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The learning curve for modified handassisted retroperitoneoscopic living donor nephrectomy



Limin Shang^{1,2}, Mengmeng Zheng^{1,2}, Zhipeng Wang^{1,2} and Yichen Zhu^{1,2*}

Abstract

Background We aimed to introduce our modified hand-assisted retroperitoneoscopic living donor nephrectomy (HARPLDN) technique and define the learning curve.

Methods One hundred thirty-eight kidney donors who underwent modified HARPLDN by the same surgeon between May 2015 and March 2022 were included. A cumulative sum (CUSUM) learning curve analysis was performed with the total operation time as the study outcome.

Results In total, the mean operative time was 138.2 ± 32.1 min. The median warm ischemic time (WIT) and estimated blood loss were 90 s and 50 ml, respectively. The learning curve for the total operative time was best modeled as a second-order polynomial with the following equation: $CUSUM_{OT}$ (min) = (-0.09 case number²) + (12.88 case number) – 67.77 (R^2 = 0.7875; p < 0.05). The CUSUM learning curve included the following three unique phases: phase 1 (the initial 41 cases), representing the initial learning curve; phase 2 (the middle 43 cases), representing expert competence; and phase 3 (the final 54 cases), representing mastery. The overall 6-month graft survival rate was 99.3%, with 94.9% immediate onset of graft function without delayed graft function and 0.7% ureteral complications.

Conclusions Our modified method is safe and effective for living donor nephrectomy and has the advantages of a shorter operating time and optimized WIT. The surgeon can become familiar with the modified HARPLDN after 41 cases and effectively perform the next 97 cases.

Keywords Cumulative sum analysis, Hand-assisted retroperitoneoscopic live donor nephrectomy, Learning curve, Living donor nephrectomy

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Background

Hand-assisted retroperitoneoscopic surgery is a hybrid of laparoscopic and open surgical techniques. Handassisted retroperitoneoscopic surgery has the following advantages: more easily retracted tissue planes; better tactile feedback through the operator's hands; easily controllable bleeding by manual compression; direct access to the renal pedicles; and avoiding potential injury to the intraperitoneal organs [1-4]. Because the advantages apply to obese patients or patients with a history of abdominal surgery, the HARPLDN procedure is widely performed worldwide. Based on the medical situation in China, our center has made some modifications to the HARPLDN procedure. We have described the surgical procedure and determined the efficacy, efficiency, and favorable surgical outcomes using a modified HARPLDN [5].

Surgical proficiency has improved tremendously with technological innovations and surgical instruments. It is necessary to evaluate how surgeons acquire new surgical techniques, the learning curve is useful for such an assessment. The cumulative sum (CUSUM) analysis has been adopted for surgical techniques; [6] however, several studies have reported the learning curves for laparoscopic donor nephrectomy (LDN), hand-assisted laparoscopic live donor nephrectomy (RPLDN), [7–9] while the learning curve for HARPLDN has rarely been described. In this study, we have introduced our modified HARPLDN technique and estimated the learning curve case number using the CUSUM method to train and guide new learner competence.

Matherials and methods

Patient

The study was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University(ethics number, 2021-P2-172-01). A single experienced urologist performed 138 consecutive modified HARPLDN surgeries between May 2015 and March 2022. The surgeon has performed>500 laparoscopic upper urinary tract procedures and performed>100 modified HARPLDNs as first surgical assistant.

All donor preoperative laboratory tests were normal. Donors underwent a preoperative computed tomography (CT) angiography to evaluate the renal vessels. Split renal function was evaluated by radionuclide dynamic renal imaging. The criteria for choosing which kidney included a single renal artery, and the kidney with better relative GFRs remained in the donor. If the blood supply and GFR were the same on each side, we chose the left kidney because of the longer renal vein.

Baseline demographic and clinical data were retrospectively retrieved from the donors and matching recipients. Intraoperative parameters, including the operative time (OT), warm ischemic time (WIT), and estimated blood loss (EBL), were analyzed. The operative time was defined as the time between skin incision and skin closure. The WIT was defined as the time between renal artery stapling and placement of the kidney on ice. Postoperative complications were classified according to the modified Clavien classification system [10]. After hospital discharge, we followed the donors in our clinic until completion of wound healing and surgical recovery. The recipients were contacted 1, 3, and 6 months, and 1 year for follow-up evaluation. Clinically evident biopsyproven acute cellular rejection (ACR) was defined based on the Banff criteria [11]. Delayed graft function (DGF) was defined as the need for dialysis within the first 7 days after transplantation.

