Laparoscopic live-donor nephrectomy

RAMASWAMY MANIKANDAN and CHANDRU P. SUNDARAM*
*Departments of Urology, The Royal Liverpool University Hospital, Liverpool, UK, and *Indiana University Hospital, Indianapolis, USA*

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INTRODUCTION

With increasing numbers of people on the renal transplant waiting list each year in every country, the onus has been to increase live donation and thus try to address this shortfall. The first living-related donor nephrectomy (DN) was reported in 1953 [1] and open DN (ODN) has been the reference standard for many years. 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 [2]. Live DN is a unique operative situation in which a healthy individual puts him or herself at risk of having a major operation to aid a sick person. Live DN accounts for ≈42% of renal transplants in the USA. ODN has a very low mortality rate of <0.03% associated with it, and provides high-quality kidneys with excellent long-term function [3]. However, it is associated with significant morbidity, including postoperative pain, pneumothorax, hernia, chronic incision pain, and a long convalescence. As a result of this it has been considered a major deterrent to voluntary kidney donation [4].

Laparoscopic DN (LDN) was first described in 1995 by Ratner *et al.* [5], in an attempt to reduce the donor morbidity associated with ODN, while at the same time hoping to mimic the good long-term results for the recipient. Over the past 10 years it has continued to develop and proponents of LDN claim that the benefits associated with LDN may be one of the reasons for increased live donations in recent years in the USA [6]. For any new technique to become established it must stand the test of time, while also being confirmed as better than the established method. Here we review the current evidence for LDN in terms of both the short- and long-term outcomes.

PRE-OPERATIVE EVALUATION

The evaluation before LDN is the same as for ODN; the absolute contraindications for renal transplantation is 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. In many transplant centres helical CT angiography and MR angiography have replaced conventional angiography. They give a better view of the renal parenchyma and the computer reconstruction shows the arterial anatomy well. Ureteric and renal anomalies are also well seen with these methods; the accuracy is ≈95% and they are quicker and cheaper [3].

TECHNICAL CONSIDERATIONS

The technique of LDN is well described [4] and we only discuss some of the important points. It is well accepted that LDN is difficult to learn and is considered to be one of the more technically challenging laparoscopic operations.

Laparoscopic harvesting of the right kidney is more technically challenging than the left, due to the short renal vein and the need to retract the liver in the transperitoneal approach. The application of the endo-GIA stapler on the right renal vein can result in a loss of 1 cm of its length. Due to the greater incidence of venous thrombosis causing graft loss in the initial series of right LDN, many institutions perform only left LDN. This may be considered against the basic tenet of renal transplantation, i.e. the better kidney should remain *in situ* for the donor. Also in women of child-bearing age, donation of the right kidney may be advantageous because pregnancy-related hydronephrosis and pyelonephritis may be more common on that side [3]. To address the problem associated with right LDN a few modifications were suggested: (a) using a subcostal incision of 5–6 cm to divide the renal artery and vein, and using this incision to remove the kidney, instead of the Pfannenstiel incision; (b) using a parallel port to the inferior vena cava to introduce the stapler; and (c) using a graft from the recipient saphenous vein to increase the length of the right renal vein [7]. These measures produced results which are comparable to left LDN. Another way to address this problem was to use the retroperitoneal approach, as described by Gill *et al.* [8]. A modified muscle-splitting Gibson incision was used to retrieve the kidney, but this approach requires adequate experience with the retroperitoneal approach. Several studies have shown that right LDN is comparable to left LDN in terms of operative duration, estimated blood loss (EBL), warm ischaemia time (WIT), complications, and more importantly, graft loss soon after surgery (Table 1) [8–10]. Whilst the short-term outcome is comparable, there are no long-term data available. Despite studies showing that outcomes for right LDN are comparable to left LDN, reluctance still persists in many centres to use right LDN.

