



## Original Research

# Structured introduction of retroperitoneoscopic donor nephrectomy provides a high level of safety and reduces the physical burden for the donor compared to an anterior mini incision: A cohort study



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## ABSTRACT

**Introduction:** A major goal in living donor kidney transplantation is to reduce the physical burden for the donor. Key-hole surgery for donor nephrectomy is a safe procedure, but concerns regarding donor safety during the learning phase might be the reason for surgeons' reluctance to change to a minimal invasive approach.

**Material and methods:** We analyzed the first 100 retroperitoneoscopic donor nephrectomies (RPDN) performed at our institution and compared the results to the last 50 mini incision donor nephrectomies (MIDN) regarding donor and recipient outcome, and analyzed the learning curves of RPDN.

**Results:** The learning phase of RPDN was very short with significantly shorter operative times compared to MIDN (118 vs. 175 min,  $p < 0.001$ ) and significantly fewer surgical complications ( $p = 0.03$ ). RPDN patients rated the physical burden ( $p = 0.01$ ) as lower, and they felt less bothered by the surgical scar ( $p = 0.03$ ).

**Conclusion:** Introducing RPDN is safe, even during the learning phase of the surgeons. Changing surgical technique from MIDN to RPDN reduces the surgical burden of the procedure. Our study might encourage more transplant centres to adopt a minimally invasive approach.

## 1. Introduction

Living kidney donation is performed with increasing frequency worldwide [1]. In Germany, the numbers remain nearly constant with 548 living kidney donations performed in 2017 in 38 hospitals. More than one third of the donor nephrectomies are reported to be performed with an open approach ([https://iqtig.org/downloads/auswertung/2017/nls/QSKH\\_NLS\\_2017\\_BUAW\\_V02\\_2018-08-01.pdf](https://iqtig.org/downloads/auswertung/2017/nls/QSKH_NLS_2017_BUAW_V02_2018-08-01.pdf); 5.2.2019). This is in contrast with European and international recommendations [2,3] recognizing the reduced physical burden for the donor by using less invasive surgical techniques.

One reason to use an open approach might be the surgeons' concerns regarding donor safety. There is no doubt that it is of the utmost importance to maximize donor safety, while minimizing the burden associated with the procedure. The technique of choice at many centers nowadays has become laparoscopic donor nephrectomy [4–6], but several studies show the same positive effects for retroperitoneoscopic donor nephrectomy (RPDN), with the benefit of shorter operation time

and shorter warm ischemia time [6–9]. Compared to open donor nephrectomy, key-hole surgery in general is associated with less post-operative pain, faster convalescence, and faster return to normal activities as well as higher patient satisfaction, whereas complication rates and graft function appear to be comparable [4,10,11].

Due to the encouraging results reported for RPDN and after an observational stay in Basel, Switzerland we decided in 2011 to change the technique of donor nephrectomy from a retroperitoneal anterior mini incision donor nephrectomy (MIDN) to RPDN.

In a medium size German transplant center with 20–30 living donations per year, three surgeons were trained on the technique following a structured program. We established a close, standardized follow-up schedule and collected prospective data with a follow-up of at least one year to ensure donor and recipient safety. Furthermore, we investigated whether patients profited from RPDN by analyzing a previously established questionnaire.

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## 2. Patients and methods

At our institution, a university medical center, 150 living donor nephrectomies were carried out between March 2009 and April 2015. Per year, 21–28 donations were performed. In March 2011, the technique of donor nephrectomy was changed from MIDN to RPDN. We compared the last 50 MIDNs to the first 100 RPDNs done by three surgeons including the learning phase of RPDN. Data of the MIDN group were collected retrospectively from the electronic patient chart, while RPDN data was collected prospectively. Furthermore, with the introduction of the new technique, a structured surgical follow-up program for the donors was established to ensure the safety of the new procedure.

Protocols of the living donor survey were reviewed and approved by the Medical Faculty's Ethical Committee (No. M-196/07). Written informed consent was obtained from all participating patients. Research was performed in accordance with the declaration of Helsinki, and the work has been reported in line with the STROCSS criteria [12].

Besides demographic data of donor and recipient, surgical complications of the donors, operation time of the donor operation (skin to skin including perfusion and preparation of the organ), time of discharge, and recipients' outcome were recorded. Furthermore, the donors' own rating of the consequences of donor nephrectomy was recorded with a questionnaire three months and one year after donation.

