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Current concepts in transplant surgery: laparoscopic living donor nephrectomy.

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Abstract

Objective: The basic idea of introducing laparoscopy in living donor nephrectomy was to obtain a potential reduction in incision-related morbidity while providing at least the same level of operative security. This study is focusing on technical aspects, outcome, results and possible current concerns of laparoscopic donor nephrectomy.

Material and Methods: From January 2001 to December 2006, 115 consecutive patients (56 open and 59 laparoscopy) underwent living donor nephrectomy at Siriraj hospital. The open and laparoscopic procedures were compared in the following categories: patient's characteristics, surgical outcomes, warm ischemic time and graft function. Here we review the current evidence for laparoscopic donor nephrectomy available in the literature.

Results: Laparoscopic donor nephrectomy was successfully done in 56 (94.9%) cases. The mean operative times (329±51 vs 220±50 minutes, $p \leq 0.001$) and warm ischemic time (180±74 vs 114±112 seconds, $p \leq 0.001$) were longer in the laparoscopic than in the open group. However, the mean length of hospital stay was significantly shorter in the laparoscopic than the open group (p=0.018). For the graft outcome, there were 6 (10%) vs 5(9%) instances of slow or delayed graft function among the recipients in laparoscopic vs the open group. One year graft survival rates were comparable between the two groups (94.3% vs 98.2% p=0.80).

Conclusion: According to our results and the results available in the literature, laparoscopic living donor nephrectomy is safe when performed with sufficient experience. However large-scale, prospective comparative studies with adequate follow-up will help to define the exact role of this procedure in renal transplantation.

Key words: Laparoscopy, Live donor nephrectomy, safety

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Introduction

Kidney transplantation is considered the definitive treatment for patients with end-stage renal disease. The number of patients awaiting transplantation has in the past for exceed the number of cadaveric organ available. Despite efforts to increase the numbers of decreased donors including acceptance of extended criteria donors, there is an at least persisting if not increasing discrepancy between cadaveric organs available for transplantation. Living donor kidney transplantation (LDKT) has emerged as an excellent alternative to cadaveric donor since the first live donor nephrectomy was successfully performed in 1952[1]. Increased use of living donor nephrectomy in recent years has counteracted the shortage of cadaveric renal donors; in 2001, for the first time, there were more living organ donors in the United States than decreased organ donors (http://www.unos.org). Scandinavian countries have the highest ratio of living donors in Europe. In Thailand, all 29 centers performing kidney transplantation also perfor-med LDKT. In 2007, Siriraj hospital transplant unit performed 51 LDKT, representing 56% (51/90) of all KT. Kidney transplant recipients from living donors have shorter time on dialysis, acceleration of damages to the cardiovascular system is prevented, and overall health-related quality of life is improved, when compared to recipients from deceased donors. Although advances in understanding transplant immunology and the development of new drugs have improved patient and graft survival, live donation remains the single most consistent factor affecting long-term survival. Living donor nephrectomy is a unique operative situation in which a healthy indivi-dual puts him or herself at risk of having a major operation to aid a sick person. When performed by conventional open incision, living donor nephrectomy is, from the technical standpoint, a rather straight forward procedure for well-trained transplant surgeons and is considered to be safe in properly investigated and selected patients. Relevant complications occur in less than 5% of the patients, and mortality rate is less than 0.14%[2,3,4]. However, it is associated with significant morbidity of the donor, including perio-perative risks, perioperative discomfort, hernia, chronic incision pain and a long convalescence. Laparoscopic donor nephrectomy (LDN) was first described in 1995 by Ratner et al.[5], in an attempt to reduce the donor morbidity associative with open donor nephrectomy (ODN), while at the same time hoping to mimic the good long-term results for the recipient. However these laparoscopic procedures are technically demanding, and are characterized by long learning curves and the possibility of life-threatening complications[6].

Laparoscopic donor nephrectomy had been performed at Division of Urology Siriraj hospital since August 2001, and we report our initial experience of surgical results in donor and the outcomes in recipients. Here we review the current evidence for LDN in terms of both donor safety and graft efficacy.