CONVERSION RATES

Reported conversion rates for LDN are 0–13.3% [11]. The most common cause for conversion to open surgery include intraoperative haemorrhage or vascular injury (65%), difficult kidney exposure or an obese donor (20%), vascular staple malfunction (12%) and loss of pneumoperitoneum (3%) [1].

HAND-ASSISTED LDN (HALDN) VS LDN

The proponents of HALDN advocate it as a means to decrease the technical difficulty, making it easier to learn, reducing graft injury, EBL and the WIT [12]. However, the method has not shown any marked difference in the outcome of patients in the medium term [13–17]. Long-term data as to whether this difference is clinically significant remain to be seen. Table 2 shows studies assessing HALDN and compared to either ODN or LDN [13–17]. The operating times are the longest for LDN

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TABLE 1 Comparison between right (R) and left (L) LDN

Variable*	[8] (R)	[8] (L)	[10] (R)	[10] (L)	[9] (R)	[9] (L)
Number	28	107	73	28	54	333
Approach	Retro	Trans	Trans	Trans	Trans	Trans
EBL, mL	107	166.2†	275 (50–2300)	250 (100–1000)	62 (20)	77 (63)†
WIT, min	5.03	4†	7.9 (2–17)	8.2 (2–17)	N/A	N/A
Operative duration, min	190.4	220.5†	218 (105–420)	280 (210–420)†	169 (25)	208 (45)†
Conversion rate, %	0	0	8	11	0	1
Recipient creatinine level [at days]	2.3 [5]	2.04 [5]	2.2 [7]	1.8 [7]	1.4 (0.5) [30]	1.5 (0.7)
Complications, %:						
during surgery	7.1	3.7	8	10	2.7‡	6.3‡
after surgery	0	1	4	11		
Graft loss	0	0	4	0	0	1

**mean, mean (range) or mean (SD); †statistically significant; ‡includes complications during and after surgery. Trans, transperitoneal; Retro, retroperitoneal; N/A, not available.*

and shortest for ODN, with HALDN intermediate.

ROBOTIC HALDN

Horgan *et al.* [18] described their first series of 12 patients undergoing robotic HALDN and compared it to the standard LDN. All the nephrectomies were on the left side. The mean operative duration was longer for robotic HALDN, at 166 min vs 110 min for LDN and 95 min for ODN. Their operative duration improved, with the last case being done in 140 min. Other variables including EBL, WIT and hospitalization, were similar to LDN. The argument for using robotic HALDN is the better length of dissected vessels obtained due to the dexterity offered by the robot, and therefore improved quality of the allograft. The technique is described in detail elsewhere [19]. Larger series are awaited.

INTRAOPERATIVE FACTORS

Pneumoperitoneum is necessary for LDN and many of the initial concerns were centred on the elevated intra-abdominal pressures in LDN, that could cause reduced perfusion, resulting in a greater risk of acute tubular necrosis or delayed graft function with increased allogenicity. This was shown in porcine models. However, these effects are prevented by intravascular volume loading [20]. Donors receive 8–10 L of volume replacement during surgery, with mannitol and frusemide to promote brisk diuresis. It is essential to maintain a low-pressure pneumoperitoneum of 12 mmHg to reduce the effects of pneumoperitoneum. During dissection of the renal artery it is intermittently bathed with a topical solution of papaverine (30 mg/mL). Once hilar dissection is completed, 25 g of mannitol is given with 20 mg of frusemide. The patient is given 3000 units of low molecular weight heparin 5 min before division of the vascular pedicle. When the ureter is divided it is observed for brisk urine output, which occasionally requires the pneumoperitoneum to be released. It is also important to ensure that both the kidney and the ureter are entirely within the extraction bag before closing it. At the end of the procedure the pneumoperitoneum should be reduced to 5 mmHg to ensure complete haemostasis.

