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Laparoscopic Living-Donor Nephrectomy: Analysis of the Existing Literature

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Abstract

Context: Laparoscopic living-donor nephrectomy (LLDN) has achieved a permanent place in renal transplantation and in some centers has replaced open donor nephrectomy as the standard technique.

Objective: To evaluate the published literature regarding the relative results and complications of open LLDN and the hybrid technique of hand-assisted LLDN.

Evidence acquisition: A systematic review of the literature was performed, searching PubMed and Web of Science. A "free text" protocol using the term *living-donor nephrectomy* was applied. Six hundred twenty-nine records were retrieved from the PubMed database and 686 records were retrieved from the Web of Science database.

Evidence synthesis: Fifty-seven comparative studies were identified in the literature search. The three techniques of open, laparoscopic, and hand-assisted laparoscopic donor nephrectomy were compared in terms of reported outcomes. With regard to the perioperative outcome parameters, laparoscopy was better than open surgery in terms of blood loss, analgesic requirements, and duration of hospital stay and convalescence. Postoperative graft function was not significantly different between the different forms of donor nephrectomy, although longer warm ischemia times are reported for laparoscopy.

Conclusions: All three techniques of live-donor nephrectomy are standard of care. The laparoscopic techniques result in less postoperative pain and estimated blood loss with shorter hospital stay, while postoperative graft function is not inferior to that after open live-donor nephrectomy.

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1. Introduction

In the half century that has passed since the first successful procedure, living-donor renal transplantation has shown superiority over cadaveric-donor renal transplantation. The advantages of live-donor renal transplantation are several. First, cold ischemia time is significantly shorter than in cadaveric-donor kidney transplantation and thus there is an almost complete absence of ischemic injury to the transplanted kidney. This results in a relative insensitivity to poor tissue matching and better long-term function [1]. Second, kidneys harvested from living donors represent perfect organs from perfectly healthy donors, ensuring a better graft and recipient survival compared with human leukocyte antigen (HLA)–matched cadaveric transplants [2]. Third, live-donor nephrectomy (LDN) reduces the waiting time for the recipient and therefore allows renal transplantation earlier, with the recipient still in better general condition and health.

LDN is unique in that it affects a healthy individual rather than a sick person. This makes it a very demanding and sophisticated surgical procedure. The safety and efficiency of the surgical technique are of utmost concern for the donor, the recipient, and the surgeon. Therefore, the surgical technique used must entail the lowest possible morbidity for the donor without compromising the functional outcome of the graft [3].

Since the early 1990s, laparoscopic techniques have been successfully adapted for various open urologic procedures, including laparoscopic living-donor nephrectomy (LLDN) which was first described in 1995 [4,5]. Because laparoscopy is generally considered to be less invasive than open surgical techniques, laparoscopy may be preferable if it can be demonstrated to achieve the same result with the same safety for the patient. While pure laparoscopic donor nephrectomy is feasible, some surgeons for reasons of safety prefer hand-assisted laparoscopy for LDN [6], with either a trans- or retroperitoneal approach.

With the introduction of laparoscopy into LDN, some centers have reported an increase in the numbers of renal transplants from living donors [2,7–9]. For the United States, the United Network of Organ Sharing (UNOS) reported that in 2005, 83% of all LDNs were performed laparoscopically [10].

However, when laparoscopic donor nephrectomy was first introduced there was great concern that this procedure would be unsafe and that longer warm ischemia times (WITs) would jeopardize postoperative graft function. The purpose of the present systematic review was to evaluate the published literature regarding the relative results and complications of open LDN, purely laparoscopic (LLDN) and retroperitoneoscopic live-donor nephrectomy (RLDN), and the hybrid technique of hand-assisted LLDN (HALLDN).

2. Evidence acquisition

A literature search was performed on the Internet using the PubMed and Web of Science. The PubMed search included a "free text" protocol using the term *living-donor nephrectomy* across the "Title" and "Abstract" fields of the records. Subsequently, the following limits were used: humans and language (English). Particular attention was paid to articles focusing on indications, results, complications, and mortality for LDN. The searches of the Web of Science databases used the same free-text protocol and the same keyword, applying the same limits.

We took into consideration all the papers published from 1997, when the first important publication about LLDN appeared in the literature, to January 2010. We retrieved 629 records from PubMed and 686 records from the Web of Science database. Studies published only as abstracts and reports from meetings were excluded.

We assessed the papers based on their different levels of evidence (level 1–4) for the various end points examined (indications, results, and complications of LLDN) and distinguished according to the grade of evidence (Phillips and Sackett, levels of evidence and grades of recommendation. Oxford Centre for Evidence-based Medicine Web site. http://www.cebm.net/%3Fo=1025). Meta-analyses of randomized clinical trials (RCTs) constitute the highest evidence (level 1a), followed by an adequately sampled single RCT (level 1b), systematic review of cohort studies (level 2a), and low-quality RCT (level 2b). Lower levels of evidence are provided by retrospective studies compared to contemporary series of patients (level 3) and by retrospective studies used historical series as control (level 4).

The following outcomes were evaluated in the review: (1) indications for LLDN and HALLDN, value of LDN, different techniques, characteristics of the patients; (2) Results for intra- and postoperative outcome after LLDN and HALLDN versus open living-donor nephrectomy (OLDN), WIT, early and late graft function; and (3) complications associated with the surgical technique.

2.1. Statistical analyses

Cumulative analysis was conducted using the Review Manager v.5, software designed for composing Cochrane Reviews (Cochrane Collaboration, Oxford, UK). Statistical analysis of dichotomous variables was carried out using odds ratio (OR) as the summary statistic, whereas continuous variables were analyzed using the weighted mean difference (MD); both were reported with 95% confidence intervals (CIs). ORs represent the odds of an adverse event occurring in the LLDN/HALLDN compared with the OLDN group, whereas MDs summarize the differences between the two groups with respect to continuous variables, accounting for sample size. Statistical heterogeneity was tested using the χ^2 test. A p value <0.10 was used to indicate heterogeneity. Random effects models were used in case of heterogeneity.

