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Hand-Assisted Laparoscopic Living-Donor Nephrectomy Versus Open Surgery: Evaluation of Surgical Trauma and Late Graft Function in 82 Patients

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ABSTRACT

Objective. We evaluated and quantified surgical trauma and late graft function in cases of hand-assisted laparoscopic living-donor nephrectomy (HALLDN) versus open living-donor nephrectom (OLDN).

Methods. This study is a retrospective nonrandomized single-center analysis. Between 1995 and January 2008, 82 patients with end-stage renal disease received kidney transplantations from living donors. Open living-donor nephrectomy was performed in 37 donors, and 45 underwent laparoscopic hand-assisted nephrectomy. Demographic data and perioperative and postoperative data, such as markers of acute phase (C-reactive protein; serum amyloid A) and biochemical markers of glomerular filtration (serum creatinine, serum cystatin C), were compared at serial time points.

Results. The mean operative times for HALLDN and OLDN were 165 min and 195 min, respectively. The average warm ischemia time was 45 seconds for laparoscopy and 87 seconds for open surgery. The evaluation of acute phase markers demonstrated a minimally invasiven nature of laparoscopy, with same late graft function compared with open surgery.

Conclusion. When the surgery was performed by experienced surgeons, hand-assisted living- donor nephrectomy showed shorter operative and warm ischemia times than open surgery, offering at least the same functional results and decreasing surgical complications compared with a completely laparoscopic technique.

ON THE half-century since the first successful procedure, living-donor renal transplantation has shown superiority over cadaveric-donor renal transplantation. Regarding the medical advantages, the evidence is convincing: The cold ischemia time in living-donor nephrectomy is significantly shorter than that of cadaveric-donor kidney transplantation; there is an almost complete absence of ischemic injury to the transplanted kidney, a relative insensitivity to poor tissue matching, and better long-term function.[1]

Since the 1990s, laparoscopy has represented an important development in urology as well as in other surgical areas. Because laparoscopy is generally less invasive than open surgical techniques, it may be preferable if it can be demonstrated to achieve the same results and patient, safety with less operative trauma. Nevertheless, this difference remains the object of debate.

In the present study, we sought to evaluate differences in the hand-assisted laparoscopic technique versus the open technique for living-donor nephrectomy. After the technique had been developed in an animal model, in 1995, Ratner demonstrated the feasibility of laparoscopic living-donor renal-transplant nephrectomy in a 40-year-old man. Thereafter, the technique advanced to become an accepted method of transplantation.[1] At present, more than 200 centers worldwide perform laparoscopic living-donor ne-

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phrectomy; more than 10,000 kidneys have been retrieved from living donors with this approach.[2]

We sought to quantify surgical trauma in hand-assisted laparoscopic living-donor nephrectomy and in open living-donor nephrectomy.

MATERIALS AND METHODS

This study was a retrospective nonrandomized single-center analysis. From 1995 to January 2008, 82 kidneys from live donors (relatives, partners) were transplanted at our center. Until 2003, 37 kidneys were removed using a conventional open technique. From 2004, the remaining 45 donors underwent laparoscopic hand-assisted donor nephrectomy. Preoperatively, all the patients underwent intravenous urography (IVU), renal scintigraphy, and digital subtraction angiography (DSA). The immunosuppressive protocol was standardized in all patients, consisting of acrolimus, methylprednisolone, and mycosh enolate-mofetil[3]. Patients with a particular immunological risk also received antithymocyte globulin (ATG) or the IL-2R inhibitor basiliximab for induction therapy. We compared demographic data (age, gender) as well as perioperative and postoperative data, including operative time, estimated blood loss, complications, length of hospital stay, analgesic requirement, and markers of systemic reaction and renal function. We measured acute phase markers (CRP: C-reactive protein; SAA: serum amyloid A) as well as biochemical markers of glomerular filtration (serum creatinine and serum cystatin C) at serial pre-, intra-, and postoperative times. The renal parameters serum creatinine (S-Crea) and serum cystatin C (S-Cyst C) of both groups were compared at 12 months postoperative S-Crea was measured using the Jaffe method (Beckmann Coulter) and S-Cyst C, using an immunonephe lometric technique (Dade Behring).

