

LAPAROSCOPIC DONOR NEPHRECTOMY IN THE REPUBLIC OF NORTH MACEDONIA

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ABSTRACT

Introduction: Hand-assisted laparoscopic living donor nephrectomy has become the technique of choice for living donor kidney donations. Since 2018, 30 procedures have been performed at our clinic using this technique. The goal of this comparative analysis was to determine how surgical technique, specifically, hand-assisted laparoscopic living donor nephrectomy with hand assistance may affect early graft function when compared to open classical nephrectomy.

Material and methods: Retrospective analyses were performed, comparing the two techniques of kidney donation. Kidney transplantation was performed with the open standard technique in both groups. The primary outcome was early graft function, and levels of urine output, and plasma creatinine were analyzed at three time points. A secondary outcome was the quality of the operative technique, which was determined by the time of warm ischemia, blood loss, and duration of surgery. Additionally, we noted all complications, length of hospital stay, and patient satisfaction.

Results: In terms of warm ischemia time, there was no statistically significant difference between donors in both groups. It is important to note that in 2 recipients from Group II we did not observe diuresis at the conclusion of the operation. The recipients' diuresis was 515 ml $\pm$ 321SD in group I and 444 ml $\pm$ 271SD in group II. At 3, 12, and 36 hours postoperatively, there were statistically significant differences in the average serum creatinine values (p 0.05) in favor of group I. Similar results were observed in the second time measurement at 12 h and the third time measurement at 36 h for serum urea levels in recipients. The difference in serum urea values between the recipients in the groups at the first measurement (3h) following surgery was not statistically significant.

Conclusion: Hand-assisted laparoscopic donor nephrectomy is recognized as a safe and effective treatment. Donors in this situation have a different profile from other surgical patients; hence, they do not undergo surgery due to their own medical condition but for an altruistic reason, and with hand-assisted living donor nephrectomy. Such patients receive all the advantages of minimally invasive surgery. The two main objectives of a donor nephrectomy are to give the recipient the best possible kidney and to ensure the donor's complete safety.

Keywords: laparoscopic living donor nephrectomy, hand assisted, open classical living donor nephrectomy, kidney transplant

INTRODUCTION

In end-stage kidney disease, transplantation remains the best treatment. A living donor kidney transplant is superior to a deceased donor kidney transplant due to better graft survival rates, improved quality of life, and better cost effectiveness [1–3]. For over a 40-year period, living-donor kidney transplantation in the Republic of North Macedonia has been performed with an open surgical approach. Living-donor kidney transplantation requires a healthy individual to undergo a major surgery where the kidney is removed through a large lateral flank lumbotomy incision. This procedure requires a long recuperation period for the donor and is associated with significant pain. In contrast, in hand-assisted laparoscopic living kidney donor nephrectomy (LDN), tiny incisions with miniaturized instruments and a camera are used for the harvesting of the kidney. This minimally invasive procedure through a smaller incision has shown superior results in terms of decreased discomfort and blood loss, enabling faster recovery, a shorter hospital stay, less complications, and a return to normal daily activities. In terms of graft function, the literature does not reveal any significant differences between those two approaches [4–7]. Nowadays, LDN has become the preferred method for procuring kidneys from living donors. In our university clinical center in November 2018 we used LDN for the first time. Up to today, 30 have been performed in total, and our aim in this comparative evaluation was to evaluate the influence of surgical technique, either LDN or open classical nephrectomy, on early graft function.

MATERIAL AND METHODS

After obtaining the internal Ethical Committee's permission and signed informed consent from all patients, we evaluated the patients who underwent LDN performed between November 2018 and December 2022 at our University Clinic for Urology, Group I. In those cases, we compared them with Group II patients who underwent open classical donor nephrectomies. We evaluated 60 pairs of patients, 30 from Group I

who underwent laparoscopic living donor nephrectomy and open classical surgery for recipient and 30 from Group II who underwent open classical surgery for living donor nephrectomy and open classical surgery for recipient. The retrospective evaluation of the charts was conducted by an independent reviewer who was not informed of patient allocation in order to ensure an unbiased evaluation.