Preoperative evaluation

The evaluation before LDN is the same as for ODN; the absolute contraindications for renal transplantation are the same for ODN and LDN. Previous abdominal surgery may make LDN more difficult, especially via the transperitoneal route. Multiple vessels are not a contraindication to LDN. Suitable donors undergo an arteriogram by way of femoral puncture, computerized tomographic angiography (CTA) or magnetic resonance angiography (MRA) to evaluate the kidney, ureter and vascular supply. CTA and MRA are preferred by most centers over formal arteriography, which is uncomfortable, cumbersome, and more inconvenient for the donor. The renal

vasculature is accurately imaged with either CTA or MRA. Three-dimensional reconstructions contribute to the sensitivity of these studies. Recently our center used this technique for preoperative evaluation (Fig 1).

Technical aspects of LDN

For laparoscopic and open techniques, several surgical approaches have been described. The currently used technical variations in laparoscopic surgery comprise of transperitoneal or retroperitoneal approach, the use of hand assistance with or without specific device, and robotic assistance.

Retroperitoneal vs transperitoneal access

A retroperitoneal or transperitoneal approach may be utilized, depending on the preference of the surgeon, the habitus of the patient, and the renal anatomy. The theoretical advantage of the retroperitoneal approach is the avoidance of post operative bowel obstruction, but the workspace is limited compared to the transperitoneal access. Although authors who are performing retroperitoneoscopic LDN describe the method as being safe and promissing, only few prospective studies with patients included up to n=29 exist[7,8,9]. No data from randomized trials exist concerning retroperitoneoscopic LDN.

Totally endoscopic vs hand-assisted LDN

These two technique differ in the timing and possible location of the incision for removal of the kidney. Without hand-assist the incision for kidney extraction is not made until the kidney is completely mobilized. Immediately before division of the renal

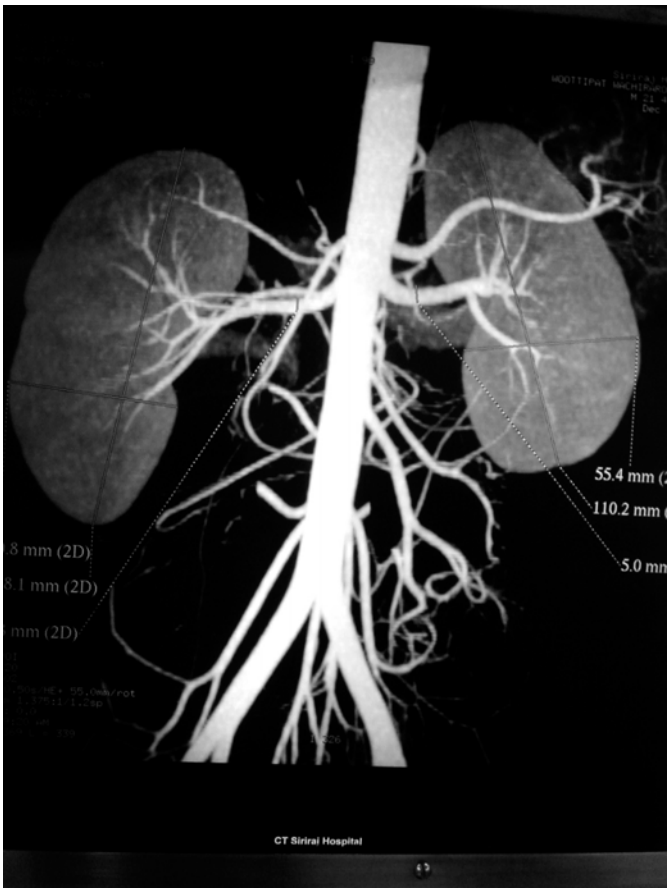


Fig 1 *A three-dimensional reconstruction of CTA demonstrates renal arterys and veins.*

vessels a 7 to 10 cm. abdominal incision, commonly lower midline or Pfannenstiel, is created for retrieval of the kidney. The free kidney is withdrawn from the abdomen by hand or with a 15-mm endocatch device (retrieval bag) inserted through a port placed in the abdominal or suprapubic incision. With the hand-assisted transabdominal procedure, a hand port is placed early in the surgery, usually by way of midline incision, and a hand is used throughout for dissection, palpation, and retraction. Advocates of hand assistance are convinced that it is faster, easier to learn, and that it adds on intraoperative safety. Reduction in operating time obviously reduces time of exposure of the kidneys to pneumoperitoneum, which has negative effects on the hemodynamics, which may affect primary graft function. However, until now, no evidence is available that, with "hand assistance" in LDN, a clinically significant reduction in injury to the graft can be achieved. Some authors not only report reduced intra-and post operative bleeding episodes in hand-assisted LDN, but also higher incidences of complications like bowel obstruction are described[10,11]. There are no major studies available comparing hand-assisted and total LDN. However, this approach may not be easily translated to donor nephrectomies as the objectives of nephrectomy differ by indication for the procedure.