### 2.1. Operation technique

The already described technique of MIDN [13] used a total retroperitoneal approach with an approximately 10 cm pararectal incision. MIDN was performed between July 2007 and March 2011 by six specialized transplant surgeons in a highly specialized department of hepatobiliary surgery and visceral transplantation. Most of the surgeons had previous experience with open donor nephrectomy, therefore no structured program was established when MIDN was introduced in 2007. In the analysis described here, we did not include the learning phase of MIDN, but the last 50 procedures performed, to compare our results in the learning phase of RPDN with a well established procedure.

RPDN was carried out as described before [14–17]. We modified the technique by using three 12 mm trocars. The first trocar was placed below the 12th rib and above the horizontal line of the translucent erector trunci muscle to prepare the retroperitoneal space with the herloon hernia balloon (Braun, Melsungen, Germany). After preparing adequate space, the first trocar was used for the camera and the second and third trocar were placed above the hip and in the lower abdomen. After preparing the renal vessels and the ureter from a dorsal approach, the kidney was released from the retroperitoneal fatty tissue. After preparing all anatomical structures, the trocar in the lower abdomen was removed and the incision was widened to a 7–8 cm gridiron incision, and a hand of the surgeon was introduced to assist the transection of the ureter and the renal vessels and the extraction of the kidney [18,19].

RPDN was adopted into clinical routine after an observational stay of two surgeons in Basel, Switzerland in 2011. Thereafter, RPDN was used as standard technique and all donor nephrectomies were performed via the retroperitoneoscopic approach. To ensure the safety of the new procedure, fixed surgical teams were established, and a structured surgical follow-up for the donors as well as a prospective database of surgical complications were introduced.

### 2.2. Donor management

All patients were evaluated as living donors by the outpatient department of our center according to the Amsterdam protocols [20]. Side decision was based on kidney function and anatomy of the renal vessels. Multiple arteries were not a contraindication. Both right and left sided nephrectomies were conducted. Donors were educated during surgical

evaluation to mobilize quickly after the operation, to take adequate pain medication and have normal oral intake as soon as possible. All patients received pain medication with piritramid and acetaminophen i. v./s.c. Every 4 h for 24 h followed by oral acetaminophen/codein, switched to acetaminophen after day three, if necessary. All patients were required to stop smoking at least four weeks prior to the operation. Oral contraception was stopped before donation. Patients were told to expect a hospital stay of five to seven days, but to discharge at their own discretion.

Physical thrombosis prophylaxis including early mobilization was carried out in all patients. Pharmacological thrombosis prophylaxis was not used routinely and was restricted to patients with risk factors. No heparin was used during organ harvesting or organ perfusion. While the bladder catheter was removed one or two days postoperatively in the MIDN group (dependent on the mobility of the patients), it was removed in the operation room after RPDN, and all donors were ambulated 6 h after the operation.

Surgical complications were recorded from the patients' electronic charts in case of MIDN and prospectively documented in a living donor database in case of RPDN during surgical follow-up visits four weeks, three and six months, and one year after donation. Surgical complications are reported for the first year post operation. Complications were graded according to the modified classification for live donor nephrectomy [21]. Follow-up was available for all but one patient. One donor in the MIDN group donating for his child was lost to follow-up without any medical problems at discharge. Complete routine follow-up until three years after donation was available for all other donors.

### 2.3. Donor questionnaire

All German-speaking donors were asked during evaluation to take part in a psychological survey to evaluate physical and psychological outcome of living kidney donation. Paper questionnaires were sent by mail with stamped return envelopes enclosed. The questionnaires were filled out at three months and one year respectively by 26 and 27 donors in the MIDN group (63% and 66% of 41 German-speaking donors) and 65 and 67 donors in the RPDN group (76% and 79% of 85 German-speaking donors). For our study, we analyzed a questionnaire based on the European Multicenter Study 'Transplantation of Organs from Living Donors' (EUROTOLD) [22]. The items relevant for our study referred to the operation and its consequences, which donors had to rate on a five-point Likert scale (0–4) with higher scores indicating more impairment. The following questions were included: "As how strong did you perceive the physical burden of the living donation?", "As how strong did you perceive the psychological burden of the living donation?", "How strong was your pain after the operation?", "How much does the surgical scar bother you?". Furthermore, in open questions, which were later categorized, they were asked to report current problems and impaired activities they attributed to the donation.

