

Long-Term Graft Function in a Randomized Clinical Trial Comparing Laparoscopic Versus Open Donor Nephrectomy

Nasser Simforoosh, Abbas Basiri, Nasser Shakhssalim, Shahram Gooran, Ali Tabibi, Ali Khoshdel, Seyed Amir Mohsen Ziaee

Abstract

Objectives: To evaluate and compare the long-term graft and survival rates in kidney transplant recipients who had undergone laparoscopic donor nephrectomy versus those who underwent open donor nephrectomy.

Materials and Methods: Our study was done with 100 cases of laparoscopic donor nephrectomy and 100 cases of open donor nephrectomy, performed between July 2001 and September 2003. Mean follow-up of recipients in this study was 6.6 ± 2.4 years (range, 1-9.3 y). This study has a longer follow-up than previous randomized clinical trials. We compared patient and graft survival in recipients of laparoscopic donor nephrectomy versus those who had open donor nephrectomy.

Results: Mean duration of kidney warm ischemia time was 8.7 ± 2.7 minutes for laparoscopic donor nephrectomy and 1.8 ± 0.92 minutes for open donor nephrectomy. There were no significant differences in 5-year graft survival between the laparoscopic donor nephrectomy and open donor nephrectomy groups (89.5% vs 84.3%; $P = .96$). There were no differences in delayed graft function between the laparoscopic donor nephrectomy and open donor nephrectomy groups (8 and 11 patients; $P = .135$). There was a significant difference in 5-year graft survival between

recipients with a history of delayed graft function and those without delayed graft function (63.2% vs 89.7%; $P = .04$). Despite a longer warm ischemia time in laparoscopic donor nephrectomy group (8.69 vs 1.87 min; $P = .0001$), warm ischemia time had no effect on graft outcome in long-term follow-up.

Conclusions: Although earlier experiences with laparoscopic donor nephrectomies were associated with concerns about long-term effects of laparoscopic donation on the graft function in the recipient, our long-term results confirm that laparoscopic donor nephrectomy provides similar graft outcome to open donor nephrectomy.

Key words: Kidney transplant, Laparoscopic donor nephrectomy, Open donor nephrectomy, Long-term follow-up

Introduction

Kidney transplant is the treatment of choice in managing most patients with end-stage renal disease.^{1,2} The gap between supply and demand is increasing. Therefore, there is global trend toward living-donor kidney transplant.^{3,4} Laparoscopic donor nephrectomy (LDN) was first introduced by Ratner and associates^{5,6} to encourage live donation, claiming less postoperative pain, smaller incision, and better cosmeses compared with open donor nephrectomy (ODN).⁶ Laparoscopic donor nephrectomy is gaining popularity and has become the standard of care for donor nephrectomy in many transplant centers.⁷⁻⁹ Although many large retrospective studies have shown the safety and efficacy of LDN,^{9,10} several randomized clinical trials (RCT) have been performed to compare LDN

From the Shahid Labbafinejad Medical Center, Urology and Nephrology Research Center (UNRC), Shahid Beheshti University, M.C. (SBMU), Tehran, I.R. Iran.

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Corresponding author: Nasser Simforoosh, 1. Urology Department of Shahid Labbafinejad Hospital, 9th Boushan St., Pasdaran Ave., Tehran, PO Box: 16666-94516, Iran.

Phone and Fax: +98 21 2258 8016 **E-mail:** simforoosh@urtc.org.ir

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and ODN with much evidence and large numbers of cases. We previously reported the first RCT comparing various outcomes between LDN and ODN in kidney transplants and found that LDN showed better donor satisfaction and less morbidity with an almost equivalent graft outcome.¹¹ This study sought to compare graft outcomes in recipients of LDN and ODN with a much longer follow-up of our previously reported RCT.

Materials and Methods

Our original prospective study included 100 cases of LDN and 100 ODN was performed between July 2001 and September 2003. They were assigned randomly to ODN and LDN groups using a balanced randomization method.¹¹ The present study has a longer follow-up than the previous study. One hundred fifty-six patients had follow-ups greater than 5 years; also, 10 patients died, and only 7 cases (2 patients in the LDN group and 5 in the ODN group) were missed during the first 5 years. Mean follow-up of recipients in this study was 6.6 ± 2.4 years (range, 1-9.3 y). All protocols were approved by the ethics committee of the institution before the study began, and the protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Written, informed consent was obtained from all patients.

