 ml/min (71-179.3).

Operative data and postoperative results are presented in Table 2. The estimated blood loss was 45.3±61.2 g in the HALDN group ; hence, no patient required blood transfusion. In comparison, the estimated blood loss in

Table 1 Donor characteristics

	HALDN (*n*=100)	OPN (*n*=15)
Historical	2003-2011	1993-2002
Total number	100	15
Age (Mean±SD) (range)	52.7±11.9 (24-79)	50.5±14.5 (20-69)
Sex (male/female)	48/52	6/9
Relative (Yes/No)	63/37	15/0
BMI (Mean±SD) (range)	22.8±3.9 (15.5-35.8)	23.1±2.8 (18.4-27.5)
Harvested side (Lt/Rt)	97/3	11/4
Serum-Creatinine (Mean±SD)	0.72±0.16 (0.4-1.2)	0.76±0.11 (0.5-0.9)
Twenty-four-hour creatinine clearance	10.2.4±20.3 (71-179.3)	106.0±16.9 (77-127.3)
ABO incompatible	29 (29%)	2 (13.3%)
Multiple renal arteries	83/17	13/2
Previous surgical history	Myoma (1) Cholecystectomy (1) C-section (1)	No

Table 2 Operative data and postoperative results

	HALDN (*n*=100)	ODN (*n*=15)	*P*-value
Blood loss (g)	45.3 ± 61.2	426.5 ± 247.6	<0.001
Operation time (min)	189±55.5	228.4 ± 35.7	<0.01
Nephrectomy (min)	149±41.6	152.6 ± 24.7	NS
WIT (min)	4.4 ± 2.5	1.5 ± 0.8	<0.001
TIT (min)	99.9 ± 49.5	60.5 ± 20.6	<0.05
Graft size (g)	172.4 ± 39.0	196.7 ± 62.5	NS
Immediate function (min)	11.1 ± 8.1	8.0 ± 4.2	NS
Delayed graft function (number)	10 (10%)	3 (20%)	NS
Postoperative hospital stay (day)	7.9 ± 3.1	13 ± 1.9	<0.001
Total hospital stay (day)	11.5 ± 4.6	26.9 ± 6.9	<0.001
Blood transfusion (number)	No	2	-
Open conversion	No	-	-

the ODN group was 426.5±247.6 g (P<0.001), requiring blood transfusion in 2 patients. The mean operating times were 189±55.5 and 228.4±35.7 min in the HALDN and ODN groups, respectively (P<0.01). However, the times until nephrectomy were not significantly different between the two groups.

The WIT and TIT in the HALDN group were significantly longer than those in the ODN group, although both times in the two groups were considered acceptable. The postoperative hospitalization period was 7.9 days in the HALDN group and 13.0 days in the ODN group (P<0.001). Of the 100 patients who underwent HALDN, 7 (7.0%) had perioperative complications (Table 3), 5 (71.5%) of which were considered as Grade 1 according to the modified Clavien grading system. Nevertheless, no mortality was encountered. Reoperation was performed in 2 patients with Grade 3b complications who developed hand port hernia requiring primary closure.

Table 3 Postoperative complications according to modified Clavien grading system

Grade 1		Management
✓ Wound infection	2	Antibiotics
✓ Sub-ileus	2	Nothing per os and infusion
✓ Rhabdomyolysis	1	Cessation of statin
Grade 3b		
✓ Hand-port hernia	2	Hernioplasty
✓ Total	7 (7%)	

The relationship between operator and operation duration, that is, the learning curve, was also investigated (Fig. 1). No significant difference was observed between operators.

Recipient outcomes between HALDN and ODN were

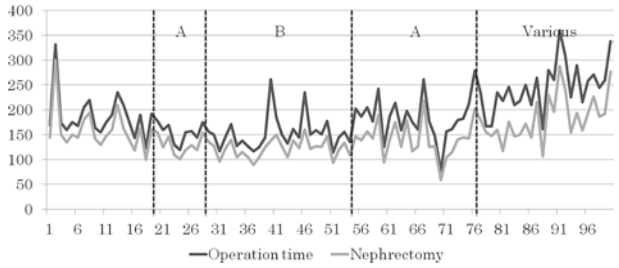

Fig. 1 Line plot on operating time and time until nephrectomy.

examined. No significant difference was observed in immediate function time between the two groups (HALDN vs. ODN group, 11.1±8.1 min vs. 8.0±4.2 min). A DGF was observed in 10% (10/100) and 20% (3/15) of the HALDN and ODN groups, respectively, with no significant difference between the two groups. Primary non-function occurred in only 1 patient (1%) because of hyperacute rejection due to inadequate blood reperfusion. The mean s-Cr levels of the recipients at 1 and 6 months were 1.06 mg/dL and 1.04 mg/dL, respectively, while those at 1 and 2 years after transplantation were 1.03 mg/dL and 1.01 mg/dL, respectively. The 1-, 3-, and 5-year actual recipient graft survival and patient survival rates were 92.7%, 91.1%, and 91.1%, and 93.7%,92.2%, and 92.2%, respectively.