2.2. Quality of the comparative studies and level of evidence

Fifty-seven comparative studies were identified in the literature search, but not a single RCT. Among the 57 evaluated papers, 29 (50.9%) compared LLDN with OLDN [3,11–38] (Table 1); 7 (12.3%) compared HALLDN with

Table 1 – Comparative studies evaluating the peri- and postoperative outcomes after purely laparoscopic and open living-donor nephrectomy

Level of evidence	Study	No. of cases, type	OPT, min	WIT, min	Postoperative pain, mg	Hospital stay, d	Complication rate, %	Graft function
1b	Oyen et al. [11]	63 LLDN 59 OLDN	180 140	4.3 1.4	28.1 36.4	6.2 6.7	12.7 6.7	–
1b	Simforoosh et al. [12]	40 LLDN 40 OLDN	251.4 135	6.6 2.09	5.4 5.9	2.21 2.13	22.5 15	Creatinine after 180 d: 123 vs 143 μmol/l
1b	Brook et al. [13]	40 LLDN 20 OLDN	135 186	3.6 2	–	–	–	Creatinine after 52 wk: 130 vs 130 μmol/l
1b	Andersen et al. [14]	63 LLDN 59 OLDN	180 140	–	14.5 18.6	6.2 6.7	–	–
1b	Kok et al. [15]	50 LLDN 50 OLDN	221 164	6 3	16 25	3 4	6–12 6	100 98
1b	Hamidi et al. [16]	63 LLDN 59 OLDN	180 140	–	13.1 17.8	6.2 6.7	11 NA	–
1b	Kok et al. [17]	50 LLDN 50 OLDN	–	–	–	3 4	6 6	–
1b	Andersen et al. [18]	63 LLDN 59 OLDN	–	–	–	–	7.9 NA	–
1b	Simforoosh et al. [19]	100 LLDN 100 OLDN	270.8 152.2	8.7 1.87	11.5 10.8	2.26 2.2	17 9	93.8 92.7
2a	Shokeir [20]	–	LLDN:105–420 OLDN: 75–310	2–17 2–12	–	–	0–31 0–19	93–100 91–100
2a	Nanidis et al. [21]	3751 LLDN 2843 OLDN	–	–		–	13.7 16.4	–
2a	Antcliffe et al. [22]	216 LLDN 822 OLDN	130–232 105–164	–	–	–	24.3 18.6	98.5 98.6
2a	Tooher et al. [23]	–	LLDN:162–370 OLDN: 95–288	2.3–7.8 1.6–7.8	–	–	5–26 0–71	93–100 91–100
2a	Merlin et al. [24]	–	LLDN:183–340 OLDN: 148–268	5 1.7	–	2.2–3.1 3.8–5.7	5–20 0–35	–
2a	Handschin et al. [25]	–	LLDN:145–340 OLDN: 95–268	3.05 1.6	36–88 60–265	1.2–11 2.6–10.5	0–30 0–35	–
2b	Power et al. [26]	100 LLDN 83 OLDN	178 159	3.5 2	–	4.7 6.8	–	97.7 98.8
2b	Wilson et al. [27]	20 LLDN 20 OLDN	165 153	5 2	19 Epidural	3 5	0 NA	Creatinine at discharge: 124.7 vs 126.4 μmol/l
2b	Chung et al. [28]	38 LLDN 38 OLDN	194.8 116.8	–	51.4 116.8	4.8 7.1	7.8 13.1	–
3b	Bachmann et al. [3]	65 RLDN 69 OLDN	152 160	2.1 1.9		11 13	26.1 24.6	Creatinine after 1 yr: 148 vs 159 μmol/l
3b	Brook et al. [29]	44 LLDN 359 OLDN	–	–	–	–	–	–
3b	Perry et al. [30]	72 LLDN 98 OLDN	–	–	–	–	–	–
3b	Percegona et al. [31]	60 LLDN 49 OLDN	–	4.13 2.36	–	5–33 5–30	–	95 87
3b	Vats et al. [32]	39 LLDN 53 OLDN	343.6 152.6	–	–	–	–	–
3b	Leventhal et al. [33]	80LLDN 50 OLDN	276 186	3.8 NA	–	2.1 3.2	11 NA	97 94
4	Derweesh et al. [34]	101 LLDN 35 OLDN	213 217	4.35 NA	–	–	–	93.1–98 94.3–100
4	Srivastava et al. [35]	342 LLDN 1000 OLDN	180 110	4.5 2	150 251	3.14 5.7	–	Creatinine after 1 yr: 151 vs 152 μmol/l
4	Troppmann et al. [36]	2685 LLDN 2847 OLDN	–	–	–	–	–	79–100 80–100
4	Bachmann et al. [37]	77 RLDN 79 OLDN	149 160	1.9 1.8	54 59	–	–	–
4	Brown et al. [38]	50 LLDN 50 OLDN	234 208	2.8 NA	–	3.5 4.7	6 10	92 94

LLDN = laparoscopic living-donor nephrectomy; OLDN = open living-donor nephrectomy; OPT = operating time; WIT = warm ischemia time.