### 2.4. Statistics

Data analysis was performed using SPSS Statistical Software for Windows, version 15.0 (SPSS Inc., Chicago). To analyze differences between groups, t-tests for independent samples or Chi-square tests (according to scale level) were applied. For all tests, probability values lower than 0.05 were considered significant. Two-tailed tests were applied. To determine the learning curves of the surgeons, a cumulative sum (CUSUM) analysis of the operation time was carried out by using SAS software (version 9.4; SAS Institute). First, cases were ordered chronologically from the first to the last date of surgery. The CUSUM for surgeon 1 (S1) was then calculated by the following formula:  $CUSUM_i = \sum_{j=1}^i (x_{ij} - \bar{x}_i)$ , with  $x_{ij}$  being the individual operation time of S1 and  $\bar{x}_i$  being the mean operation time of S1. The CUSUM of two surgeons was plotted, and the learning curves were compared to each other [23,24].

**Table 1**  
Demographic and preoperative clinical characteristics of MIDN and RPDN donors.

	MIDN N = 50	RPDN N = 100	P
Donor age (years) (mean and range)	52.1 (25.0–79.0)	54.0 (27.0–76.8)	n.s.
Donor BMI (mean and range)	25.5 (18.5–33.8)	25.8 (19.8–35.3)	n.s.
Female donors	30 (60%)	67 (67%)	n.s.
S-creatinine (mg/dl) before donation (mean and range)	0.8 (0.5–1.2)	0.8 (0.4–1.2)	n.s.

MIDN: mini incision donor nephrectomy, RPDN: retroperitoneoscopic donor nephrectomy; n.s.: not significant.

### 3. Results

#### 3.1. Patient characteristics

Table 1 shows demographic and preoperative clinical characteristics for all donors in the MIDN and the RPDN group. With a mean age of 52.1 and 54.0 years at the time of donation, there was no significant difference between MIDN and RPDN donors. In both groups, the majority of donors were female. There were no significant differences between MIDN and RPDN donors regarding mean BMI and mean serum-creatinine.

#### 3.2. Surgical procedure and postoperative clinical data

Table 2 shows surgical and postoperative clinical data. In the MIDN group, 66% right donor nephrectomies were performed, in the RPDN group 58%. Mean operation time was significantly shorter in the RPDN group (118 min vs. 175 min,  $p < 0.001$ ). The first warm ischemia time in the RPDN group was about 3 min (mean: 199 s, range: 94–440 s). This data was not measured in MIDN.

The mean length of hospital stay was significantly shorter in the RPDN group (4.9 days vs. 6.3 days,  $p < 0.001$ ). One patient was excluded from this analysis in the RPDN group. This was a mother accompanying her disabled (adult) child until discharge of the recipient. The mean serum-creatinine one year after donation was comparable between the groups (1.2 mg/dl in both groups). There was no donor mortality or donor dialysis observed.

#### 3.3. Surgical complications of the donors

Table 3 shows intra- and postoperative complications within one year after donation.

In the MIDN group, 14 complications occurred in 13 patients (26%). Most complications were mild. One patient suffered from two potentially life-threatening complications (lung embolism and small bowel injury). A second patient needed a resection of a granuloma of the vocal cord, possibly related to the intubation.

In the RPDN group, 12 complications occurred in 12 patients (12%).

**Table 2**  
Surgical data and postoperative clinical characteristics of MIDN and RPDN donors.

	MIDN	RPDN	P
Right sided nephrectomies	33 (66%)	58 (58%)	n.s.
Kidneys with multiple arteries	11 (22%)	18 (18%)	n.s.
Skin to skin time (min) (mean and range)	175 (112–250)	118 (70–271)	$< 0.001$
Time to discharge after donation (days) (mean and range)	6.3 (3–12)	4.9 (3–13)	$< 0.001$
S-creatinine (mg/dl) 1 year after donation (mean and range)	1.2 (0.8–1.8)	1.2 (0.8–1.9)	n.s.

MIDN: mini incision donor nephrectomy, RPDN: retroperitoneoscopic donor nephrectomy; n.s.: not significant.