Recipient and graft survival and serum creatinine levels were recorded during follow-up. As reported previously,¹¹ eligibility criteria including donor body mass index $< 28 \text{ kg/m}^2$, no complexity in donor renal vessels, recipient age of 18 to 65 years, and an absence of hemolytic uremic syndrome or focal segmental glomerulosclerosis in recipients. The LDN or ODN was performed by 2 cosurgeons (68 ODN and 69 LDN by N.S. and 32 ODN and 31 LDN by A.B.) on the left kidney in all patients. The kidney was transplanted by the same urologist who performed nephrectomy.

Warm ischemia time (WIT) is defined as *the time from renal artery occlusion to kidney immersion in ice-slush*, and cold ischemia time is defined as *the time between kidney immersion in ice-slush and graft revascularization*. Graft failure is defined as *the need for renal replacement therapy from any cause* and delayed graft function (DGF) is defined as *a serum creatinine value of $> 309.4 \mu\text{mol/L}$ on the third day after transplant*. Both techniques of donor nephrectomy

have been described previously.¹² Briefly the surgical technique used for ODN was the standard retroperitoneal flank approach. For LDN, under general anesthesia and using a transperitoneal approach in the modified flank position, a video laparoscope was introduced through a 12-mm umbilical port 12-mm pararectal, and 5-mm epigastric ports were used for the dissecting instruments. For ligating renal vessels, simple metal clips were used. The kidney was extracted manually from the abdominal cavity by the surgeon via a Pfannenstiel incision. Immunosuppression was similar for the 2 groups: We used cyclosporine, mycophenolate mofetil, and prednisolone. Antithymocyte globulin was used if indicated.

Survival curves were constructed using the Kaplan-Meier method, and the log-rank test was applied to compare groups for patient and graft survival. Baseline characteristics were compared using the *t*, chi-square, and the Fisher exact tests. The WIT groups were compared using an analysis of variance with the Bonferroni correction. Spearman's rank correlation coefficient also was used to evaluate correlations. The Cox proportional hazards regression model was applied to evaluate influential factors on survival. *P* values less than .05 were considered significant.

Results

Characteristics of patients in both groups have been described elsewhere.¹¹ Three kidney recipients in the ODN group, but none in the LDN group were related to the donor in the first degree. Patients in both groups were comparable regarding the number, age, sex (Table 1), and immunosuppressive regimen. The recipients' outcome (including graft and recipient survival and graft function during follow-up) is shown in Table 1 and Figures 1 and 2.

Long-term follow-up outcomes

Overall 5-year patient survival was 94.4% and 5-year death-censored graft survival was 83.7%. There were no significant differences between male and female patients regarding 5-year patient survival ($P = .6$) and 5-year graft survival ($P = .92$). There were no significant differences in 5-year patient survival (91.9% and 96.7%; $P = .48$) and 5-year death-censored graft survival (84.3% and 89.5%; $P = .96$) when ODN and LDN were

Figure 1. Patient Survival Curve Constructed by the Kaplan-Meier Method

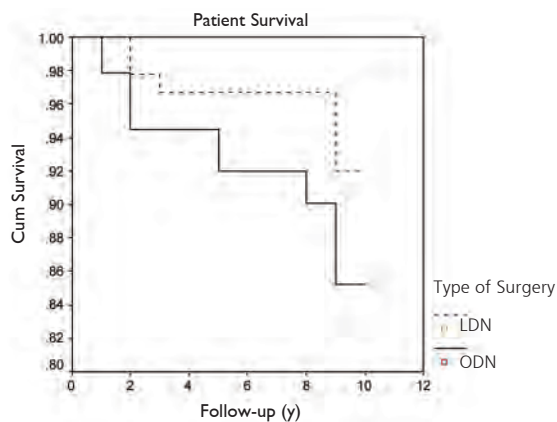
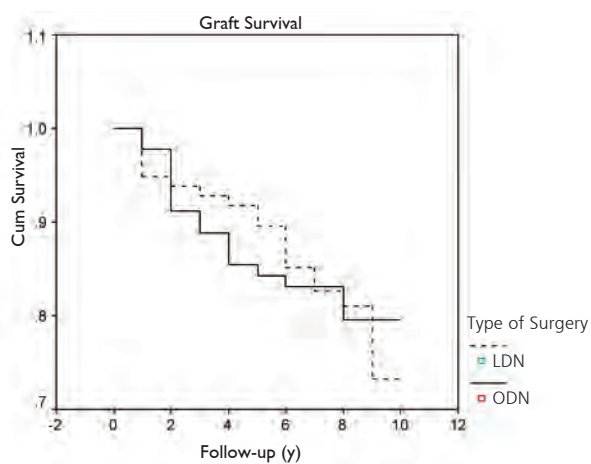