WIT

The WIT is defined as the time from which the renal vessels are ligated during harvesting to when the temperature of the kidney is reduced to 4 °C. Two randomized trials and other studies showed a significantly shorter WIT in patients undergoing ODN than LDN [11,21,22]. The mean (range) WIT for LDN is ≈5 (1.3–7.8) min and ≈2.5 (1.3–7.8) min for ODN. There is also evidence that the WIT is significantly lower for HALDN than LDN [14,16]. However, the short-term follow up failed to show that this had any effect in terms of increased graft rejection or in graft survival in patients undergoing LDN. A study assessing the United Network for Organ Sharing (UNOS) database comparing 2734 LDNs with 2576 ODNs showed that although patients having LDN had a significantly higher creatinine level at discharge, creatinine levels assessed later, rejection rates and short-term graft survival were the same [6]. This is in agreement with other studies [23,24].

EBL

It was consistently shown that LDN causes less blood loss than ODN; HALDN causes the least blood loss when compared to LDN and ODN [25] (Table 2 and Table 3 [4,21,22,26–28]. Transfusion rates during surgery were 0–10% for LDN and 0–7% for ODN, and after surgery were 1–7% for LDN and 3–5% for ODN [11] (Table 3).

SPECIAL SITUATIONS

In a study comparing 41 markedly obese patients, with a mean body mass index of 39.3 kg/m^2, with a control group of 41 with a mean body mass index of 24.3 kg/m^2, Jacobs *et al.* [29] found that although surgery was significantly longer in the markedly obese, the postoperative recovery, analgesic requirements, complications and recipient function were equivalent in both groups.

A very small retrospective study showed that LDN could be safe in elderly patients; the mean (range) age in this group of patients was 69.5 (65–74) years [30].

TABLE 2 Comparison between HALDN, ODN and LDN

Variable	[13]	[15]	[16]	[14]	[17]
Comparison	HALDN vs ODN	HALDN vs ODN	HALDN vs LDN vs ODN	HALDN vs ODN vs LDN	LDN vs HALDN
Remarks	Randomized trial	Non-randomized comparative study in two institutions	Non-randomized Patients having R DN only offered ODN	Retrospective; mainly left DN. Minimal data for ODN	Randomized trial: mostly left DN
Follow-up, months	6–12*	18	15 (7)	12	6
HALDN, n	23	60	17	23	20
EBL, mL	156 (148, 50–600)	82.9 (61.8)†	167 (70)† for HALDN	100–200	97.4 (73)
WIT, min	3.05 (2, 1.5–10.4)†	2 (0.5)	2 (2)† for ODN	1.6 (0.2)† for HALDN: no data on ODN	2.25 (0.8)
Operating room duration, min	206 (32, 150–282)†	240 (88.4)	249 (42)† for ODN	165 (12)† for HALDN: no data on ODN	219 (28)† for LDN
Conversion rate, %	0	0	0	4	0
Complication rates, %	Ureter 9 17 minor	3.3 re-exploration 1.6 ureteric	0	8.6 ileus	5 pneumonia, 5 ileus 5, chylous ascites
Pain	59 (62, 9–310)† morphine	35.5 (19.5)† parenteral narcotic	N/A	N/A	28.3 (14.8) mg morphine
Hospital stay, days	1.7 (0.9, 0–5)†	3.5 (0.7)	2 (2)† for LDN and HALDN	2 (0.1)	2.1 (0.5)
Serum creatinine level, mg/dL	1.7 (0.7) [7 days]	1.4 (nadir)	1.8 [5 days and 2 months]	1.7 [1 week]	1.31 (0.5) [7 days]
[at sample time]	1.2 (0.4) [3 months]†		1.7 [15 months]	1.5 [12 months]	1.3 (0.6) [6 months]
Graft loss, %	13	8	0	17, acute rejection	0
Convalescence, weeks	11/23 at 6†	4 (0.5)†	3.6 (2)† for LDN, HALDN	N/A	N/A
ODN, n	27	31	55	19	
EBL, mL	216 (280, 50–1300)	364 (449)†	167 (70)	100–200	
WIT, min	1.6 (0.95, 0.5–4.96)	N/A	2 + 1	N/A	
Operating room duration, min	125 (36, 70–224)	265 (50.5)	163 (24)† for ODN	N/A	
Complication rate, %	Ureter 4 Minor 15	Pneumothorax 6.4 Ureter 3	Fever 4	N/A	
Pain	111 (96, 12–458)	198 (57.7)†	N/A	N/A	
Hospital stay, days	2.6 (0.7, 1–4)	4.5 (1.2)†	3 (2)	N/A	
Serum creatinine level, mg/dL	2.1 (1.5) [7 days] 1.5 (0.4) [3 months]†	1.3 (nadir)	1.7 [5 days and 2 months] 1.5 [15 months]	1.9 [1 week] 1.5 [12 months]	
Graft loss, %	4	22	0	14, acute rejection	
Convalescence, weeks	5/26 at 6	9.2 (3.9)†	5.9 (2)	N/A	
LDN, n			28	11	20
EBL, mL			200 (107)	100–200	141.5 (221.8)
WIT, min			3 (2)	3.9 (0.3)	2.6 (1.2)
Operating room duration, min			306 (40)	186 (6)	200 (20.8)
Conversion rate, %			0	0	0
Complications, %			3.5 umbilical hernia	one deep vein thrombosis one hernia	5, urinary leak 15, wound infection 5, atelectasis
Pain			N/A	N/A	22.1 (14.0) mg morphine
Hospital stay, days			2 (2)	1.6 (1.3)	1.9 (0.5)
Serum creatinine level, mg/dL			1.4 [5 days, 2 months, and 15 months]	2.0 [1 week and 1.6 [12 months]	1.25 (0.5) [7 days] 0.98 (0.5) [6 months]
Graft loss			0	one, acute rejection	0
Convalescence, weeks			3.3 (2)	N/A	N/A