Modified HARPLDN procedure

The modified HARPLDN was used in all donor nephrectomies with patients in the full-flank, mid-lumbar flexion position. The surgical techniques have been described previously, [5] as briefly following in Fig. 1: the kidney was dissected from the adipose capsule using scissors in the avascular area rather than an ultrasonic scalpel; a 6-7 cm mini-open muscle-splitting incision was made with blunt dissection, which was performed parallel to the direction of the muscle fibers to separate the muscle tissue. Then, the surgeon inserted a hand through this mini-incision and simultaneously re-established the pneumoretroperitoneum without a hand-assisted port. At the same time, the time-zero donor kidney biopsy was obtained. Using the hand to place traction on the kidney, thus extending the renal artery or vein to the maximum length with transection using Hem-o-lock clips.

Cumulative sum analysis

The CUSUM technique was used for quantitative assessment of the learning curve. It calculates the running total of differences between the individual data points and the mean of all data points, and can therefore be performed recursively. The 138 cases were ordered chronologically, from the earliest-to-the latest surgery dates. The operative time for each case is denoted by x_i , and the mean operative time for all cases is denoted by μ .

CUSUM
$$_{OT} = \sum_{i=1}^{n} (x_i - \mu)$$

The CUSUM_{OT1} is the difference between the actual OT for the first case and the mean OT. CUSUM_{OT2} is the CUSUM_{OT1} added to the difference between the OT for the second case and the mean OT. The recursive process continued until the CUSUM_{OT} for the last case was calculated.



Fig. 1 Unique steps in modified HARPLDN technique. **a** The scope port is A, surgeon operated using ports B (12 mm) and C (5 mm), port D (5 mm) is for the assistant; **b** The kidney was dissected using scissors in the avascular area;**c** Modified mini-open muscle splitting Gibson incision; **d** This incision allowed hand-assistance to be achieved without hand-assisted device and rapid kidney extraction; **e** The time-zero donor kidney biopsy **f** The transection of renal artery

Statistical analysis

Continuous data are shown as mean \pm SD and categorical variables are expressed as count (%). To compare phases 1, 2, and 3, the categorical variables were analyzed with a chi-square test or Fisher's exact test, and the continuous variables were analyzed with analysis of variance. IBM SPSS Statistics 25 was used for statistical analyses. *P*-value<0.05 was considered statistically significant.

Results

Donor baseline characteristics are listed in Table 1. The study population included 51 (37.0%) males and 63 (63.0%) females with a mean age and body mass index (BMI) of 51.7 ± 7.2 years and 24.4 ± 2.9 kg/m², respectively. The median American Society Anesthesiologists (ASA) score was 2, accounting for 67.4% of the study population. Seven donors had hypertension (HTN) and one donor had diabetes mellitus (DM). 23.9% of the subjects had a history of abdominal surgery. All kidney donations were performed using the left kidney. The mean operative time was 138.2 ± 32.1 min. The median WIT and EBL were 90 s and 50 ml, respectively. The mean length of stay was 12.9 ± 3.5 days. The mean time for drainage tube removal was 4.9 ± 2.3 days.

Figure 2 shows the operation times plotted in chronological case order, and the $\rm CUSUM_{OT}$ learning curve was best modeled as a second-order polynomial with the

following equation: $CUSUM_{OT}$ (in minute) = (-0.09 case number²) + (12.88 case number - 67.77). The highest R [2] value was 0.7875 (p<0.05). Analysis of the CUSUM_{OT} demonstrated that the learning curve reached a plateau phase between cases 41 and 84. The consistent decline of CUSUM for OT after case 84 indicated the achievement of the learning curve at that point. Therefore, we could divide the learning process into the following three phases: phase 1 (the initial 41 cases); phase 2 (the middle 43 cases); and phase 3 (the final 54 cases). Comparisons among the three phases are presented in Table 1. Donor demographic characteristics were not significantly different among the three phases, excluding the age, ASA score, and the donor relationship to the recipient. The operative time was significantly decreased in phase 3 compared to phase 1 (p=0.005); however, the decrease was not significant from phase 1-to-phase 2 (p=0.191). The WIT was significantly decreased in phase 3 (p=0.005) compared to phase 1 and significantly decreased in phase 2 compared to phase 1 (p < 0.001). The EBL in phases 2 and 3 was less than phase 1, but the differences were not statistically significant. The mean removal time of the drainage tube was progressively shorter among the three phases (p=0.011).