All patients undertook standard protocol procedures before surgery including a full medical and surgery history, laboratory evaluations, cardiology evaluation (EKG, echocardiography), and chest X-rays. Patients who were on chronic dialysis were dialyzed 24 hours before the renal transplant surgery.

The same surgical and anesthesia teams performed all transplantations in this evaluation.

Standard anesthesia protocol was used in all patients: regular non-invasive monitoring (EKG with 5 leads, non-invasive blood pressure, and pulse oximetry) before induction of anesthesia. At that time, in donor patients who underwent an open classical surgical procedure, an epidural catheter was placed, as well as in recipients without contraindication for epidural anesthesia. To avoid any interaction with the evaluated parameters, the epidural catheter was not used until the end of the surgery. Anesthesia was induced and maintained with remifentanyl (0.5 mcg/kg for induction, followed by 0.25 mcg/kg for maintenance) and propofol (3 mg/kg for induction, followed by 0.5–2 mg/kg for maintenance). Intubation was facilitated with atracurium (0.55 mg/kg). Mechanical ventilation was with a mixture of oxygen and air at 50% each, with tidal volumes of 6–8 ml/kg, and respiratory rates adjusted according to CO₂ levels between 35 and 40 mm Hg on Datex Ohmeda Avance S-5 ventilators. After induction and intubation, a central venous catheter and arterial line were placed for invasive hemodynamic monitoring.

The primary outcome was early graft function, and levels of urine output and plasma creatinine were analyzed at three time points: the 3rd, 12th, and 36th hours after the surgery. A secondary outcome was the quality of the operative technique. This was determined by the time of warm ischemia, blood loss, and duration of surgery. Additionally, we noted all complications, length of hospital stay and patient satisfaction.

RESULTS

We evaluated 60 pairs of patients, Group I ($n = 30$ pairs) for LDN and Group II ($n = 30$ pairs) for open classical donor nephrectomy. One donor was excluded from analysis who started LDN, but conversion was done due to obesity and a previous surgery in open classical nephrectomy. The baseline demographic characteristics were similar with respect to sex, age, American Society of Anesthesiologists physical classification (ASA), and body mass index (BMI). Demographic and clinical characteristics of the patients are shown in Table 1. There was no statistical difference observed between the demographic data of the patients. Only one patient from the classical open nephrectomy group had bleeding after surgery and was treated conservatively without any operative revision. Except for 4 patients in Group I who did not need hemodialysis and 2 patients in Group II, all of the patients underwent hemodialysis 24 hours prior to surgery.

Results from ischemia time: warm and cold are shown in Table 2. There was no statistically significant difference in warm ischemia time between groups. It is important that in 2 patients from Group II, we were not able to achieve diuresis at the end of the surgery. Diuresis in the groups were $515 \text{ ml} \pm 321\text{SD}$ for group I vs $444 \text{ ml} \pm 271\text{SD}$ for group II ($p=0.3$).

Table 2. Warm and cold ischemia time in groups

Parameter	Group I	Group II	p
Warm ischemia time (min)	$1,8730 \pm 0,49406$	$2,0150 \pm 0,62368$	0.3
Cold ischemia time (min)	$137,5000 \pm 12,50862$	$149,5000 \pm 38,62619$	0.1

The blood creatinine and urea values (mmol/L) for both groups at 3, 12, and 36 hours postoperatively are shown in Table 3 and Table 4. There were statistically significant variations between the average values of serum creatinine in the interval between 3, 12, and 36 hours ($p = 0.05$ in favor of Group I). As for serum urea levels, statistical significance was observed in the second and third time measurements in favor of Group I. In the first measurement, 3h after surgery, the difference in the value of serum urea between groups was not statistically significant.