Technique of Hand-Assisted Laparoscopic Living-Donor Nephrectomy

After induction of general anesthesia, a nasogastric tube and a transurethral catheter were placed to decompress the stomach and bladder. The patient was secured to the operating table in a semiflank position. A transperitoneal approach was used in all patients. A Veress needle was inserted periumbilically to establish pneumoperitoneum by injection of carbon dioxide. With an initial intra-abdominal pressure of 12 to 15 mm Hg, a 12-mm trocar was placed above the umbilicus after removal of the Veress needle.

The endoscopic 0° camera was introduced for inspection of the abdominal cavity. Thereafter, three additional trocars were inserted under direct vision: two 12-mm trocars in the ipsilateral midclavicular line, and a 10-mm trocar just below the xiphoid process. Occasionally, a fourth trocar (5 mm) was used in the anterior axillary line below the umbilicus. Then the intra-abdominal pressure was lowered to 10–12 mm Hg at which it was maintained.

The peritoneum was incised along the line of Toldt using electrosurgical scissors and grasping forceps. The colon was mobilized and retracted medially. The ureter was identified above the iliac vessels crossing to expose renal hilum. When the kidney was totally mobilized, an extended skin incision between the working trocars was performed. In this way, the surgeon could introduce his hand into the retroperitoneal space without losing the pneumoperitoneum.

After clamping the ureter above its iliac vessel crossover, a bolus of heparin (150 U/kg) was given to the patient, to reduce the risk of intravenous thrombosis during the ischemic phase. Dissection of the remaining fat and connective tissue was continued for complete mobilization of the kidney. Subsequently, the renal artery and vein were secured with a vascular stapler. The renal vein was dissected first, followed by the renal artery, thus achieving a longer perfusion of the kidney and reducing the warm ischemia time. The extracted kidney was immediately perfused with histzdine-tryptophane-ketoglutarate solution (HTK) before transplantation. Then the patient was reversed with prothrombin.

Statistical Analysis

The data are shown as mean values ± standard deviations. The statistical analysis was performed using Graphpad Instat 3 (GraphPad Software, CA, USA). Comparisons between groups were performed using unpaired *t* tests (Mann-Whitney, 95% CI). In all calculations, a P value of $<.05$ was considered to be significant.

RESULTS

Preoperative Data

The mean age of the 45 patients who underwent hand-assisted laparoscopic living-donor nephrectomy was 44 ± 13 years, and the mean age of the 37 patients who underwent open living-donor nephrectomy was 40 ± 14 years (Table 1).

Perioperative Data

The mean operative times for HALLDN and OLDN were 165 min and 195 min, respectively. The average warm ischemia time was 45 seconds for laparoscopy and 87 seconds for open surgery. The hospital stay (4 vs. 7 days) showed a faster recovery among patients in the laparoscopic group (Table 1).

The preoperative and intraoperative serum concentrations of CRP were almost identical in both groups at times of measurement of T0, T1, and T2. At six hours postoperative (time of measurement T3) as well as at 12, 24, and 48 hours postoperative (times of measurement T4, T5, and T6), CRP values averaged 20% to 40% lower in the laparoscopic group than in the open group (Figure 1).

Table 1. Pre-, Intra-, and Postoperative Data ($P < .05$)

	Open Living-Donor Nephrectomy (OLDN)	Hand-Assisted Laparoscopic Living-Donor Nephrectomy (HALLDN)
Number of patients	37	45
Age (y, mean ± SD)	40 ± 14	44 ± 13
Ratio male/female	3.9	3.3
Immunsuppression regimen		
triple	28/37	34/45
triple+1	9/37	11/45
Mean operative time (min)	195 (150–240)	165 (120–210)
Mean estimated blood loss (mL)	110	60
Average time of warm ischemia (s):	87 (61–112)	45 (30–60)
Resumption of oral intake (d)	2.7	1.4
Hospital stay (d)	7	4

At timepoint T2, the intraoperative serum SAA values were lower in the laparoscopic group than the open group, remaining lower subsequently (Figure 2). Regarding renal function, serum markers of glomerular filtration rate in the recipient (S-Crea; Fig. 5) showed an initial relevant reduction at 12 hours postoperative (time of measurement T4), rapidly reducing the values at 24, 48, and 72 hours postoperative (times of measurement T5, T6, and T7). Two weeks after transplantation (time of measurement T8), the creatinine recovered to nadir levels.