Discussion

Approximately 1,500 living-donor kidney transplantations are performed every year in Japan. Approximately 80% of all medical facilities in Japan perform laparoscopic surgery[8]. Preoperative assessment of the safety of living-donor HALDN and donor selection are performed according to the guidelines established by the Amsterdam Forum on the Care of the Live Kidney Donors, its social acceptability, and the ethical guidelines of the Japan Society for Transplantation[9]. In the present study, we report our experience with 100 cases of HALDN performed between 2003 and 2011 at our center. Patient outcomes were compared between these cases of HALDN and those of 15 ODNs performed between January 1995 and June 2003. The difference in number of patients here is large. This was because only 10 living donor renal transplantations were performed at this center over the 3 years prior to the introduction of HALDN. Over the first 9 years following the introduction of HALDN in 2003, the number of living donors tripled. We believe that this increase was due to the fact that HALDN reduces the burden on the donor. In the present study, the first 20 HALDN procedures were performed under the supervision of an instructor in 54 patients. Subsequent procedures were then performed independently by each surgeon. The reductions in blood loss, operative time, and length of hospital stay were marked, with a significant difference between the two groups. Significant differences in the increases in WIT and TIT were observed. A DGF was observed in 10 patients. Delayed graft function is a consequence of acute tubular necrosis due to prolonged ischemia/reperfusion injury during handling and implantation of the donated graft[10]. In the present series, both immediate and DGF were comparable between the HALDN and ODN groups. Dialysis was indicated based on a reduction in the amount of urine ; early recovery of renal function was observed in 7 patients during the follow-up period (until 2010). No DGF has been observed since the start of postoperative rehydration in 2011.

In addition to obstruction due to incarceration of the small intestine in the trocar port, suturing the peritoneum using a fine GraNee needle or Cartor-Thomason closure system (Harada Corporation), held with suturing forceps, may also have been responsible for the decreasing amount of drained blood observed in transplant recipients since 2010.

Postoperative management was introduced in 2007 according to the clinical course of the recipients. Recipient outcomes varied as there were cases of abdominal distension due to postoperative delayed bowel peristalsis and defecation disorders, for which oral antibiotics were administered pre- and postoperatively, resulting in relief of symptoms. One donor developed diabetes 3 years postoperatively and underwent medical treatment while discontinuing dialysis temporarily. In Europe and the United States, the incidence rates of postoperative chronic kidney disease (CKD) and end-stage renal disease (ESRD) after donor nephrectomy are 12% and 0.04-0.5%, respectively, based on a long-term prognosis study. In a donor study in Japan, 94% of postoperative CKD cases were classified as stage 3. At our center, approximately 80% were classified as stage 3 CKD. Recently, the development of renal dysfunction or CKD, even among low-risk kidney donors, has been considered a risk factor for developing diabetes and cardiovascular disease, especially in older donors. Donors are provided with monthly routine follow-up examinations at our center, which are then reduced to annual follow-up visits in an outpatient setting. Postoperative multidisciplinary follow-up examinations are performed at 1, 3, 6, and 12 months, or once a year by a transplant surgeon or nephrologist. None of the present series of patients at our center developed ESRD.

Not all the data for the factors influencing the learning curve were obtained for Dr. A, as shown in Figure 1. The number of transplantations performed per year at 10 transplant centers, in particular, was difficult to obtain. Since 2011, preoperative radiological evaluation of a donor's anatomy, including the renal, lumbar, and gonadal veins, has become part of the standard trans-

plantation procedure at our center, as these anatomical areas have great impact on preventing bleeding and reducing operative time.