Table 3. Serum cretinin (mmol/L) in 3.12 and 36 hours after the surgery.

Creatinin	GrouI	Group II	p
3H after surgery	$501,70 \pm 150,942$	$608,70 \pm 66,364$	0.01
12H after aurgery	$351,30 \pm 137,079$	$474,40 \pm 118,379$	0.00
36H after surgery	$218,70 \pm 105,738$	$324,00 \pm 134,722$	0.01

Table 4. Serum urea level (mmom/L) in 3.12 and 36 hours after the surgery.

Urea	Group I	Group II	p
3H after surgery	$12,64 \pm 4,565$	$13,82 \pm 1,882$	0.19
12H after aurgery	$12,67 \pm 4,653$	$14,94 \pm 3,521$	0.03
36H after surgery	$13,34 \pm 4,902$	$15,90 \pm 6,127$	0.07

DISCUSSION

LDN is considered a complex procedure and requires an experienced medical team with excellent laparoscopic skills. According to Higashihara and Siqueira, 30 LN are required to

Table 1. Demographic data and operative data

	Group I donors	Group II donors	Group I recipients	Group II recipients
Gender M/F	7/23	6/24	23/7	24/6
Age (years)	58 ± 9	54 ± 9	37 ± 12	31 ± 9
Kidney (left/right)	27/3	15/15	/	/
BMI (kg/m^2)	24 ± 10	23.4 ± 11	22 ± 9	23.5 ± 7
ASA classification I/ II/ III	0 / 17/ 13	0 /20/ 10	1 / 3 / 26	2/ 28
Month on dialysis	/	/	11 ± 4.8	11 ± 4.3
Anesthesia time (min)	192 ± 30	203 ± 31	240 ± 27	230 ± 31
Surgery time (min)	175 ± 35	140 ± 25	220 ± 40	215 ± 40
Blood loss (ml)	105 ± 40	240 ± 80	350 ± 60	410 ± 50
Warm ischemia time (sec)	1.8 ± 0.4	2.0 ± 0.6	72 ± 9	133 ± 37
Cold ischemia time (min)	137 ± 38	149 ± 38	/	/
Postoperative hospital stay	5.1 ± 0.7	6.7 ± 1.7	18 ± 7	20 ± 6
Complications	/	1	/	/
Death	/	/	/	/

overcome the learning curve and two proficient surgeons in LN to start an LDN program [3]. LDN has been preferred due to a longer renal vein and overall better technical ease, because right-side LDN requires the liver to be retracted, and duplicate clamping of the vena cava is challenging [3, 8]. In our series, only three cases of the LDN were right-sided, and due to the straight division of the renal vein at the vena cava vascular staplers, we lost approximately 1 cm of renal vein as compared to an open, classical surgical approach. This is described by Ratner and his coauthors in their article: 1 to 1.5 cm of renal vein can be lost compared to open and LDN [9]. This can generate some difficulties in graft anastomosis and can lead to vascular complications and possible graft loss [10]. Modifications are proposed to facilitate the safe harvesting of the right kidney through a laparoscopic approach. In our institution, hand assisted LDN is performed through an upper quadrant transverse incision. Vessel separation, kidney evacuation, and cavotomy repair are performed through this incision [11–13].

In Scandinavian countries, internal and external iliac veins are divided, which raises the external iliac vein higher up and circumvents the difficult anastomosis. The retrospective multi-institutional analysis done by Buell et al. covered 97 right LDNs done for different reasons (smaller right kidney, cyst in right kidney, multiple vessels on the left side kidney) [14]. In our case, the reasons for right-side LDN were multiple vessels in the left kidneys. We did not have any conversions to open nephrectomy due to bleeding or anatomical anomalies, as described in the literature. We had one conversion due to obesity and scars from previous surgery. There are concerns about ureteral length in LDN harvesting as well. In a randomized controlled trial by Berends and coauthors, the structural and functional aspects of LDN and an open one are being studied. They show similar results for renal vessels as for ureteral length, which was significantly higher in the LDN group for both left and right LDN. Ureteral injuries occur more often in LDN than during open donor nephrectomy (0–11%) versus 0–6%, respectively [15, 16]. In our series, we did not have any ureteral injuries or report any unwanted events. Technical modifications, an experienced surgical team, and subsequent trauma led to decreased complications in our case series. Refinements in surgical technique allowed a reduction in the incidence of ureteral complications in the evaluation of Ratner et al. [17].