Late graft function

In the open donor nephrectomy group, data of 37 transplant graft recipients were analysed. Of these, 31 transplants functioned well at the end of the first year. Of the remaining 6 recipients, 3 transplants never resumed their function, 1 patient died within the 1st year after transplantation for heart disease, 2 grafts had to be removed after the transplantation due to acute rejection. Among the laparoscopic nephrectomy group, we analyzed 45 transplanted recipients at one year. During this period, one graft had lost function and one transplaned graft had never resumed function. Furthermore, one patient died due to non-Hodgkin lymphoma. The other patients lost function owing to humoral reactions. Furthermore, both parameters of glomerular filtration rate that characterize renal function-

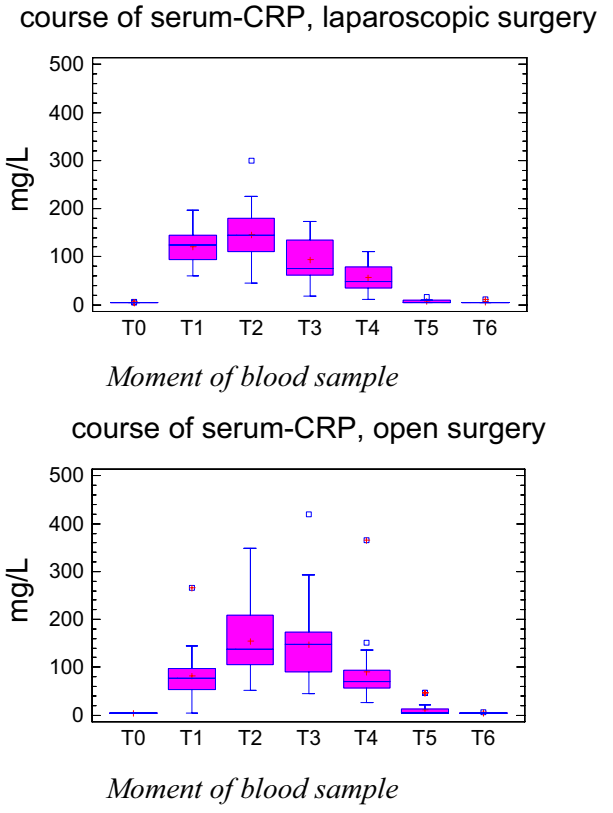

Fig 1. C-Reactive protein (CRP) (mg/L) ($P < .05$).

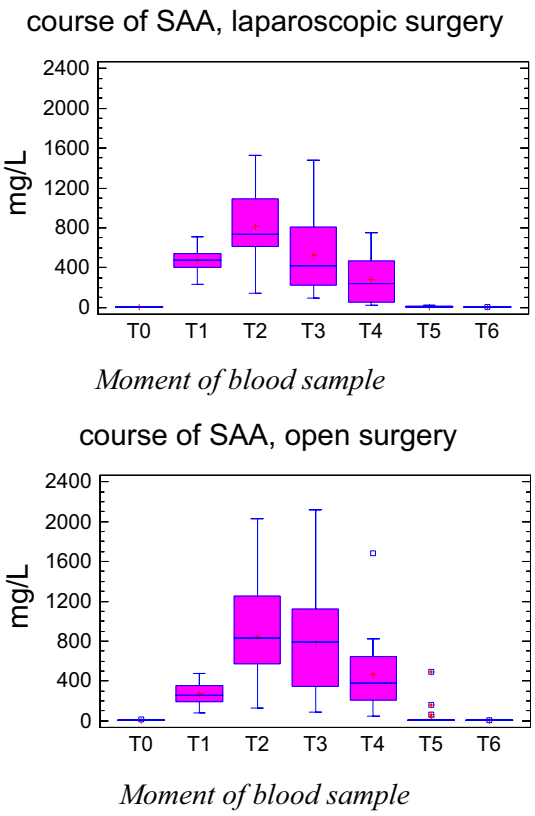

Fig 2. Serum amyloid A (SAA) (mg/L) ($P < .05$).