All donor operations were successfully completed. The intra- and post-operative complications of the donors are presented in Table 2. No significant differences were detected among the three phases (p=0.81).

Table 1 Interphase comparisons of donor's characteristics

	Total (n = 138)	Phase 1 (<i>n</i> = 41)	Phase 2 (<i>n</i> =43)	Phase 3 (n = 54)	<i>P-</i> Value
Patient characteristics					
Age, years	51.7 ± 7.2	49.8±7.1	50.7±5.7	53.9 ± 7.8	0.010*
Gender					
male	51(37.0%)	19(46.3%)	14(32.6%)	18(33.3%)	0.331
female	87(63.0%)	22(53.7%)	29(67.4%)	36(66.7%)	
Height, cm	163.5 ± 7.1	164.6±7.8	163.3±6.5	163.0 ± 7.1	0.523
Weight, Kg	65.5±9.8	67.1±10.4	65.0±9.9	64.7±9.2	0.466
BMI, Kg/m2	24.4 ± 2.9	24.7 ± 3.0	24.4±3.1	24.3±2.6	0.783
ASA score					
1	43(31.2%)	18(43.9%)	16(37.2%)	9(16.7%)	0.004*
2	93(67.4%)	23(56.1%)	25(58.1%)	45(83.3%)	
3	2(1.4%)	0(0.0%)	2(4.7%)	0(0.0%)	
HTN, %	7(5.1%)	1(2.4%)	1(2.3%)	5(9.3%)	0.297
DM, %	1(0.7%)	0(0.0%)	0(0.0%)	1(1.9%)	1.000
Relationship to recipient					
Father/mother	120(87.0%)	31(75.6%)	38(88.4%)	51(94.4%)	0.022*
Spouse	4(2.9%)	4(9.8%)	0(0.0%)	0(0.0%)	
Brother/sister	14(10.1%)	6(14.6%)	5(11.6%)	3(5.6%)	
History of abdominal surgery	33(23.9%)	11(26.8%)	11(5.6%)	11(20.4%)	0.730
Preoperative HB; g/L	136.2 ± 15.2	133.9 ± 16.5	135.7 ± 15.4	138.4±13.8	0.349
Preoperative SCr; µmol/L	65.8 ± 12.0	72.2±11.6	61.4±11.6	64.4 ± 10.7	<0.001*
Intraoperative parameters					
Operation time; min	138.2±32.1	148.3±31.2	139.3 ± 33.3	129.6 ± 29.8	0.017*
Warm ischemic time; s	90(30-300)	120(90-300)	90(30-180)	90(50-220)	<0.001*
Estimated blood loss; ml	50(10-300)	50(10-300)	50(20-200)	50(15-100)	0.065
Postoperative outcomes					
Postoperative HB; g/L	124.1 ± 14.0	123.0 ± 14.4	124.3 ± 15.2	124.9 ± 13.0	0.802
Postoperative SCr; µmol/L	104.8 ± 22.2	106.9 ± 24.3	98.9±21.0	107.9 ± 20.8	0.108
The decline in HB level; g/L	12.1±9.2	10.9 ± 10.7	11.4±9.2	13.5 ± 7.9	0.348
Length of stay; days	12.9 ± 3.5	13.0 ± 2.7	12.5 ± 3.4	13.2 ± 4.1	0.585
Drainage tube removal time	4.9±2.3	5.5 ± 2.5	4.7±1.9	4.1±2.1	0.011*
Reoperation	1(0.7%)	0(0.0%)	1(2.3%)	0(0.0%)	0.609
Readmission	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	

*Statistically significant

Postoperative complications in phases 1, 2, and 3 occurred in 16 (39.0%), 9 (20.9%), and 13 (24.1%) cases, respectively. Twenty-four patients (17.4%) had grade I complications, the main manifestations of which were electrolyte disturbances and mild elevation of transaminases. Fourteen patients (10.1%) had postoperative complications defined as grade II or higher. One patient was Grade IV who required reoperation for a postoperative delayed hemorrhage in whom a Hem-o-lock clip on the renal artery was detached.