**Telephone follow-up; †statistically significant difference; N/A, not available. Values are mean, mean (SD, range) or mean (SD), except where stated otherwise.*

TABLE 3 Intraoperative variables during LDN

Study	N patients	EBL, mL	WIT, min	Op room time, min	Conversion, %	Remarks
Oyen *et al.* [21]						
LDN	63	N/A	4.3	180	6.3	Randomized prospective trial
ODN	59	N/A	1.4*	140*		
Simforoosh *et al.* [22]						
LDN	100	N/A	8.70	270.8	1	Randomized, prospective trial
ODN	100	N/A	1.87*	152.2*		
Ratner *et al.* [4]						
LDN	70	266 (174)	N/A	230 (29)	N/A	Historical controls used in study
ODN	20	393 (335)*	N/A	183 (48)*		
Rawlins [28]						
LDN	100	102	2.3	231	1	Comparative series
ODN	50	193*	N/A	209*		
Flowers *et al.* [27]						Report from same institution as [26]
LDN	70	122.3	N/A	226.3	6	Historical age matched controls used.
ODN	65	408*	N/A	212.8		
Jacobs *et al.* [26]	738	128 (194)	2.81	202 (52.4)	1.6	Largest LDN series from one institution
Indiana University†	250	115 (285)	2.2 (1)	199 (50)	1.6	Retrospective study

**Statistically significant difference; †Unpublished data; N/A, not available. Values are mean or mean (SD) except where stated otherwise.*

Multiple renal vessels and other anomalies are not contraindications for LDN. The presence of multiple renal arteries may require arterial reconstruction before transplantation of the kidney in the recipient. In a comparison of 17 patients with multiple renal arteries undergoing either ODN (nine) or LDN (eight) the mean duration of the operation, complications and the recipient outcomes at the end of 1 year were similar in the two groups [31]. Other studies also showed that LDN can be safe in patients with multiple renal arteries [4].

COMPLICATIONS

URETERIC COMPLICATIONS

There was a much higher rate of ureteric complications in initial series of LDN (9.1%) from the John Hopkins. This was mainly due to a more extensive dissection of the ureter, resulting in ischaemia to the ureter. Therefore caution must be exercised by avoiding aggressive dissection of the ureter. With technical modifications by which all the tissue lateral to the gonadal vein are preserved, thus maintaining a good ureteric blood supply, this complication has been reduced significantly (3%) [4].