Table 2 – Comparative studies evaluating the peri- and postoperative outcomes after hand-assisted laparoscopic and open living-donor nephrectomy

Level of evidence	Study	No. of cases, type	OPT, min	WIT, min	Postoperative pain, mg	Hospital stay, d	Complication rate, %	Graft function
1b	Wolf et al. [39]	23 HALLDN 27 OLDN	206 125	3.5 1.6	59 111	1.7 2.6	12.7 6.7	Creatinine after 3 mo: 120 vs 150 μmol/l
3b	Tsuchiya et al. [40]	62 HALLDN 27 OLDN	241.5–260.5 225.3–225.8	2.8–3.3 1.8	–	9.3–10.8 11.5–12.6	3.2 NA	Creatinine after 6 mo: 160 vs 160 μmol/l
3b	Stifelman et al. [41]	60 HALLDN 31 OLDN	240 265	2.01 NA	35.5 198	3.5 4.5	3 2	Creatinine after 1 wk: 130 vs 140 μmol/l
3b	Kercher et al. [42]	30 HALLDN 30 OLDN	275 180	1.2 1.7	–	3.4 4.1	–	–
3b	Sansalone et al. [43]	23 HALLDN 139 OLDN	185 140	–	–	5 9	–	Creatinine after 7.9 yr: 120 vs 120 μmol/l
4	Lee et al. [44]	85 HALLDN 115 OLDN	191.5 184	2.1 1.4	–	–	7.1 0.7	98 97
4	Shrestha et al. [45]	11 HALLDN 71 OLDN	–	–	–	–	–	–

HALLDN = hand-assisted laparoscopic living-donor nephrectomy; OLDN = open living-donor nephrectomy; OPT = operating time; WIT = warm ischemia time.

Table 3 – Comparative studies evaluating the peri- and postoperative outcomes after laparoscopic living-donor nephrectomy with hand-assisted laparoscopic living-donor nephrectomy

Level of evidence	Study	No. of cases, type	OPT, min	WIT, min	Postoperative pain, mg	Hospital stay, d	Complication rate, %	Graft function
1b	Bargman et al. [46]	20 LLDN 20 HALLDN	200 219	2.6 2.2	22.1 28.3	1.9 2.1	12.7 6.7	Creatinine after 6 mo: 98 vs 130 μmol/l
2a	Kokkinos et al. [47]	174 LLDN 202 HALLDN	208–311 165–294	3–5.4 1.6–4.4	–	–	5.9 10.3	–
3b	Percegona et al. [48]	34 LLDN 21 HALLDN	184 191	3.8 4.2	–	2.6 3.6	8.8 28.6	–
4	Kocak et al. [49]	482 LLDN 318 HALLDN	–	–	–	1.6 1.2	3.3 2.2	Creatinine after 1 wk: 190 vs 120 μmol/l

HALLDN = hand-assisted laparoscopic living-donor nephrectomy; LLDN = laparoscopic living-donor nephrectomy; OPT = operating time; WIT = warm ischemia time.

Table 4 – Comparative studies evaluating the peri- and postoperative outcomes after laparoscopic living-donor nephrectomy (LLDN) with hand-assisted laparoscopic living donor nephrectomy (HALLDN) and open living donor nephrectomy (OLDN)

Level of evidence	Study	No. of cases, type	OPT, min	WIT, min	Postoperative pain, mg	Hospital stay, d	Complication rate, %	Graft function
2a	Manikandan et al. [50]	–	219 165 249	1.6 2 1.5–10	22.1 14 198	3 2.6–4.5 NA	–	Creatinine after 15 mo 150 vs 150 vs 150 μmol
2b	Yuzawa et al. [9]	441 LLDN 16 HALLDN 254 OLDN	244 243 192	5.3 NA NA	–	8.5 8.5 11.1	5.6 5.5 NA	–
2b	El-Galley et al. [51]	28 LLDN 17 HALLDN 55 OLDN	180–306 155–294 163	3 2 2	–	2 2 3	3 2	Creatinine after 15 mo: 140 vs 165 vs 155 μmol
3b	Ruiz-Deya et al. [52]	10 LLDN 23 HALLDN 19 OLDN	215.4 165 NA	3.9 1.6 NA	0 75 NA	1.6 2 NA	–	Creatinine after 6 mo: 150 vs 170 vs 160 μmol
4	Ruszat et al. [6]	14 LLDN 34 HALLDN 69 OLDN	212 192 160	3.9 2.1 1.9	–	13 11 13	57.1 26.5 24.6	–

OPT = operating time; WIT = warm ischemia time.

OLDN [39–45] (Table 2); 4 (7.1%) compared LLDN with HALLDN [46–49] (Table 3); 5 (8.8%) compared LLDN with HALLDN and OLDN [6,9,50–52] (Table 4); 6 (10.6%) compared right and left nephrectomy with a purely laparoscopic or hand-assisted technique [53–58]; 2 (3.5%) (level of evidence 2b [59] and level of evidence 3 b [40]) compared old and young living kidney donors who underwent a LLDN; 1 (1.7%) retrospective study with a level of evidence 3b compared the first and the last 100 consecutive LLDN [60]; 1 (1.7%) retrospective study (level of evidence 3b) compared multiple versus single arteries in LLDN [61]; 1 (1.7%) retrospective study used a historical series as control (level of evidence 4) comparing early and late results related to the learning curve for LLDN [62]; and 1 (1.7%) retrospective study used a historical series as control (level of evidence 4), comparing obese and nonobese donors [63].

3. Evidence synthesis

3.1. *Indications and exclusion criteria*

Regarding the indications or exclusion criteria for donors for the different techniques of donor nephrectomy, there were no studies comparing these with relevant outcome parameters. Instead, most studies stated their exclusion criteria for the respective techniques based on surgeon opinion.

In general, selecting an appropriate donor for LDN required a careful evaluation and the involvement of various medical disciplines. Prospective donors needed to be of good general health and at low risk of comorbidity resulting from removal of one kidney. Thus all acute and chronic diseases, including malignancy, needed to be ruled out. In addition, a prospective donor had to be fit to undergo surgery and have acceptable renal anatomy, including the vascular supply [64,65].