Table 3 shows the recipient characteristics. The recipients had a mean age of 30.4 ± 7.8 years and a mean BMI of 22.1 ± 3.6 kg/m². All patients were ABO compatible. Overall, delayed graft function rate was 5.1%, and ure-teral complication rate was 0.7%. For the recipients at our institution, we observed 1 (0.7%) patient with ACR and graft losses at 2-weeks post-transplant. Six-month graft

survival was 99.3%. There were no significant differences in the recipient characteristics among the three phases.

Discussion

The demand for live donor kidney transplants is continually increasing due to organ shortage and superior graft survival [12]. The most important aspect of LDN is donor safety and donated kidney function [13, 14]. Since Ratner et al. performed the first successful LDN at John Hopkins, [15] many surgical techniques have been developed to improve the outcomes of the donor and the graft, including retroperitoneoscopic, hand-assisted, roboticassisted(RA), and laparoscopic single-site surgery (LESS). Among the surgical techniques, the HARPLDN is more frequently used clinically. Recent reviews highlight that a HARPLDN has the advantages of fewer intraperitoneal complications and offers a clear advantage in achieving



Fig. 2 Learning curve graph fitted by CUSUM. Operation time (black line) and cumulative sum (CUSUM)_{OT} (blue line) plotted against case number. The red line represents the best fit for the plot using a second-order polynomial with the following equation: $CUSUM_{OT} = -0.09033 \times case number^2 + 12.88 \times case number - 67.77 (R^2 = 0.7875)$, corresponding to the 3 distinct phases of the operation time

hemostasis in major bleeding [2, 16–18]. Our institution has used the HARPLDN technique and made some modifications, including shorter hospital stays, pain duration, and recovery period, as well as the benefits of the open approach, such as effective control of the renal vessels and fast retrieval of the graft.

In the present study, the mean operative time was 138.2 ± 32.1 min. The median WIT and EBL were 90 s and 50 ml, respectively. The OT and WIT were decreased in the modified HARPLDN, while the EBL was similar

compared to minimally invasive donor nephrectomy, including LDN, RPLDN, HALDN, HARPLDN, RALDN, and LESS-LDN; Table 4 shows a detailed comparison [3, 14, 19, 20]. No open conversions or blood transfusions were required in donors. The incidence of postoperative complications was 27.5%; [10] however, the rate of complications defined as grade II or higher, which prolong the length of hospital stay and are potentially lifethreatening, was 10.1%. Based on published reports, the complication rates in the present study are acceptable

Table 2 Donors intra- and post-operative complications	Table 2	Donor's intra- and	post-operative complications
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Complications	Total (<i>n</i> = 138)	Phase 1 (<i>n</i> =41)	Phase 2 (<i>n</i> = 43)	Phase 3
				(n=54)
Intro-operative				
complications				
renal vessel injury	0	0	0	0
adrenal gland injury	0	0	0	0
abdominal visceral injury	0	0	0	0
open conversion	0	0	0	0
Post-operative				
complications				
Grade I				
Electrolyte disturbance	20	9	4	7
Abnormal liver function	4	2	1	1
Grade II				
Chylous leakage	11	3	3	5
Grade III				
Retroperitoneal hematoma	2	2	0	0
Grade IV				
Hemorrhagic shock	1	0	1	0

[21]. The 1-year graft survival rate is 99.3% [20]. The studies included in a systematic review and meta-analysis

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Table 3	Internhase	comparisons	of recipient	t characteristics
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showed a similar 1-year graft survival range of 96.2–98.2% [21]. One recipient (0.7%) had a ureterostenosis, so regular replacement of the ureteral stent was required. This finding is in agreement with the systematic review that reported a ureteral complication rate in the range of 0.5-6.4% [3]. In general, the recipients in our study had good transplant outcomes.

Our study evaluated one surgeon's operative competency based on the operative time and divided the cohort into phases corresponding to the surgeon's learning curve. The CUSUM analysis showed that during phase 1 (41 cases), a surgeon with experience in retroperitoneoscopic urologic operations, but no LDN, could complete the initial learning phase. After an additional 43 cases, expert competency was achieved. After achieving competency of the modified HARPLDN, the surgeon reduced the operative time.