Warm ischemia time is the time when the harvested kidney is still at body temperature with the blood supply cut off from the circulation before the start of perfusion. Due to the longer extraction time, warm ischemia time (WIT) is a major concern in LDN compared to open donor nephrectomy [18]. Any increase in WIT, it was thought, would lead to poor graft function. This was disclaimed by various authors and studies, showing no difference in graft function and recipient outcome depending on the slightly different WIT. They showed a range of WIT between 95 and 300 seconds [19, 20]. Our evaluation shows the same results as those described by our colleagues. Although WIT was prolonged in the LDN group, there was no repercussion on graft function. From history, there are reports of a longer WIT for LDN, at 102 seconds; this time is shortened to 75 seconds in hand assisted LDN. Nowadays WIT in LDN is almost identical with open classical donor nephrectomy [18–20].

In our series, WIT was within the range reported in the previous literature. Furthermore, our WIT maintained a time of 149 ± 53 STDV. This time is comparable with the one of Jacobs, who covered 738 cases of LDN performed over a period of six years [21]. With increased experience and a learning curve, this WIT can be reduced, although no evidence exists in the literature showing a correlation between WIT and early graft function or the level of serum creatinine during the first three months [22]. Jacobs et al. compared WIT 3 min. vs. >3 min. and WIT 5 min., 5–10 min., and >10 min. Prolonged WIT did not appear to have an effect on serum creatinine dehydrogenase level and graft function in the first three months after transplantation [21]. Although we did not evaluate the long-term graft survival in our investigation, several trials evaluated the effect of WIT on long-term graft function, showing no difference in outcome or serum creatinine as well [23].

According to the literature review, risk factors potentially affecting graft function and impairing kidney recovery are age, donor/recipient relationship, mismatched donors, warm ischemia time, cold ischemia time, and preservation time [23, 24]. We did not include cadaveric transplantation patients in our analysis. All of our donors were living donor transplant pairs in a family relationship. The mean age of donors in Group I was 58 ± 9 SD, and 54 ± 9 SD in Group II. The recipients' mean age was 37 ± 12 SD in group I vs. 31 ± 9 in group II. We did not notice any statistical

significance between groups in terms of warm and cold ischemia time, and since it was a living donor transplant, we did not preserve the kidneys. On the contrary, in larger transplant centers, preserving and packing the graft is the standard procedure for living donor transplants.

In the systematic review reported by Handschin et al., there is no significant difference in the rate of acute kidney rejection between LDN and open donor nephrectomy [16]. Similar results were shown in the University of Maryland series with more than 700 participants [21]. Our results are similar to those presented in the literature. We did not notice any acute kidney rejection in our series of 60 cases.

There are currently many studies available comparing LDN to open classical nephrectomy [17]. Those studies suggest the many benefits of LDN, including reduced blood loss, length of hospital stay, time to resume diet, analgesic requirements, and time to return to normal activities. Those recuperation times are one-third or two-thirds shorter than the equivalent ones for open classical nephrectomies. Esthetic results are better in LDN as well. All of those above-mentioned factors contribute to the increased rate of living donor transplants. This happened to be the case in Baltimore, where the living donor transplant rate increased to 100% when the laparoscopic technique was introduced [17, 25].