Another large series reported a 2% rate of ureteric complications [26]. In the randomized trial by Simforoosh *et al.* [22] the ureteric complication rate for ODN was 2%, compared to none for LDN. In our series of 250 patients (unpublished data), 4.4% of the first 150 recipients developed ureteric stricture. We have since modified our technique to stent the ureter in the recipient. There have been no cases of ureteric stenosis in the last 100 patients after the ureteric implantation technique was modified to include a stent for 4–6 weeks.

OTHER COMPLICATIONS

The main complications from LDN seem to be mechanical, due to either injury of the spleen or bowel. Injuries can also result when using the stapler or when retrieving the kidney. Vascular complications, in particular injury to the renal artery or vein, are more common in LDN. In comparison, pulmonary complications are more common in ODN and this can be largely explained by the incision used in ODN. Wound complications including wound infection, haematoma, seroma or incisional hernia can occur in both types of operation [11]. The re-operative rate for LDN is 1–8% [25]; the complications are listed in Table 4 [21,22,26,32].

HOSPITAL STAY AND CONVALESCENCE

Analgesic requirement, hospital stay and the convalescence period are much shorter for LDN and HALDN than for ODN in most series [11]. The two randomized trials comparing LDN with ODN failed to show any difference in the hospital stay, while the only randomized trial comparing HALDN with ODN showed that those undergoing HALDN had a shorter hospital stay [13,21,22]. Return to normal activities, use of analgesia after discharge and return to work is much quicker after LDN and HALDN than ODN [4,12,13,33] (Table 5 [4,21,22,24,27,34]).

RECIPIENT OUTCOME AND GRAFT FUNCTION

The initial concerns about LDN and the recipient outcome were the longer operative duration and the pneumoperitoneum, resulting in problems with graft functioning. Early graft functioning is important, as studies have shown that poor early graft function may have an impact on long-term graft survival [35,36]. There is a lack of uniformity in defining what exactly constitutes delayed graft function. Some of the definitions include: (a) the need for dialysis within 72 h after transplantation; (b) serum creatinine level of >3 mg/dL at 5 days after surgery; (c) urine output of <1 L in the first 24 h or a decrease in serum creatinine level of <20–30%. To date, none of the comparative studies between LDN and ODN have shown that the recipient outcome, in

TABLE 4 Complications, as n (%), of LDN

Study	N patients	Re-exploration	Haemorrhage	Bowel injury	Splenic injury	Ureteric	Wound-related	Pneumonia	Other
Oyen *et al.* [21]									
LDN	63	4 (6.3)*	2 (3.1)	2 (3.1)†	0	1 (1.6)	2 (3.1)	0	3 (4.7)
ODN	59	0	0	0	0	0	2 (3.3)	1 (1.6)	0
Simforoosh *et al.* [22]									
LDN	100	1 (1)	4 (4)	1 (1)	2 (2)	0	0	0	1 (TP)
ODN	100	2 (2)	1 (1)	0	0	2 (2)	0	0	3 (1) (LY) 1 (1) (TP) 1 (1) DVT
Ratner *et al.* [32]									
LDN	171	1 (0.6)	6 (3.5)	1 (0.6)	0	N/A	6 (3.5%)	1 (0.6)	7 (4) (TP)
Jacobs *et al.* [26]								1 (0.1)	
LDN	738	6 (0.8)	13 (1.8)	2 (0.3)	15 (2)	33 (4.4)	0	–	7 (1) P
Indiana University‡									
LDN	250	3 (1.2)	7 (2.8)	1 (0.4)	1 (0.4)	3 (1.2)	8 (2.4)	1 (0.4)	1 (0.4) I 1 (0.4) LY