Learning curves involving LDN techniques have been previously reported, but assessment of training and competency has differed. Learning curves involving LDN techniques are largely due to the prior experience of the surgeon and objective learner-based metrics. Chin et al. [7] reported that the learning curve for LDN by general

	Total	Phase 1	Phase 2	Phase 3	P-
	(<i>n</i> = 138)	(<i>n</i> =41)	(n=43)	(<i>n</i> = 54)	Value
Age, years	30.4±7.8	30.0±7.7	29.2±8.0	31.5±7.7	0.341
Gender					
male	103(74.6%)	33(80.5%)	33(76.7%)	37(68.5%)	0.385
female	35(25.4%)	8(19.5%)	10(23.3%)	17(31.5%)	
Height, cm	169.8±8.1	169.9 ± 8.2	169.6±8.0	169.9±8.3	0.971
Weight, Kg	64.0 ± 13.2	64.4 ± 13.0	63.1 ± 12.8	64.4 ± 13.8	0.860
BMI, Kg/m2	22.1 ± 3.6	22.2 ± 3.5	21.8 ± 3.7	22.2 ± 3.8	0.879
Dialysis type					
Hemodialysis	115(83.3%)	34(82.9%)	36(83.7%)	45(83.3%)	0.995
Peritoneal dialysis	23(16.7%)	7(17.1%)	7(16.3%)	9(16.7%)	
Dialysis vintage					
<1 year	81(58.7%)	27(65.9%)	18(41.9%)	36(66.7%)	0.026*
>1 year	57(41.3%)	14(34.1%)	25(58.1%)	18(33.3%)	
ABO incompatibility	0	0	0	0	
Delayed graft function	7(5.1%)	2(4.9%)	2(4.7%)	3(5.6%)	1.000
Acute cellular rejection	1(0.7%)	1(2.4%)	0(0.0%)	0(0.0%)	0.297
Graft losses	1(0.7%)	1(2.4%)	0(0.0%)	0(0.0%)	0.297
SCr at 1 week, µmol/L	135.2±130.7	123.6±88.2	142.4±157.8	138.2±135.7	0.789
SCr at 1 month, µmol/L	126.4±78.4	115.1±33.0	132.5±88.1	130.0±93.2	0.550
SCr at 3 months, µmol/L	123.2±110.3	115.7±28.1	111.9±24.8	137.4±172.1	0.471
SCr at 6 months, µmol/L	112.8±26.7	112.2±22.7	111.9±23.6	114.1±31.7	0.907
*Statistically significant					

 Table 4
 Comparison of surgical details among minimally invasive donor nephrectomy

	LDN	RPLDN	HALDN	HARPLDN	RALDN	LESS-LDN
Operation time; min(range)	138~221	191~248	133~205	141~211	150~235	144~362
Warm ischemic time; min(range)	3.2~6.0	2.2~5.6	3.0~3.2	2.5~4.3	1.5~5.8	2.0~9.0
Estimated blood loss; ml(range)	50~200	50~100	50~120	100~315	30~146	10~250

surgeons, defined by operative complications and bleeding, plateaued after 150 cases and the operative time decreased significantly. A systematic review indicated that the learning curve, defined by a decreased operative time, averaged 35 LDNs for attending surgeons, most of whom had prior laparoscopy or open nephrectomy experience [8]. This comparison showed the effects of technical skills on the learning curve. Pal et al. [9] reported that the RPLDN learning curve was 35 cases for a surgeon trained in retroperitoneoscopic surgery and implementing RPLDN independently after observing 20 cases. Another study showed that the surgeon becomes proficient with RPLDN over 30 consecutive cases, with a smooth transition from LDN-to-RLDN [17]. A riskadjusted cumulative summation learning curve analysis indicated that novice transplant surgery fellows who had just completed a general surgery residency training rotation exhibited peak performance and proficiency in HALDN by 24-28 and 35-38 cases, respectively. This study overcame the effects of donor risk factors and prior surgical experience to assure objectivity [22]. The CUSUM model demonstrated an initial learning phase for HARPLDN of 32 cases by a urologist who had performed 1000 retroperitoneoscopic procedures [23]. There is little evidence regarding the learning curve for RALDN. A randomized controlled trial showed that among surgeons familiar with LDN, transitioning to the robotic-assisted approach appears to have a relatively steep learning curve of 20 cases based on a comparison of the LDN and RALDN procedures [24]. A clinical study suggested that LESS-DN has a long learning curve defined by the operative time using CUSUM analysis. Specifically, > 60 cases performed by a surgeon with significant clinical experience in laparoendoscopic donor nephrectomy to demonstrate skill in LESS-LDN [25]. The most recent cohort study based on CUSUM analysis concluded that 23, 45, and 26 LDN, HARPLDN, and RALDN cases were required by transplant fellows and surgical residents to demonstrate proficiency [20]. The aforementioned studies reported that previous experience with kidney transplantation and advanced laparoscopic skills are essential and shorten the learning curve. According to published studies, considering the surgeon's level of experience prior to practicing and the observed perioperative metrics, the learning curve associated with our method was shorter than the LDN, LESS-DN, and RALDN learning curves and comparable to the RPLDN, HALDN, and HARPLDN learning curves.