Robotic assistance in live donor nephrectomy

There are only few descriptions on robotic-assisted LDN which performed in few centers with good initial results[12]. The argument for using robotic-assisted LDN is the better length of dissected vessels obtained due to the dexterity offered by the robot, and therefore improved quality of allograft. Robotics is not generally available, is expensive, and adds on complexity. Larger series are awaited.

Technique and results for LDN at Siriraj hospital

We perform a totally transperitoneal LDN in a technique which is based on the initially proposed technique[5]. However hand assisted LDN was used in selected cases in the early experience of our series. The side of nephrectomy depends on the separately measured renal function and vascular anatomy as evaluated by CTA. Usually, the inferior functionary kidney and/or the kidney with a single arterial supply is removed. In patients with regular anatomy, left-sided nephrectomy is preferred. The entire procedure is performed only with laparoscopic instruments. Only after a completed dissection of the kidney, a low Pfannenstical incision. Hand assistance (without introduction of a hand port) was used only for the extraction of the kidney [Fig 2].



Fig 2 *Intraoperative picture shows port positions and small Pfannenstiel incision for retrieval of the kidney.*

We have offered LDN since August 2001. Over this time period (August 2001 to February 2009) 113 living donor nephrectomy were performed. Over that time period we continued to perform ODN (Fig 3) according to donor preference and the availability of



Fig 3 *Intraoperative picture shows a large flank incision in ODN*

laparoscopic surgeons. From January 2001 to December 2006, We reviewed the clinical outcomes of 115 consecutive LDKT (56 open and 59 laparoscopy) performed at division of urology Siriraj hospital to determine whether the type of donor nephrectomy, laparoscopy versus open, affects the operative outcomes and graft function[13].

Laparoscopic donor nephrectomy was successfully performed in 56 (94.9%) cases and converted to open in 3 (5.1%) cases due to renal vein injury and intraoperative bleeding. The demographic data in terms of patient's age, sex were similar in the two groups. The mean operative times (329±51 vs. 220±50 minutes, p=<0.001) and warm ischemic time (180±74 vs. 114±112 seconds, p=<0.001) were longer in the laparoscopic than in the open group. There was no statistically significant difference in mean estimated blood loss (278±351 vs. 366±454 ml, p=0.7), mean time for resuming oral intake (0.92±0.33 vs. 1.07±0.42 days, p=0.052) and indwelling urinary catheter time (3.01±1.27 vs. 2.89±0.91 days, p=0.87) between the open and the laparoscopic groups. However, the mean length of hospital stay was significantly shorter in the laparoscopic than the open group (p=0.018). For the graft outcome, there were 6(10%) vs. 5(9%) instances of slow or delayed graft function among the recipients in laparoscopic vs. the open group. The recipient mean calculated GFR of the laparoscopic and the open groups at 1 week and at 1 year were 51.03±23.80 vs. 54.54±23.12 ml/min (p=0.57) and 98.58±35.76 vs.100.93±38.32 ml/min (p=0.77), respectively. One year graft survival rates were comparable between the two groups (94.3% vs. 98.2%, p=0.80). (Fig 4)