**One patient with forgotten sponge excluded; †both patients obese; ‡Unpublished data. P, pneumothorax; I, ileus; TP, transient thigh paresthesia; LY, lymphocoele; DVT, deep vein thrombosis.*

terms of graft function, graft survival or the incidence of rejection, is significantly different between the groups [6,11,22,23]. Suzuki *et al.* [37] reported a 5-year graft survival of 82% for LDN vs 89% for ODN. Troppmann *et al.* [6,36], assessing the UNOS database, found that in the comparison between 2576 ODN and 2734 LDN, the incidence of delayed graft function was 5% and 5.9% ($P = 0.18$). Although the serum creatinine decrease or the urine production in the first 24 h were not significantly different between the groups, more patients in the LDN group had a creatinine level at discharge of >1.4 mg/dL (1116 in ODN vs 1274 LDN, $P = 0.002$). The shorter hospital stay in the LDN group, and that the recipients in the LDN group were slightly older than in the ODN group, may be contributing factors to this. The two groups were not exactly matched, in that the LDN group recipients had slightly better residual function than the ODN recipients. However, at a follow-up of 1 year there was no significant difference between the groups in terms of serum creatinine level, acute rejection (17.4% ODN, 18.2% LDN) or graft survival (94.1% vs 94.4%) in the two groups [6].

In the randomized trial [22] 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.

TABLE 5 Hospital stay and convalescence

Study	Hospital stay, days		Return to work, days	
	ODN	LDN	ODN	LDN
Oyen *et al.* [21]	6.2	6.7	N/A	N/A
Simforoosh *et al.* [22]	2.13	2.21	N/A	N/A
Ratner *et al.* [4]	5.7 (1.7)	3 (0.9)	N/A	N/A
Lennerling *et al.* [34]	6 (1–38)	5 (2–39)	7 (1–16)	6 (2–19)
Flowers *et al.* [27]	4.5	2.2*	51.5	15.9*
Khauli *et al.* [24]	5.0 (0.8)	3.4 (0.9)*	27.4 (11.1)	10 (3)*

**Statistically significant difference. Values are mean, mean (range) or mean (SD).*

QUALITY OF LIFE

Perry *et al.* [33] evaluated pain and health-related quality of life after surgery using the Short-Form-36 version 2 between patients undergoing LDN and mini-incision ODN. The mean bodily pain scores 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. The cosmetic results of LDN seem to be much better than ODN and this may be a factor for donor satisfaction [22].

COST IMPLICATIONS

Renal transplantation is much more cost-effective than haemodialysis. 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 [22]. However, the shorter hospital stay and return of the donor to work earlier should negate the costs [11,25]. The cost implications for the donor may be more

important, as it may be a barrier to voluntary donation [3]. Most of the studies assessing the cost comparisons between ODN and LDN use either selective costing or fail to state how the costs were derived [11]. Because live DN 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.

CONCLUSION

LDN continues to develop as an alternative to ODN; LDN is certainly better than ODN in terms of blood loss, analgesic requirement, hospital stay, convalescence and cosmesis. The longer surgery and WIT are factors that count against 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. A bias still exists in many centres to perform a left LDN, although this is slowly changing. Whilst in the short term LDN has similar outcomes in terms of graft function and graft survival, long-term data are still lacking, which will hopefully be available in the next few years. Many of the published comparative studies between ODN and LDN use historical controls for ODN. The difficulty in performing large-scale randomized studies in procedures such as DN are well known and therefore large-scale, prospective comparative studies with an adequate follow-up will help to define the exact role of LDN in renal transplantation.

CONFLICT OF INTEREST

None declared.

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Correspondence: Ramaswamy Manikandan, 15 Langtree Close, Ellenbrook, Manchester M28 7XT, UK.
e-mail: armanikan2000@gmail.com

Abbreviations: **(L)(O)(HA)DN**, (laparoscopic) (open) (hand-assisted) donor nephrectomy; **EBL**, estimated blood loss; **WIT**, warm ischaemia time; **UNOS**, United Network for Organ Sharing.