Open donor nephrectomy, compared to LDN hand-assisted, as in our series, has a shorter surgery time: 140 ± 25 min vs. 175 ± 35 min. There seems to be enough data, according to a recent systematic review, to say that renal function and renal blood flow are both impaired during pneumoperitoneum. Preoperative renal function, hydration, level of pneumoperitoneum, patient placement, and duration of pneumoperitoneum are some of the variables that affect how much the drop will be [26].

CONCLUSION

Open surgery can currently be replaced with a safe and efficient laparoscopic procedure. Hand-assisted laparoscopic donor nephrectomy is recognized as a safe and effective treatment, thanks in large part to the advancements in technology and surgical methods. Donors in this situation have a different profile from other surgical patients; hence, they do not undergo surgery due

to their own medical condition but for an altruistic reason. With hand-assisted laparoscopic living donor nephrectomy, they receive all the advantages of minimally invasive surgery with outcomes that are on par with those of open classic surgery in terms of graft function and receiver outcome. Laparoscopic donor nephrectomy has been developed as a way to increase the appeal of renal donation to potential donors. The two main objectives of a donor nephrectomy are to give the recipient the best possible kidney and to ensure the donor's complete safety.

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Резиме

ЛАПАРОСКОПСКА НЕФРЕКТОМИЈА НА ДАРИТЕЛ НА БУБРЕГ ЗА ТРАНСПЛАНТАЦИЈА ВО РС МАКЕДОНИЈА

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Вовед: Лапароскопската нефректомија на жив дарител на бубрег за трансплантација потпомогната со рака стана техника од избор за трансплантација од жив донор. Од 2018 година оваа процедура започна да се изведува и на нашата клиника. Целта на оваа компаративна анализа беше да се одреди дали хируршката процедура, поточно лапароскопската нефректомија од жив дарител потпомогната со рака може да влијае на функцијата на графтоот споредено со отворената класична нефректомија.

Материјали и методи: Ретроспективна компаративна анализа беше спроведена на двете техники на нефректомија на даватели на бубрег за трансплантација. Трансплантацијата на бубрег беше изведена со отворена класична метода кај двете групи. Примарен исход беше раната функција на графтоот, нивото на диуреза и плазма-концентрацијата на креатинин, кои беа анализирани во три временски точки. Секундарен исход беа квалитетот на оперативната техника детерминирана од времето на топла исхемија, крвозагубата и времетраењето на интервенцијата. Дополнително беа нотирани сите компликации, должината на болничкиот престој и задоволството на пациентите.

Резултати: Во однос на топлата исхемија, не добивме статистички сигнификантни резултати меѓу давателите на бубрег од двете групи. Важно за нагласување е дека кај двајца реципиенти од група II не забележавме диуреза на завршување на интервенцијата. Диурезата на примателите на бубрег беше $515 \text{ ml} \pm 321\text{SD}$ во група I и $444 \text{ ml} \pm 271\text{SD}$ кај група II. Во временските точки од 3, 12, и 36 часа постоперативно имаше статистички сигнификантна разлика во просечното ниво на серумскиот креатинин ($p < 0,05$) во прилог на групата I. Слични резултатите се добија и за втората и третата временска точка, 12 и 36 часа постоперативно за серумската вредност на уреа кај примателите на бубрег. Само во првата временска точка, 3 часа постоперативно, испитуваните вредности на серумската уреа беа статистички неситнификантни.

Заклучок: Лапароскопската нефректомија на жив дарител на бубрег потпомогна со рака е препознаена како безбедна и ефикасна процедура. Давателите на бубрег во оваа констелација имаат различен профил од другите хируршки пациенти. Тие не подлегнуваат на операција поради сопствена медицинска потреба, туку од алтруистична природа. Поради тоа, давателите на бубрег ги имаат придобивките на оваа минимално инвазивна хирургија, чии главни цели се да им се овозможи на примателите на бубрег најдобар можен графт по најбезбеден начин.

Клучни зборови: лапароскопска нефректомија на жив дарител, потпомогната со рака, отворена класична нефректомија на жив дарител на бубрег, трансплантација на бубрег