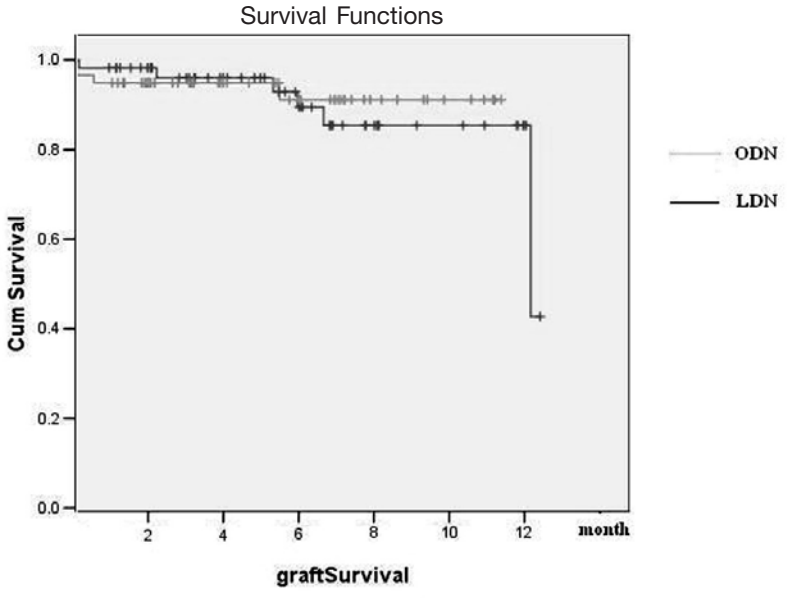


Fig 4 *One year graft survival rates according to surgical procedure.*

Results of laparoscopic vs conventional open donor nephrectomy: external evidence.

Donor factors

Safety

Although in two recent reviews published by Handschin[2] and Tooher [3] conclude that LDN is as safe as ODN, donor deaths after LDN because of gas embolism and hemorrhage are described[14,15]. However for ODN 5 donor deaths had occurred among 19,368 LDKT and estimated that the perioperative mortality associated with ODN in the USA was at least 0.03%[16]. In general, safely in very experienced hands seems to be equal or even better after LDN, and the rate of incision related complications is less when compared with ODN.

Conversion rates

Reported conversion rates for LDN are 0-13.3%[3]. Reasons for conversion were vascular injuries, difficult kidney exposure or an obese donor, vascular staple malfunction and splenic and bowel injuries.

Operative parameters

A meta-analysis reported by Nanidis[17] concluded that total blood loss was significantly lower in the LDN including Hand assisted group compared with ODN by 74.23ml. ($p<0.001$). Both operative and warm ischemic times were significantly shorter in ODN group by 51.92 minutes ($p<0.001$) and 102.01 seconds ($P<0.001$), respectively.

Postoperative complications

Gastrointestinal complications interms of bowel injury, bowel obstruction, internal hernia and pancreatitis were more common with LDN. On the other hand, pulmonary complications, as well as thrombotic complications were more common with ODN. Wound complications including wound infection or abscess, wound hematoma or seroma and incisional hernia, were reported in patients with ODN.

Proper selection of nephrectomy side

Traditionally, the left kidney has been preferred for organ donation, as the available renal vein length is longer. A major concern about right kidneys is technically more difficult. At one time, right side renal donation was considered only in instances of disparate renal size or function, or abnormal vasculature to the preferred left kidney. In a recent prospective study, Kay et al, compared the anatomy and function of right and left kidneys retrieved by LDN[18]. Left kidneys had longer renal veins (38 vs 27mm, $p<0.05$), although there were no differences in arterial length. Three of 18 right kidneys (17%) required bench renal vein lengthening using recipient saphenous vein grafting. The functional results of right and left kidneys were equal. At the moment, there are no relevant arguments against laparoscopic right donor nephrectomy.

Multiple vessels

Multiple renal vessels are not contraindications for LDN. There are several studies showing no differences between donor and recipient outcome if more than one artery or vein were present[19,20, 21,22]. Overall; ODN and LDN can be performed safely also in donors and recipients if multiple vessel exist and when proper vascular techniques for back table reconstruction including all small accepony vessels are applied

Learning curve

Exact effects, risks and limitations of learning curves in LDN are difficult to estimate. LDN is surely

the more demanding and challenging procedure than ODN. Descriptions vary from 20% major complications during the first 50 cases and 6% during cases 200-250[23] to 30% major complications during the first 30 laparoscopic cases with no complications during the next 50 LDN[24], but there are also reports of series without an apparent learning curve effect[25].

Reconvalescense and quality of life

The necessary amount of pain medication and the time it has to be supplied is reduced after LDN. Return to the usual activities such as driving a car or return to work is accelerated by at least 1 week. Hospital stay can be reduced when economically desirable by 1-2 days[2-4]. Perry et al.[26] evaluated pain and health related quality of life after surgery between patients undergoing LDN and miniincision ODN. The mean bodily pain score at all times after surgery were significantly less in the LDN group. The mean physical functioning score and emotional score significantly favoured the LDN group.