Irrespective of the chosen technique of LDN, the left kidney was generally preferred for renal transplantation by most surgeons because of its longer vein, which facilitated the vascular anastomotic procedure [2,3,6,25,54–57,62, 66–74]. The right kidney was selected when significant anatomic variations of the left renal vascular supply were seen on preoperative donor angiography [2,3,26,27,54,56, 70–72,75], or if split renal function on nuclear scintigraphy was <40% in the right kidney, according to the principle that the kidney with the better function remains with the donor [55–58,68,70–72,74,75].

In the 1990s, the use of kidneys with multiple renal arteries from live donors was discouraged because of a perceived increased technical difficulty of completing more than one arterial anastomosis within a short time, with resulting prolonged warm ischemia for at least part of the renal allograft [4]. Poorly controlled hypertension after transplantation, resulting from segmental infarction of the allograft, was reported in some cases [5].

Since then, the use of live-donor kidneys with double renal arteries has increased and this anomaly is no longer considered a contraindication since it can be transplanted with a minimal risk of technical failure [69,75].

Controversy still exists about the surgical feasibility of a LLDN of the right kidney. Most urologists have considered this more challenging because of the required retraction of the liver, the short right renal vein, and the presence of friable venous branches draining into the inferior vena cava in proximity to the right renal vein. They suggested removing the right kidney laparoscopically only if there was a clear advantage to the donor to retain the left kidney [76,77]. However, some urologists affirmed the opposite: that right-sided LLDN did not represent a difficult technique if performed by surgeons with sufficient laparoscopic experience, offering results equal to that of left-sided LLDN [25,54,55,57,70–72,76].

Similarly, different opinions were given in the literature regarding the contraindications to LLDN. Some authors stated previous extensive abdominal surgery as the only contraindication for laparoscopy [2,6]. Obesity was a contraindication in the opinion of others and whether to exclude a potential donor from laparoscopic donor nephrectomy techniques based on body mass index (BMI) still remains a topic of dispute. Early experience with laparoscopic surgery led to the belief that a BMI >30 resulted in higher complication rates [6,64]. Recent studies, however, reported that markedly obese donors had no increase in operative blood loss, postoperative serum creatinine, or major complications compared with nonobese donors [25,26,66,67]. Only one study, however, reported poorer outcomes in obese male donors (level of evidence 4) [63].

Generally, and probably irrespective of surgical technique, obese renal donors may have an increased risk of developing chronic medical disease with a solitary kidney as obesity represents a serious threat to health and is linked to the risk of later developing hypertension or diabetes. At present there are no studies specifically addressing the issue of the long-term medical risks for living renal donors. For reasons of technical difficulty, many urologists refrained from performing donor nephrectomy laparoscopically on markedly obese donors.

Two studies assessed donor age as a potential risk factor [40,59] and reported small significant deficiencies with respect to postoperative pain, social functioning, and mental health in older compared with younger donors. However, in general, older donors seemed to have similar surgical outcome and postoperative quality of life when compared with younger donors.

Summarizing, the exclusion criteria for LLDN were represented by comorbidity, acute or chronic disease and malignancy of the donor, previous extended abdominal surgery, and, in some cases, obesity.

3.2. *Surgical technique*

Regarding the technical aspects of LDN, three different techniques were reported: purely transperitoneal laparoscopic (ie, LLDN), hand-assisted laparoscopic (HALLDN), and retroperitoneoscopic (RLDN).

The proponents of pure LLDN advocated the potential minimal invasiveness of this procedure with perceived better cosmetic results and advised this method for donors who place great importance on postoperative cosmetic appearance. Some surgeons also preferred this approach for small donors who did not have enough intra-abdominal space for HALLDN [46,48,49,51]. The proponents of HALLDN believed that this technique was generally faster to perform than LLDN and that it was safer with lower risk for conversion to open surgery. It was also argued that significantly shorter WITs were reported for HALLDN compared to LLDN [47,76].

The proponents of the retroperitoneoscopic approach (RLDN) believed that this procedure allowed an easier access to the renal hilum with better exposure for the

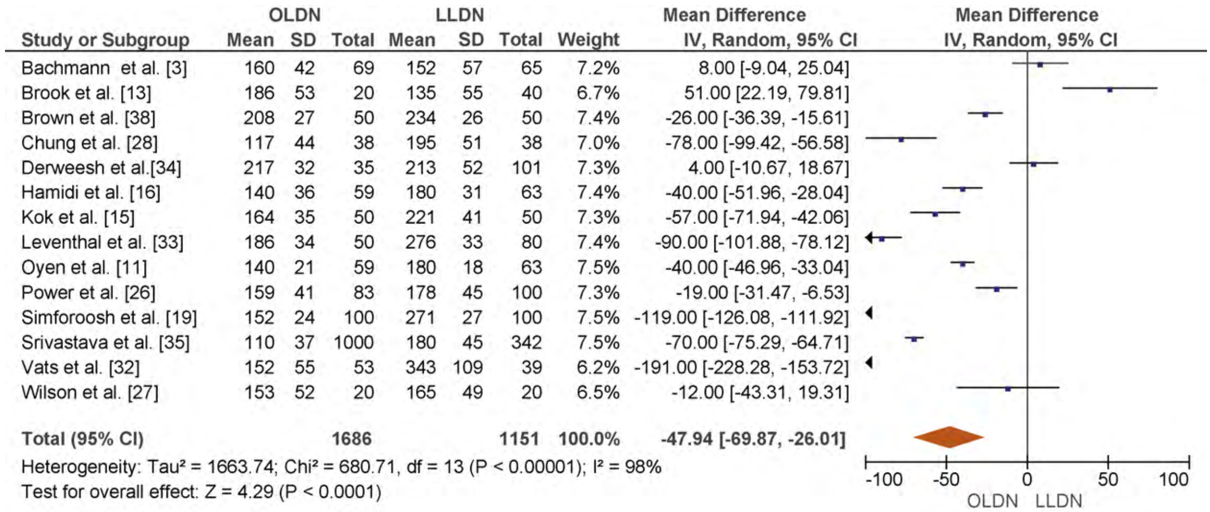

Fig. 1 – Forrest plot of open living-donor nephrectomy versus laparoscopic living-donor nephrectomy for operative time.
CI = confidence interval; SD = standard deviation; IV = inversed variance, df = degree of freedom; OLDN = open living donor nephrectomy; LLDN = laparoscopic living donor nephrectomy.

dissection of the renal vessels, with an adequate WIT, and that it was followed by less postoperative pain and a lower complication rate compared with other laparoscopic techniques [3,6,37].