**Table 3**  
Surgical complications of MIDN and RPDN donors.

GRADE	COMPLICATION	MIDN N = 50	RPDN N = 100
1	Urinary tract infection	5 (10%)	2 (2%)
	Other infections	3 (6%)	0
	Gastritis	1 (2%)	1 (1%)
	Prolongation of warm ischemia time	–	1 (1%)
	Mild wound complications	0	2 (2%)
	Unplanned visit due to pain or other complaints	2 (4%)	5 (5%)
2A	None		
	Granuloma of the vocal cord	1 (2%)	0
2B	Conversion to open surgery/extension of gridiron incision	–	1 (1%)
3	Lung embolism	1 (2%)	0
	Small bowel injury	1 (2%)	0

MIDN: mini incision donor nephrectomy, RPDN: retroperitoneoscopic donor nephrectomy.

All complications were mild. In one patient, the gridiron incision had to be extended to attend a laceration of the vena cava. No blood transfusions were given, but bleeding exceeded 500 ml. In one patient, bleeding  $< 500$  ml from the renal vein led to prolongation of warm ischemia time to 7 min without negative consequences for the donor or the recipient.

In the RPDN group, a lower percentage of donors had surgical complications in the first year compared to the MIDN group ( $p = 0.03$ ).

Within three years, during routine visits in the transplant center, five patients (10%) in the MIDN group reported complaints about the scar: four patients reported hernia/relaxation of the abdominal wall, one patient had esthetical complaints. In the RPDN group, one patient suffered from persistent pain, and one patient reported a trocar hernia.

#### 3.4. Recipient outcome

There were no significant differences regarding age, BMI, or immunological risk of the recipient between the groups (Table 4). The time to complete the anastomosis of the renal vessels in the recipient was shorter in the RPDN group compared to the MIDN group ( $p < 0.001$ ). In two cases in the RPDN group, transplantation was carried out with a double J stent due to parenchymal lesion of the donor kidney in one and a short ureter in the second case. No venous reconstruction was necessary in either group. No venous thrombosis was seen. Delayed graft function and early graft loss within the first year were not different between the groups.

**Table 4**  
Recipient characteristics and clinical data.

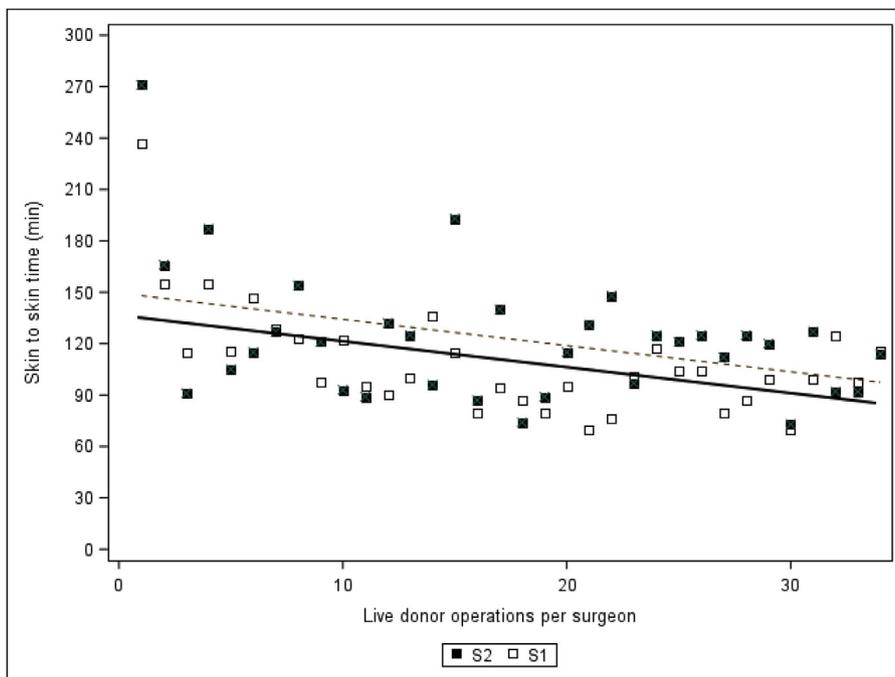
	MIDN	RPDN	P
Recipient age (years) (mean and range)	42.5 (1.2–74.7)	43.3 (1.5–77.1)	n.s.
Recipient BMI <sup>a</sup> (mean and range)	25.2 (18.3–38.3)	24.7 (18.5–35.6)	n.s.
Immunological risk patients <sup>b</sup>	11 (22%)	23 (23%)	n.s.
Anastomosis of renal vessels (min) <sup>c</sup> (mean and range)	38 (15–64)	30 (13–56)	$< 0.001$
Delayed graft function	6 (12%)	6 (6%)	n.s.
Graft loss within 1 year	4 (8%)	3 (3%)	n.s.