Cost implications

LDN has the potential to be more expensive due to the longer surgery and the use of disposable instruments. In developing countries the use of reusable laparoscopic instruments such as trocars has lowered the cost of LDN considerably[27]. However, the shorter hospital stay and return of the donor to work earlier should negate the cost. Because live donor nephrectomy imposes both a health and financial cost on the otherwise healthy donor, cost studies comparing ODN and LDN should ideally include both direct and indirect costs, as well as benefits both to the donor and recipients.

Recipient factors

Graft loss and injury due to technical problems.

Single graft loss due to technical problem was reported following ODN. On the other hand, at least 15 graft losses due to technical problem, following LDN were recorded[28]. The most common factor was vascular complications thought to arise from technical errors in handling a short renal vein with thin walls that was prone to dehiscence[29]. One graft loss was reported due to fracture of the graft during manipulations by the EndocatchTM bag[30]. In a series of 738 LDNs Jacobs et al. reported that the endovascular stapler created 37 extra arteries for implantation in cases with a short common stem of the main renal artery[31].

Graft functions

The initial concerns about LDN and the recipient outcome were the longer operative duration and the pneumoperitoneum, resulting in problems with graft functioning. During early experience with LDN increased warm ischemia time resulted in an increased proportion of delayed graft function. With increased experience LDN and ODN have shown comparable graft function at short-term follow up. One study[32] evaluated factors related to potential delayed graft function after LDN. Identified variable included recipient age, human leukocyte antigen (HLA) mismatched donor-recipient pairs, ischemia time, and transplantation of kidneys from a female donor into a male recipient. No variables associated with the laparoscopic technique itself were associated with poor graft function. In randomized trial [27] comparing ODN and LDN, graft function was no different between

the groups, as measured by the serum creatinine level. Graft survival (93.8% in LDN and 92.7% in ODN) and recipient deaths were also not significantly different (two LDN vs three ODN) at a follow up of 1 year.

Discussion

In the two recent systemic review published by Handshin[2] and Tooher[3], have demonstrated the safety of LDN as the primary means of procurement from live donors. Since then, three further RCT have been published[22,27,33]. Unfortunately, due to relative small numbers of patients included, heterogeneity of variations on how main postoperative endpoints were evaluated, no substantial definitive evidence especially regarding the end point donor safety was added by their RCT. Our experience have shown significantly shortened hospital stay and equivalent graft function with LDN compared with ODN.

However, LDN is still perceived as an experimental method at several major centers around the world. A recent survey of 131 transplantation centers, which collectively account for greater than 70% of the transplantation volume in 12 European countries, found that only 40% of all live donor nephrectomies were performed laparoscopically[34]. A higher rate of adoption ranging from 67% to 84%, has been reported in the US[35]. As our knowledge only 3 of 29 centers perform LDN in Thailand. The reasons cited for not offering LDN include perceived poorer graft quality, higher donor complication rates, lack of evidence of benefit, higher cost, and a steep learning curve. In our first 59 laparoscopic donor nephrectomies demonstrated equivalent graft function and similar rates of slow or delayed graft function comparable to the ODN. A lack of surgeon experience is also an important factor limiting the adoption of LDN. Nevertheless, donor mortality has remained very low since the development of this procedure-comparable to that of the open approach and morbidity has decreased as surgeons have gained experience[36]. In our center, surgeons started LDN after gained more experience in laparoscopic ablative nephrectomy.

As the rate of end stage renal disease increase, there is a need for the donor pool to be widened. Living related donors still represent the largest potential source of transplantable kidneys. Decreasing surgical morbidity can incentivize there donors. Indeed, a study from Johns Hopkins University found that 47% of donors would not have donated kidneys if LDN was not available[37]. It should be the mission of centers without LDN experience to find ways to safely introduce this approach into their program. We must continue to seek out ways to further decrease morbidity for our kidney donors.

Conclusion

LDN continues to develop as an alternative to ODN; LDN is certainly better than ODN in term of blood loss, analgesic requirement, hospital stay, convalescence and cosmesis. The longer surgery and warm ischemic time are factors that count againt it, although in the short term these have failed to have any effect on recipient outcome or graft survival. Donor satisfaction remains higher with LDN. Although the number of centers that perform laparoscopic donor nephrectomy increases, most centers still practice open donor nephrectomy. Open techniques will probably remain their place in the surgical armamentarium because the majority of transplant centers perform a small number of live donor nephrectomies only. It seems critical to have gained procedure related learning experience before performing LDN indepently.

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