Essentially, the choice for the technique of LDN must be based on surgeon preference. In a procedure where minute mistakes will potentially harm both the donor and the recipient, the technical proficiency must be extremely high and therefore each surgeon must use the technique with which he or she feels most comfortable.

3.3. *Outcomes*

3.3.1. *Comparing OLDN and LLDN*

Table 1 and Figs. 1 and 2 summarize the results from the studies comparing LLDN and OLDN. Four studies reported a significantly longer operating time (OPT) for LLDN compared to OLDN [11,12,15,19], while one study [13] reported a shorter OPT for LLDN. All five studies reported a significantly longer WIT in LLDN compared to OLDN. For LLDN, less postoperative pain (end point postoperative requirements for analgesia) and shorter hospital stay compared with OLDN was seen.

These findings were confirmed by most of the systematic reviews [20,21,23–25] except for one [22], which reported no significant difference between OLDN and LLDN concerning OPT and WIT. This latter systematic review also reported less postoperative pain and a shorter hospital stay for OLDN.

In nonrandomized prospective studies [26–28] and in retrospective studies [3,26–28,30,33–36,38] essentially the same peri- and postoperative outcomes were reported for OLDN and for LLDN. In none of these studies was there any significant difference between the OLDN and the LLDN groups concerning the postoperative graft function and graft survival.

Assessing the UNOS database, Troppmann et al. [36] analyzed the reported results of 2576 OLDN and 2734 LLDN. In this database, the incidence of delayed graft function was

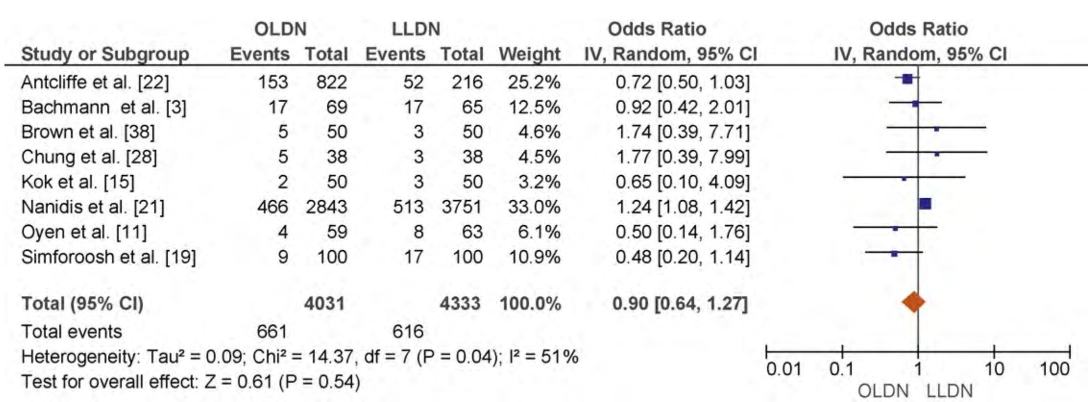

Fig. 2 – Forrest plot of open living-donor nephrectomy versus laparoscopic living-donor nephrectomy for overall donor complications.
OR = odds ratio; CI = confidence interval; SD = standard deviation; df = degree of freedom; OLDN = open living donor nephrectomy; LLDN = laparoscopic living donor nephrectomy.

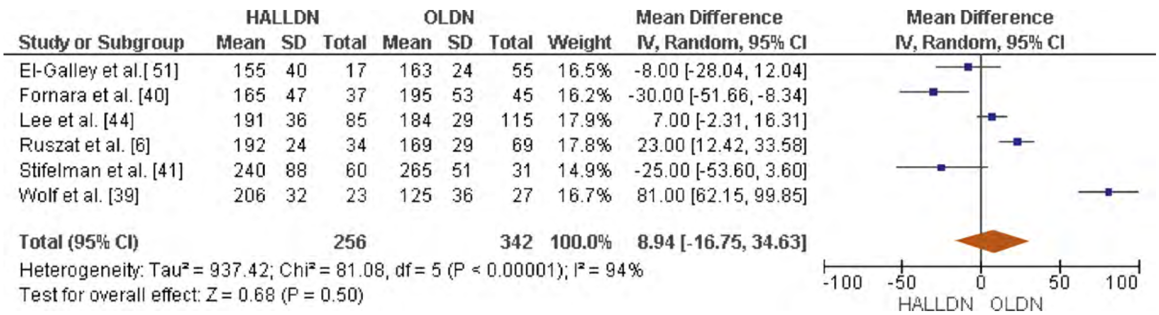

Fig. 3 – Forrest plot of open living-donor nephrectomy versus hand-assisted laparoscopic living-donor nephrectomy for operative time.
CI = confidence interval; SD = standard deviation; IV = inversed variance; df = degree of freedom; OLDN = open living donor nephrectomy; HALLDN = hand-assisted laparoscopic living donor nephrectomy.

5% in OLDN grafts and 5.9% in LLDN grafts ($p = 0.18$). However, significantly more patients in the LLDN group had a serum creatinine at discharge of >1.4 mg/dl (1116 in OLDN vs 1274 LLDN, $p = 0.002$), although the decrease in serum creatinine and the urine volume during the first 24 h were not significantly different between the two groups. At 1 yr postoperatively, there was no significant difference between the OLDN and LLDN groups in the UNOS database regarding serum creatinine level, frequency of acute rejections (17.4% OLDN, 18.2% LLDN), and graft survival (94.1% vs 94.4%).