S-Crea and S-Cyst C-showed no significant difference between the groups at one year after transplantation (Table 2; Figs 3 and 4).

DISCUSSION

Laparoscopic living-donor nephrectomy has revolutionized kidney transplantation. This surgical technique, introduced in 1995, has become an accepted method of kidney harvest for transplantation.[1] Initially, LLDN was met with criticism, because a new method always has to be measured against the "gold standard" of the established surgical approach.[2]

Table 2. Graft Function and Biochemical Markers of Glomerular Filration Rate (GFR) One Year After Transplantation

	OLDN	HALLDN
Graft function		
One-year post transplant graft function	31/37 (83.8%)	42/45 (93%)
Biochemical marker of GFR		
S-Crea (μmol/L, mean ± SD) 1 year post transplant	154 ± 55.4	147 ± 45.9*
S-Cyst C (mg/L, mean ± SD) 1 year post transplant	1.91 ± 0.74	1.56 ± 0.49*

S-Crea, serum creatinine (μmol/L); S-Cyst C, serum cystatin C (mg/L).
*$P = .05$.

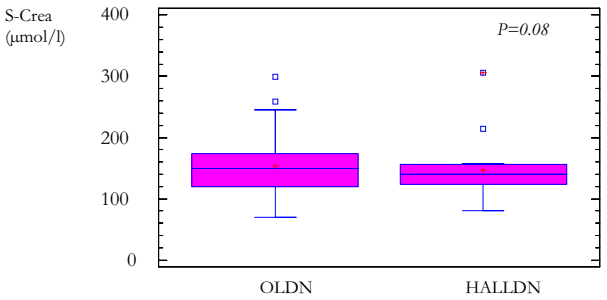

Fig 3. Serum creatinine (S-Crea) one year after transplantation in recipients of open (OLDN) and hand-assisted laparoscopic living-donor nephrectomy (HALLDN).

Increased warm ischemia times of 3 to 5 minutes after LLDN were the main point of criticism.[3] The increased warm ischemia time associated with laparoscopy was criticized because it may predispose to rejection and increase the proportion of delayed graft function. The development of HALLDN reduced the warm ischemia time, making it similar to open nephrectomy.[4] Therefore, our reasons for choosing HALLDN over a completely laparoscopic technique were as follows. First, HALLDN is generally considered to be quicker to perform than the completely laparoscopic approach. Second, HALLDN was safe for all of our donors, none of whom required conversion to the open approach. Even though HALLDN 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 HALLDN were significantly shorter than those for the completely laparoscopic technique.

In the 1990s, when laparoscopic living-donor nephrectomy was established, there was a relatively high complication rate owing to ureteral injuries and loss of organs resulting from the laparoscopic extraction. Such complications have been reduced to a low level after completion of the initial learning curve that accompanies every new surgical technique.[5] Recovery time for patients undergoing laparoscopic surgery was clearly faster and better.

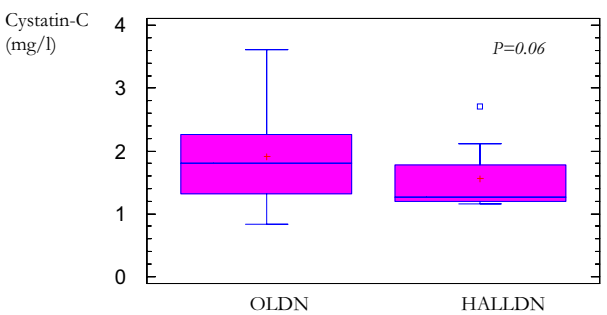

Fig 4. Serum cystatin-C one year after transplantation in recipients of open (OLDN) and hand-assisted laparoscopic living-donor nephrectomy (HALLDN).