The operative time is often used to study learning curves. Nevertheless, a shorter operation time does not necessarily result in improved clinical outcomes. An improvement in clinical outcomes reflects an improvement in surgical techniques. Therefore, in addition to surgical time, the prognosis of donors and recovery of renal allograft function in recipients were included in the present study for learning curve analysis. Although the EBL was not clearly different among the phases, the EBL had a gradually decreasing trend along the learning curve. The gradually decreasing trend for drainage tube removal time represents donor recovery. Conversion to open surgery, re-operation, re-admission, and major postoperative complications (grade \geq III) may be preferred learning curve outcomes because these measures verify the safety of the procedure and are of critical importance from the donor perspective. In the current study the conversion rates to open surgery, re-operation, re-admission, and major complications were 0%, 0.7%, 0%, and 2.1%, respectively, percentages that are comparable to the percentages reported in international studies. Moreover, a significant reduction in WIT was demonstrated, which is short enough to achieve acceptable DGF rates in recipients. The results are less than the findings of former studies that compared hand-assisted technical modifications to LDN and concluded that the hand-assisted technique was associated with a shorter operative time and WIT [4, 26]. In conclusion, our technique resulted in excellent donor and recipient outcomes.

The main advantage of the current study is because our center is one of the earliest centers to conduct LDN procedures in China, our center has experienced several challenges and attempts in the early stages, and this experience is potentially useful as a reference to beginners preparing to perform LDN procedures. Furthermore, we compared the learning curves of different minimally invasive LDN procedures and analyzed the influence of surgeon experience and measures of surgical performance on the learning curve.

We should point out that our study had some limitations. First, our study was a retrospective analysis and we only analyzed cases performed by one surgeon at our center. Second, there was selection bias, although our donors were not selected. In addition, if the operative time is subdivided according to the steps of each procedure, the CUSUM analysis could be a more accurate and useful analysis to guide training.

Conclusions

In conclusion, our unique hand-assisted approach is a safe, effective procedure for LDN, in which a significant decrease in operative time and WIT benefit both donors and recipients. The surgeon completes the initial learning phase of the modified HARPLDN after 41 cases and can be performed with proficiency after 87 cases.

Abbreviations

HARPLDN	Hand-Assisted Retroperitoneoscopic Living Donor Nephrectomy
CUSUM	Cumulative Sum Method
WIT	Warm Ischemic Time
LDN	Laparoscopic Donor Nephrectomy

HALDN	Hand-Assisted Laparoscopic Donor Nephrectomy
RPLDN	Retroperitoneoscopic Live Donor Nephrectomy
CT	Computed Tomography
OT	Operating Time
EBL	Estimated Blood Loss
ACR	Acute Cellular Rejection
DGF	Delayed Graft Function
ASA	American Society of Anesthesiologists
RALDN	Robotic-Assisted Laparoscopic Donor Nephrectomy
LESS-DN	Laparoscopic Single-Site Donor Nephrectomy

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Author contributions

Y. Z. proposed and designed the framework of this study. L. S. completed the collation and pre-processing of the raw data required for subsequent analysis. L. S., M. Z., and Z. W. performed a detailed analysis of the data and drafted this manuscript. All authors were involved in revising it and approved the version to be published. All authors have participated sufficiently in this work and take responsibility for appropriate portions of the content. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations. The project was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University with the ethics number 2021-P2-172-01. The need for written informed consent to participate was waived by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University due to retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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