3.3.2. Comparing OLDN and HALLDN

Table 2 and Fig. 3 summarize the results from the studies comparing HALLDN and OLDN. There was only one RCT on this topic and this reported both a significantly shorter OPT (125 vs 206 min) as well as shorter WIT (96 vs 183s) for OLDN than for HALLDN. The same RCT found lower postoperative pain and shorter hospital stays for HALLDN and no difference in the postoperative creatinine course [39]. Also, HALLDN was associated with a shorter period of reconvalescence compared with the OLDN technique.

Greco et al. [40], in a retrospective case series comparing historic OLDN and HALLDN controls, reported a shorter WIT and a shorter postoperative recovery time for HALLDN (level of evidence 4). Measured levels of postoperative serum indicators of surgical trauma were better for HALLDN, with a faster recovery time for the patients.

Similar findings were reported by two other nonrandomized studies comparing HALLDN and OLDN [41,42]. In a recent large case series of 199 patients, HALLDN was reported to have shorter OPT as well as recovery times, and fewer complications compared with OLDN [42].

Thus, the evidence comparing OLDN and HALLDN exclusively came from retrospective case series comparing with either historic or contemporary controls. Despite this limitation, the evidence uniformly suggested that HALLDN had advantages in surgical time, recovery time, and morbidity with the same functional transplant results [39–45].

3.3.3. Comparing LLDN with HALLDN

Table 3 and Figs. 4 and 5 summarize the results from the studies comparing LLDN with HALLDN. All the published studies comparing these two laparoscopic techniques essentially reported no significant differences regarding mean OPT, WIT, length of hospital stay, use of intravenous analgesia, and graft function [46–49].

Bargman et al. [46] reported the only randomized trial between LLDN and HALLDN with comparable outcomes, no difference in postoperative pain or complication rates, and

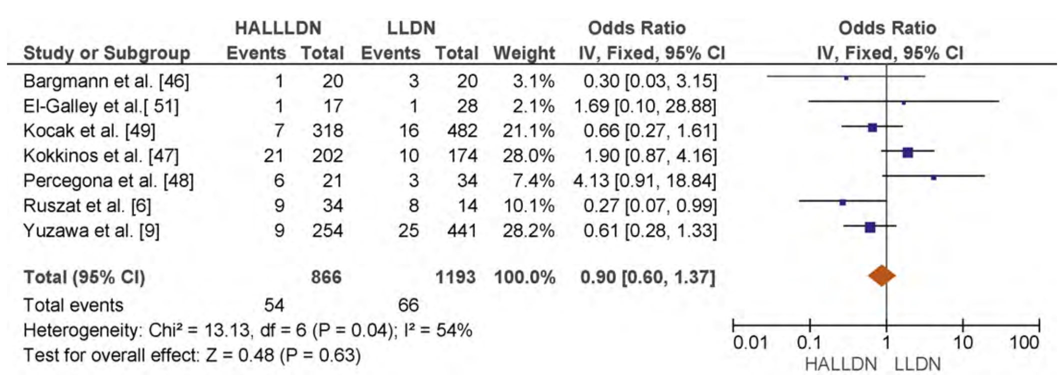

Fig. 4 – Forrest plot of hand-assisted laparoscopic living donor nephrectomy versus laparoscopic living donor nephrectomy for overall donor complications.
OR = odds ratio; CI = confidence interval; SD = standard deviation; df = degree of freedom; HALLDN = hand-assisted laparoscopic living donor nephrectomy; LLDN = laparoscopic living donor nephrectomy.

Study or Subgroup	HALLDN Mean	HALLDN SD	HALLDN Total	LLDN Mean	LLDN SD	LLDN Total	Weight	Mean Difference IV, Random, 95% CI
Bargmann et al. [46]	219	28	20	200	21	20	25.6%	19.00 [3.66, 34.34]
El-Galley et al.[51]	155	40	17	180	56	28	23.1%	-25.00 [-53.14, 3.14]
Ruiz-Deya et al. [52]	165	12	23	215	12	10	26.4%	-50.00 [-58.91, -41.09]
Ruszat et al. [6]	192	24	34	212	34	14	24.9%	-20.00 [-39.55, -0.45]
Total (95% CI)			**94**			**72**	**100.0%**	**-19.09 [-55.03, 16.84]**

Heterogeneity: Tau² = 1250.93; Chi² = 59.66, df = 3 (P < 0.00001); I² = 95%
Test for overall effect: Z = 1.04 (P = 0.30)

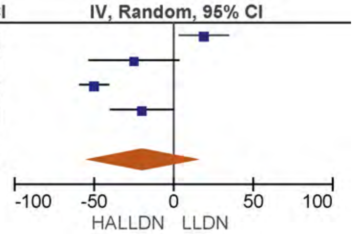

Fig. 5 – Forrest plot of hand-assisted laparoscopic living-donor nephrectomy versus laparoscopic living-donor nephrectomy for operative time.
CI = confidence interval; SD = standard deviation; IV = inversed variance; df = degree of freedom; HALLDN = hand-assisted laparoscopic living donor nephrectomy; LLDN = laparoscopic living donor nephrectomy.

no difference between the two groups in the donors' SF-36 quality of life assessment at 1 and 3 mo postoperatively.

3.3.4. Comparing LLDN with HALLDN and OLDN

Table 4 and Figs. 6 and 7 summarize the results from the studies comparing LLDN with HALLDN and OLDN.

The available studies–one each at: level of evidence 4 [6], level of evidence 2b [9], level of evidence 2a [50], level of evidence 2b [51], and level of evidence 3b [52]–comparing LLDN (both transperitoneal or retroperitoneal) with either HALLDN or open surgery reported comparable outcomes regarding OPT, WIT, and graft function. Shorter hospital stay and less postoperative pain were reported for laparoscopy (both LLDN and HALLDN) compared with OLDN.