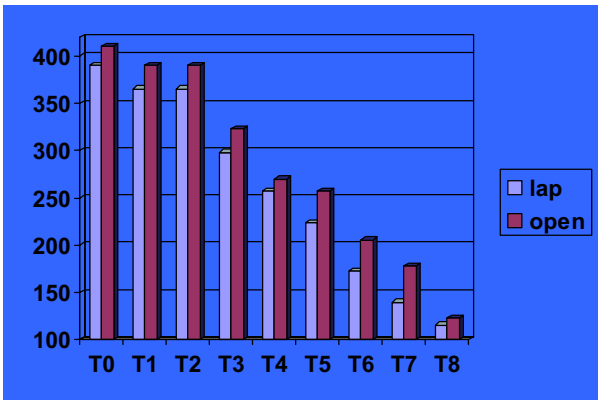

Fig 5. Creatinine (µmol/L) time course in recipient ($P < .05$).

Our results correspond to those in the literature.[3–19] Moreover, they showed that with the use of a hand-assisted technique by an experienced surgeon, we achieved an average warm ischemia time of 45 seconds, confirming advantages for patients undergoing a laparoscopic procedure with reduced operative trauma and a shorter postoperative donor course.[20] We discharged the donors on postoperative day four.

A commonly cited disincentive to offering donors the option of laparoscopic kidney procurement—as already mentioned—concerns the graft quality. In the present report, we compared renal function (as determined by recipient serum creatinine and urine output) between HALLDN and open donor groups. They were similar. Delayed kidney graft function is a consequence of acute tubular necrosis (ATN) due to prolonged ischemia/reperfusion injury during handling and implantation of the donated graft. However, in the present series both rates of delayed graft function were similars suggesting no further aggravation of ischemia/reperfusion injury of donated organ by the hand-assisted laparoscopic technique.

To evaluate renal function parameters, we used serum creatinine and serum cystatin C, the latter more exactly reflecting glomerular filtration rate (GFR), because creatinine is subject to large interindividual variations. In addition, changes in kidney function result in clinically measurable increases in serum creatinine if at least 50% of the nephron apparatus is damaged. Serum cystatin C is a low-molecular-weight protein (13 kD) produced by nearly all eucaryotic cells. In this study, the rate of late graft function as measured by GFR at one year after transplantation was not significantly different between recipients of open versus laparoscopically hand-assisted harvested organs. Furthermore, our data on late graft function in HALLDN suggested that the clinical impact of the much-discussed possible impairment of kidney function due to an increase in intraabdominal pressure by CO2 pneumoperitoneum leading to reduced renal blood flow is questionable.

A parallel study on the impact of the operative technique, in particular, laparoscopic hand-assisted versus open-donor

nephrectomy, on the function of the donor's remaining kidney at our center revealed that up to one year after the procedures, there was no significant difference in the GFRs.[16]

In conclusion, the increasing numbers of terminally ill patients with renal insufficiency in central Europe, the long waiting times for kidney transplants, and the organ shortage together have led to an increased proportion of living-donor nephrectomies.[16]

When the procedure is performed by experienced surgeons, hand-assisted living-donor nephrectomy shows shorter operative and warm ischemia times than open surgery, offering at least the same functional results and decreasing surgical complications compared with a completely laparoscopic technique.[13] The various laboratory measurements obtained from our patient sample showed no disadvantages regarding transplanted kidney function in the recipient.

The reduced hospitalization time results in cost reduction and allows donors to return to work quickly. The explanation of the risks of the procedure to the donor and preparation for the procedure must be optimized. In addition, strict criteria should be established to decide in favor of either laparoscopic or open nephrectomy. A well established kidney transplant center should have mastery of both operative techniques and be able to offer them to patients.