Figure 2. Graft Survival Curve Constructed by the Kaplan-Meier Method



compared. Both groups had the same graft function as measured by the serum creatinine value and the glomerular filtration rate calculation on the last follow-up visit ($P = .55$ and $P = .91$; Table 1).

Recipient outcomes in delayed graft function and nondelayed graft function patients

Total number of patients with DGF was 19 (ODN = 8, LDN = 11). Five-year death-censored graft survival was worse in allografts after DGF compared with allografts without DGF ($P = .04$) (Table 2). Although WIT was slightly longer in patients with DGF versus those without (6.2 min and 5.2 min) on Cox regression analysis, WIT had no significant effect on survival ($P = .99$).

Effect of warm ischemia time on graft outcomes in laparoscopic donor nephrectomy recipients

The mean kidney WIT was 8.7 ± 2.7 minutes (range, 4-17 min). Long-term graft loss and the mean level

of the last serum creatinine visit were not significantly different between the groups ($P = .55$). There was no statistically significant difference in long-term graft function among the 3 categories of WIT (Table 3). Nor were there any significant correlations between the last serum creatinine values and WIT on Spearman's rank correlation coefficient test ($P = .98$). Thirteen recipients died during follow-up (4 in the LDN group: cardiovascular event in 2, pulmonary emboli in 1, and advanced adenocarcinoma in 1; and 9 in the ODN group: uremia and infection in 1, pneumonia in 1, cardiovascular in 2, lymphoma in 1, head trauma in 1, pulmonary emboli in 1, and unknown in 2).

Table 1. Comparison of Long-Term Graft Outcomes in LDN and ODN Groups

	LDN	ODN	P Value
Number	100	100	
Age (y), mean (SD)	35.7 (11.4)	38.6 (11.7)	.08
Follow-up (d)	2422 (890)	2245 (1005)	.19
Serum creatinine ($\mu\text{mol/L}$), mean (SD)	110.50 (0.72)	1.52 (0.61)	.55
GFR (mL/min/1.73m^2), mean(SD)	59.7 (23.9)	59.2 (20.4)	.91
Death, (percentage)	4.1	9.5	.16
Overall functioning graft, (percentage)	80.6	81.7	.86
5-year patient survival, (percentage)	91.9	96.7	.48
5-year graft survival, (percentage)	84.3	89.5	.96

Abbreviations: GFR, glomerular filtration rate; LDN, laparoscopic donor nephrectomy; ODN, open donor nephrectomy

Table 2. Comparing Recipient Outcomes in Patients With and Without DGF

	With DGF	Without DGF	P Value
Patients, n	19	181	
Age (y), mean(SD)	35.3 (10.1)	37.4 (11.8)	.47
Male sex, percentage	73.7	61.9	.45
5-year-patient survival, percentage	100	93.9	.29
5-year-graft survival, percentage	63.2	89.7	.04
Serum creatinine ($\mu\text{mol/L}$), mean (SD)	194.48 (1.2)	1.5 (0.6)	.001
Warm ischemia time (min), mean (SD)	6.2 (4.8)	5.2 (3.9)	.99

Abbreviations: DGF, delayed graft function

Table 3. Warm Ischemia Time and Graft Outcome in LDN Recipients

WIT (min)	Number of Patients	Mean Serum Creatinine ($\mu\text{mol/L}$)	SE	95% Confidence Interval
4-6	21	135.25	0.15	1.23-1.83
6.1-10	52	129.95	0.10	1.26-1.68
>10	23	166.19	0.16	1.56-2.19