El-Galley et al. [51] reported similar graft function for laparoscopic and open donor nephrectomy with LLDN and HALLDN patients returning to normal physical activities (3.3 ± 2 wk for LLDN, 3.6 ± 2 wk for HALLDN and 5.9 ± 4 wk for OLDN, $p < 0.001$) and to work (3.7 ± 1.8 wk for LLDN, 4.2 ± 2 wk for HALLDN and 5.9 ± 2 wk for OLDN, $p < 0.001$) significantly earlier than OLDN patients.

Among the noncomparative studies, Alcaraz et al. [2] reported their experience with 60 donors. The mean WIT was 185 ± 82 s, with two cases where WIT exceeded 4 min.

Study or Subgroup	OLDN Mean	OLDN SD	OLDN Total	LLDN+HALLDN Mean	LLDN+HALLDN SD	LLDN+HALLDN Total	Weight	Mean Difference IV, Random, 95% CI
Brook et al. [13]	2	0.9	20	3.6	0.9	40	17.0%	-1.60 [-2.08, -1.12]
El-Galley et al.[51]	2	1	55	3	2	28	15.5%	-1.00 [-1.79, -0.21]
Lee et al. [44]	1.4	0.9	115	2.1	0.7	85	17.9%	-0.70 [-0.92, -0.48]
Merlin et al. [24]	1.7	1.5	0	5	1.8	0		Not estimable
Ruszat et al. [6]	1.9	0.4	69	3.9	1	14	16.8%	-2.00 [-2.53, -1.47]
Srivastava et al. [35]	2	2	1000	4.5	2	342	17.9%	-2.50 [-2.75, -2.25]
Wolf et al. [39]	1.6	0.9	27	3.5	2	23	14.9%	-1.90 [-2.79, -1.01]
Total (95% CI)			**1286**			**532**	**100.0%**	**-1.62 [-2.42, -0.82]**

Heterogeneity: Tau² = 0.92; Chi² = 119.17, df = 5 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.97 (P < 0.0001)

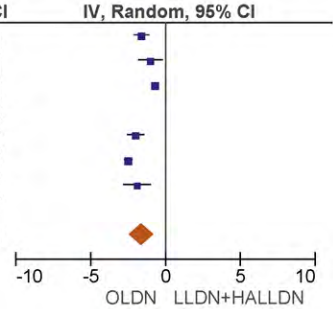

Fig. 6 – Forrest plot of open living donor nephrectomy versus laparoscopic living-donor nephrectomy plus hand-assisted laparoscopic living-donor nephrectomy for warm ischemia time.
CI = confidence interval; SD = standard deviation; IV = inversed variance; df = degree of freedom; OLDN = open living donor nephrectomy; LLDN = laparoscopic living donor nephrectomy; HALLDN = hand-assisted laparoscopic living donor nephrectomy.

Study or Subgroup	OLDN Mean	OLDN SD	OLDN Total	LLDN/HALLDN Mean	LLDN/HALLDN SD	LLDN/HALLDN Total	Weight	Mean Difference IV, Random, 95% CI
El-Galley et al.[51]	3	2	55	2	2	17	9.2%	1.00 [-0.09, 2.09]
El-Galley et al.[51]	3	2	55	2	2	28	12.3%	1.00 [0.09, 1.91]
Ruszat et al. [6]	13	2	69	11	2	34	14.4%	2.00 [1.18, 2.82]
Ruszat et al. [6]	13	2	69	13	3	14	4.4%	0.00 [-1.64, 1.64]
Stifelman et al. [41]	4.5	1.2	31	3.5	0.7	60	29.7%	1.00 [0.54, 1.46]
Wolf et al. [39]	2.6	0.7	27	1.7	0.9	23	30.1%	0.90 [0.45, 1.35]
Total (95% CI)			**306**			**176**	**100.0%**	**1.07 [0.71, 1.43]**

Heterogeneity: Tau² = 0.06; Chi² = 7.20, df = 5 (P = 0.21); I² = 31%
Test for overall effect: Z = 5.83 (P < 0.00001)

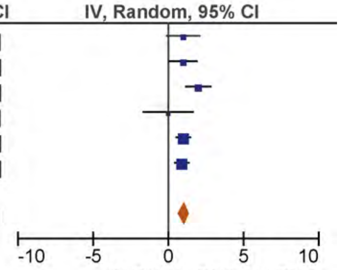

Fig. 7 – Forrest plot of open living-donor nephrectomy versus laparoscopic living-donor nephrectomy plus hand-assisted laparoscopic living-donor nephrectomy for duration of hospital stay.
CI = confidence interval; SD = standard deviation; IV = inversed variance; df = degree of freedom; OLDN = open living donor nephrectomy; LLDN = laparoscopic living donor nephrectomy; HALLDN = hand-assisted laparoscopic living donor nephrectomy.

The postoperative creatinine nadir was achieved on post-transplant day 3 on average, and patient and graft survival at 1 yr was 100% and 95%, respectively.

Bollens et al. [72] reported for right-sided LLDN a mean WIT of 135 s and mean recipient glomerular filtration rate of 67.3 ml/min after 30 d without any graft losses.

In conclusion, the real benefits of a laparoscopic technique compared with OLDN were represented by lower postoperative pain, shorter hospital stays, a shorter period of convalescence, and an earlier return to normal physical activities, while no differences were reported about the outcomes regarding the graft function.

3.4. Complications

When LLDN was established as a new technique, it was associated with a high reported complication rate, with ureteral injuries, and resulting loss of organs. Reported complications have been markedly reduced in more recent series, apparently with increasing experience [78].