REFERENCES

1. Rettkowski O, Hamza A, Markau S, Osten B, Fornara P: Ten years of laparoscopic living donor nephrectomy: retrospect and prospect from the nephrologist's point of view. Transplant Proc 39:30, 2007

2. Ebeling V, Tuerk I, Deger S, Giessing M, Loening SA: Laparoscopic living donor nephrectomy. Pro and contra. Transplant Link Nierentransplantation, S. 101, 2002

3. Stoffel F, Forster TH, Steiger J, Gasser TC, Sulser T: Hand-assisted laparoscopic living donor nephrectomy. Urologe A 41:258, 2002

4. Kokkinos C, Nanidis T, Antcliffe D, Darzi AW, Tekkis P, Papalois V: Comparison of laparoscopic versus hand-assisted live donor nephrectomy. Transplantation 83:41, 2007

5. Fisher PC, Montgomery JS, Johnston WK, Wolf JS: 200 consecutive hand assisted laparoscopic donor nephrectomies: evolution of operative technique and outcomes. J Urol 175:1439, 2006

6. Oyen O, Andersen M, Mathisen L, et al: Laparoscopic versus open living-donor nephrectomy: experience from a prospective, randomized, single-center study focusing on donor safety. Transplantation 79:1236, 2005

7. Goel MC, Modlin CS, Mottoo AM, et al: Fate of donor kidney: laparoscopic versus open technique. J Urol 172:2326, 2004

8. Fornara P, Doehn C, Seyfarth M, Jocham D: Why is urological laparoscopy minimally invasive? Eur Urol 37:241, 2000

9. Kercher K, Dahl D, Harland R, Blute R, Gallagher K, Litwin D: Hand-assisted laparoscopic donor nephrectomy minimizes warm ischemia. Urology 58:152, 2001

10. Percegona LS, Meyer F, Machado C, Bignelli AT, Riella MC, Santos LS: Hand-assisted laparoscopic nephrectomy in living donors. Transplant Proc 38:1870, 2006

11. Derweesh IH, Goldfarb DA, Abreu SC, et al: Laparoscopic live donor nephrectomy has equivalent early and late renal function outcomes compared with open donor nephrectomy. Urology 65: 862, 2005

12. Giessing M, Deger S, Schoenberger B, Tuerk I, Loening SA: Laparoscopic living donor nephrectomy: from alternative to standard procedure. Transplant Proc 35:2093, 2003

13. Breda A, Veale J, Liao J, Schulam PG: Complications of laparoscopic living donor nephrectomy and their management: the UCLA experience. Urology 69:49, 2007

14. Chin EH, Hazzan D, Herron DM, et al: Laparoscopic donor nephrectomy: intraoperative safety, immediate morbidity, and delayed complications with 500 cases. Surg Endosc 21:521, 2007

15. Bollens R, Mikhaski D, Espinoza BP, et al: Laparoscopic live donor right nephrectomy: a new technique to maximize the length of the renal vein using a modified Endo GIA Stapler. Eur Urol 51:1326, 2007

16. Hamza A, Wagner S, Weigand K, et al: Transperitoneal, hand-assisted laparoscopic donor nephrectomy: surveillance of renal function by immune monitoring. Transplant Proc 40:895, 2008

17. Minnee RC, Bemelman F, Kox C, et al: Comparison of hand-assisted laparoscopic and open donor nephrectomy in living donors. Int J Urol 15:206, 2008

18. Lee KS, Hong JH, Jeon SS, Choi HY, Kim SJ, Lee SW: Comparison of graft survival in live donor nephrectomy: hand-assisted laparoscopic v open procedures. J Endourol. 21:866, 2007

19. Alcaraz A, Rosales A, Guirado L, Díaz JM, Musquera M, Villavicencio H: Early experience of a living donor kidney transplant program. Eur Urol 50:542, 2006

20. Fornara P, Doehn C, Friedrich HJ, Jocham D: Nonrandomized comparison of open flank versus laparoscopic nephrectomy in 249 patients with benign renal disease. Eur Urol 40:24, 2001