Abbreviations: LDN, laparoscopic donor nephrectomy; SE, standard error; WIT, warm ischemia time

Discussion

Donor nephrectomy is considered a unique operation because it exposes a person in complete health to potential complications of major surgery for the benefit of the recipient. Therefore, donor safety should be the first priority in a kidney transplant. A prior RCT with a large number of the cases demonstrated that LDN resulted in better donor satisfaction and morbidity when compared with ODN in long-term follow-up.¹¹ The same study showed that long-term graft survival was almost similar in LDN and ODN (93.8% and 92.7%).¹¹ Therefore, despite slower allograft recovery shown in LDN, our longer follow-up rules out the possible negative effect of pneumoperitoneum and longer WIT on graft outcome.

In the present study, graft outcomes of 100 LDNs and 100 ODNs were compared using a longer follow-up than a prior RCT.¹¹ Five-year graft survival in LDN and ODN were 89.5% and 84.3%. Therefore, graft survival is 5% more in LDN compared with ODN. Although, this is not clinically significant, long-term follow-up of 2 other RCTs carried out by Nicholson and associates¹³ and Dolsand associates¹⁴ were 5% superior in LDN when compared with ODN. Greco and associates published a systematic review after analysis of more than 50 comparative studies about the different techniques of donor nephrectomy (open, laparoscopy, hand-assisted laparoscopy) according to perioperative parameters and graft outcome, and concluded that even though WITs are longer in the laparoscopic group, postoperative graft function was not significantly different between these 3 modalities.¹⁵ Surprisingly, Goel and associates¹⁶ reported significantly better long-term graft function in LDN compared with ODN. These findings must be confirmed by more retrospective and prospective comparative studies with longer follow-ups.

Owing to possible deleterious effect of longer WIT seen in LDN, one may try to recover the kidney rapidly to decrease the WIT at the expense of potential traumatic injury to the donor or the graft. Because a LDN is associated with a longer WIT, it has been postulated that it carries a higher risk of reperfusion injury and dysfunction in the allograft. In deceased-donor transplant, it has been shown

that there was no difference in graft function with the different lengths of WIT < 35 minutes.¹⁷ Retrospective studies have shown that different lengths of WIT do not have deleterious effects on graft outcomes.¹⁸ We previously reported the effects of different lengths of WIT on graft outcomes in LDN in 3 different prospective times, and found no significant difference in any group.¹⁹

To the best of our knowledge, prospective studies with longer follow-ups measuring the effect of different levels of WIT on graft outcomes are lacking. In the present prospective study with median follow-up of 6.4 years, it is demonstrated that there is no significant difference in graft outcome when it is compared in 3 groups of LDN recipients with different lengths of WIT (4-6 min, 6.1-10 min, and 10.1-17 min). It should be emphasized that one should not rush to decrease the WIT at the expense of endangering the donor and the graft.

In a systematic review, Tooher and associates⁹ showed that although the WIT in a LDN seems longer when compared with an ODN, this is not reflected in higher numbers of a DGF for a LDN. In the present randomized study with a longer follow-up, there was no significant difference between the numbers of DGF in the LDN recipients with different levels of WIT (Table 3). Likewise, the numbers of DGF in LDNs and ODNs were not statistically different ($P = .135$). Nevertheless, recipients with DGF had worse graft outcomes compared to those without DGF (63.2% and 89.7%; $P = .04$). In a large retrospective study, Nogueira and associates²⁰ reported worse graft outcomes in long-term follow-up in recipients with DGF compared with those without DGF. This also has been reported by Patrizia,²¹ from data provided by the United Network for Organ Sharing. Surprisingly, in our study, the recipient who underwent kidney transplant with a WIT of 17 minutes had a serum creatinine level of 88.4 $\mu\text{mol/L}$ in 7.5 years after surgery.

Conclusions

Although earlier experiences with LDN have been associated with long-term effects of laparoscopic donation on the graft function in recipient, our long-term results confirm that a LDN has similar graft outcomes compared with an ODN. Every effort

should be made to decrease early graft dysfunction in an LDN and an ODN to further improve graft outcomes in the recipient. Delayed graft function leads to worse graft outcomes, both in LDN and ODN with no difference in either group. There is no relation in WIT up to 17 minutes and long-term graft outcome.

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