Originally, the purpose of hand-assisted laparoscopic surgery was to avoid or deal promptly with unexpected heavy bleeding[11-14]. It is considered relatively safe, with only an acceptable amount of bleeding occurring in the cases we have encountered so far at our center. One of the limitations of laparoscopic surgery is that it only allows a limited field of view. This suggests the need to further improve the safety of hemostasis techniques, which would enable surgeons to perform such surgery under direct vision. The present results revealed that the standard procedures involved in HALDN led to a reduction in the amount of bleeding and operative time between surgeons compared with ODN. Hand-assisted manipulation of the organ yields a protective effect and reduces operation time. No difference was observed in the rate of complications. The recent increase in the number of patients undergoing HALDN at our facility has provided an advantage in terms of learning this procedure. Making sure that a minimum level of competency has been achieved before allowing the surgeon to perform HALDN alone has increased safety and efficacy. Skilled and careful excision of the donor kidney has reduced the incidence of intraoperative complications such as bleeding.

Showing better results in terms of blood loss, analgesic requirement, length of hospital stay, convalescence, and cosmesis, HALDN continues to offer a strong alternative to ODN. Recently, single-incision laparoscopic surgery has been introduced and is believed to offer a cosmetic advantage. Assuming that safety is assured, reduction of pain must be a future goal. However, further data on a greater number of kidney transplants is necessary to determine the optimum approach. Work is being done to further ensure the safety of the clinical path and competency in both surgeon and assistants, and to alleviate pain. Compared to with before its introduction, the establishment of HALDN should contribute to further expanding the pool of potential donors.

Overall, donor satisfaction was better in the HALDN group than in the ODN group[15]. Based on our findings, HALDN may be considered a safe procedure, making it more appealing to potential living kidney donors, which will, hopefully, increase the living donor pool at our center.

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生体腎ドナー手術における腹腔鏡下腎採取術の有用性

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【要旨】【緒言】2010 年 7 月に改正臓器移植法が施行され、脳死下臓器提供件数は増加傾向にある。しかし、わが国はドナー不足が慢性化しており、移植件数の殆どを生体臓器移植により賄われている。今回、われわれは当施設におけるドナー腎採取術における安全性を各因子に分類し検討した。

【対象】2003 年 7 月に生体腎ドナー手術対して腹腔鏡補助下用手的腎採取術（Hand-assisted laparoscopic donor nephrectomy ; HALDNx）を導入し、2011 年 12 月までに 100 例の生体ドナー腎採取術を施行した、それ以前の従来方の開腹腎採取術 15 例と比較した。

【方法】術前評価、手術側の因子として出血量、手術時間、摘出時間、合併症発生率、ドナーの腎提供前後の腎機能、レシピエントの移植後腎機能。生着率、生存率について検討した。

また、ドナーチームのメンバーを指導者、術者 2 名の出血量、手術時間、摘出時間それぞれについて検討を加え Learning curve の有無を検討した。

【結果】HALDN 群は平均年齢 52.7±11.9 歳、ODN 群は 50.5±14.5。男 48 例、女 52 例。左 97 例、右 3 例。平均手術時間は 189±55.5 分、腎摘出までの時間は平均 149±41.6 分。HALDN 群の出血量の平均は 45.3±61.2 g、ODN 群に比して有意に減少している。輸血症例や､開腹への移行症例は認めなかった。初尿時間は平均 11.1±8.1 分。10 例（10%）に遅発性腎機能発現を認めた。複数動脈を 17 例に認めた。合併症は創部感染 2 例。正中創ヘルニア 2 例（修復術）、横紋筋融解症 1 例であった。術後はドナーのサーベイランスを行い、現在までドナーは全例社会復帰している。移植腎機能は 1 ヵ月、6 ヵ月、1 年、2 年で 1.06 mg/dl、1.04 mg/dl、1.03 mg/dl、1.01 mg/dl と経過している。生着率は 92.7%（1 年）、91.1%（3 年）、91.1%（5 年）、生存率は 93.7%（1 年）、92.2%（3 年）、92.2%（5 年）であった。

【考察】日本において 1,000 例の生体腎移植が行われている。そのうち腹腔鏡手術が 70% 占めている。生体腎ドナーの選択にはアムステルダム宣言に則り施行されており、社会的、倫理的に基準を日本移植学会によりガイドラインとして規程されている。2003 年 7 月から生体腎ドナーとして腹腔鏡下腎採取術を 100 例施行した。1995 年から 2003 年の間では 10 例の生体腎移植術を施行したが、腹腔鏡下手術を開始し腎移植数は増加傾向に移行した。腹腔鏡手術導入がドナープール拡大に寄与したと考えている。

〈キーワード〉 腎移植、生体ドナー腎採取術、用手補助的手術、成績