The reported donor complication rate in recent series was not significantly different between open and laparoscopic techniques. Reported intraoperative complications of laparoscopic donor nephrectomy were pleural laceration; ureteral injury; bleeding; injuries to the liver, spleen, or diaphragm; and conversion to open surgery. Reported postoperative complications were hematoma, fever, wound pain, pneumonia, bowel paralysis, nausea, wound infection, urinary tract infection, graft loss, reoperation, ureteral stricture, or lymphocele formation [3,6,65,76,78,79].

Reported conversion rates for LLDN were 0–13.3% [23]. An analysis of reasons to convert reported in one series included intraoperative hemorrhage or vascular injury (65%), difficult kidney exposure or donor obesity (20%), vascular staple malfunction (12%), and loss of pneumoperitoneum (3%) [50].

Early LLDN series [4] reported a relatively high rate of postoperative ureteral complications (9.1%), which could have been due to extensive ureteral dissection with resulting distal ureteral ischemia. Subsequently, some authors reported a reduced rate of this complication (3%) with technical modifications by which all the tissue lateral to the gonadal vein was preserved, thus maintaining a good ureteral blood supply. Breda et al. [79] reported that, in their opinion, gonadal vein preservation with the specimen during laparoscopic donor nephrectomy was not required, but preservation of the periureteral blood supply was sufficient to prevent ureteral strictures.

Another series reported a 2% rate of ureteral complications [56]. In a randomized trial by Simforoosh et al. [19] the ureteral complication rate for OLDN was 2%, compared with 0% for LLDN.

The main complications of LLDN seemed to be due to injury to the spleen or the bowel. These could result from using a stapler or when retrieving the kidney [23]. Vascular complications, in particular injury to the renal artery or vein, have been reduced with improvements in experience and technique.

Pulmonary complications were more common with OLDN and this was explained by the incision needed for OLDN [50].

Wound complications, including infection, hematoma, seroma, or incisional hernia, could occur in all types of operation and they did not seem to be procedure specific [23].

In conclusion, the high-grade complications associated with LLDN were represented by ureteral injury; bleeding; injuries to the liver, spleen, or diaphragm; and graft loss.

3.5. Mortality after living kidney donation

Matas et al. [80] conducted a survey of transplant centers in the United States to address donor mortality rates. Of 10 828 analyzed donors, 2 died and 1 was in a persistent vegetative state because of intraoperative bleeding related to hypotension (a total of 0.03%). A concern was that all three of these donors had undergone LLDN. In the same year, Vastag [81] reported that five donors died shortly after LDN: two from pulmonary embolisms, one patient from acute hemorrhage, and one from respiratory failure (with one death unaccounted for). In addition, seven other kidney donors had died "well after surgery."

There is a possibility of overlap between the five cases of Vastag and the three of Matas et al. Nevertheless, these mortality cases were not reported in some studies published at a later date [82]. For this reason, concern has arisen that there is an underreporting of severe complications, specifically mortality of living kidney donors. In their review, Shokeir et al. [20] found that according to the published literature, underreporting of donor mortality and graft losses following laparoscopic donor nephrectomy was serious and mostly omitted when the techniques were assessed in review articles.

By 1974, five donor deaths had occurred in the early postoperative period after OLDN. Between 1974 and 1980, no perioperative mortalities were reported [20]. From January 1980 to January 1991, Najarian et al. [83] surveyed all members of the American Society of Transplant Surgeons about donor mortality at their institutions. Among 19 368 LDNs, they documented five early deaths and estimated that the perioperative mortality associated with OLDN in the United States was at least 0.03%. Pulmonary embolisms were the major cause of death. Since 1991, no perioperative mortalities have been recorded following OLDN [20]. Actually, 0.03% mortality remains a stable rate for both OLDN and LLDN.

Shokeir, in his literature review of data published until October 2006, found 11 perioperative donor deaths for laparoscopic and 10 for open donor nephrectomies and concluded that there may be underreporting of donor mortality [20].

4. Conclusions

Our analysis suggests that based on published series, both techniques of donor nephrectomy have comparable complications and equal functional graft outcomes. Laparoscopic techniques of donor nephrectomy may have advantages in postoperative recovery and duration of pain, but these differences are difficult to quantify and difficult to assess in their impact on long-term outcome. Laparoscopic techniques of donor nephrectomy have reported disadvantages in terms of longer OPT and longer WIT. However, the available evidence suggests that the longer WITs do not result in reduced graft function or survival, with the caveat that follow-up for transplantations following laparoscopic donor nephrectomy is still considerably shorter than for the open donor techniques.

Not surprisingly, most evidence in this field comes from case series and most of them are retrospective. While this constitutes a drawback, it is evident that prospective randomized trials are extremely difficult to perform in this field.

There is justifiable concern that underreporting of major complications in LDN was, and perhaps may be, an issue; therefore, national or international registries should be established for all LDNs.

As LDN always is a highly demanding as well as highly elective procedure, the greatest care for an uncomplicated outcome will be warranted. Based on the evidence, both LLDN and OLDN can be considered standard of care in experienced hands. LLDN seems to offer advantages in terms of measured blood loss, postoperative analgesic requirements, and length of hospital stay, and disadvantages in terms of surgical time and WIT. Whether the advantages outweigh the disadvantages cannot be assessed definitively at present–long-term follow-up data on graft survival and RCTs comparing OLDN and LLDN are missing–and will require further evidence. Thus, at present, individual judgment and experience will determine the technique.

Author contributions: Francesco Greco had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Greco, Hoda, Alcaraz, Bachmann, Hakenberg, Fornara.
Acquisition of data: Greco.
Analysis and interpretation of data: Greco, Hoda.
Drafting of the manuscript: Greco.
Critical revision of the manuscript for important intellectual content: Alcaraz, Bachmann, Hakenberg, Fornara.
Statistical analysis: Hoda.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Alcaraz, Bachmann, Hakenberg, Fornara.
Other (specify): None.

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