MIDN: mini incision donor nephrectomy, RPDN: retroperitoneoscopic donor nephrectomy; n.s.: not significant.

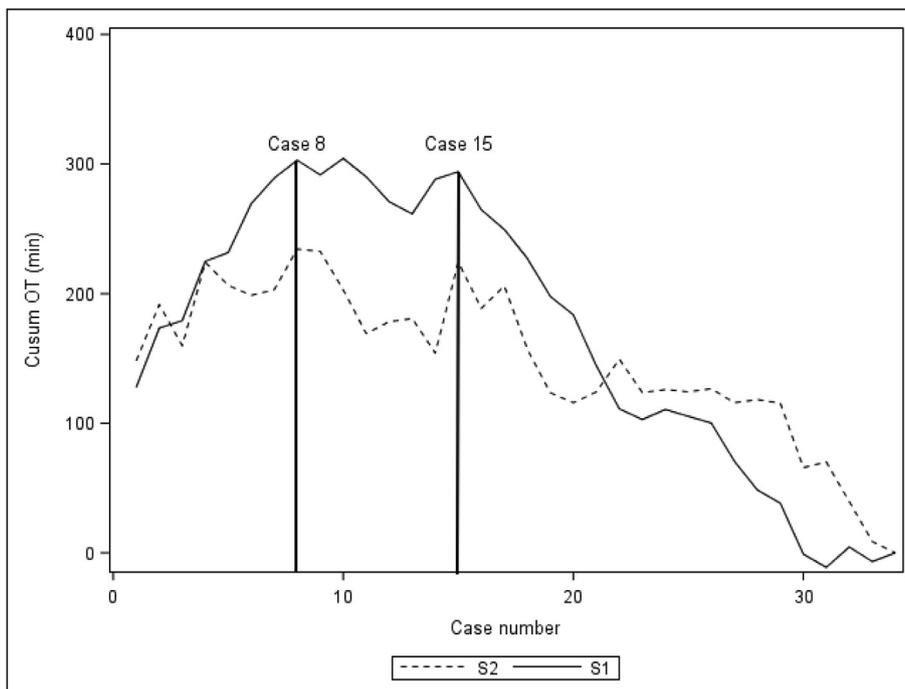
<sup>a</sup> For adults only.

<sup>b</sup> Retransplantation or ABO-incompatible.

<sup>c</sup> Recorded for 40 of 50 MIDN and 83 of 100 RPDN.



A



B

**Fig. 1.** a Operation times (OT) of the first 35 live donor operations of surgeon 1 (S1) (dotted linear trend line and open boxes) and surgeon 2 (S2) (black line and black boxes).b: CUSUM analysis of the operation times (OT) of the first 35 operations performed by surgeon 1 and 2 (S1 and S2) demonstrating an initial learning phase of about eight cases and a decline of the curve and the end of the learning phase at about 15 cases.

For the CUSUM analysis, cases were ordered chronologically from the first to the last date of surgery. The CUSUM for S1 was then calculated by the following formula:  $CUSUM_i = \sum_{j=1}^i (x_{ij} - \bar{x}_i)$ , with  $x_{ij}$  being the individual OT of S1 and  $\bar{x}_i$  being the mean OT of S1.

### 3.5. Learning curves

RPDN was introduced by surgeon 1 (S1), who had experience with more than 200 MIDNs, after an observation stay at the Basel transplant center [14–16]. We intended to perform RPDN in fixed teams, with the most experienced surgeon (S1) doing the first 20 operations together with surgeon 2 (S2), and S2 taking over the operation after participating in at least 20 operations. In actual fact, S1 performed the first 31 donations together with S2 in most cases, before S2 took over the operation together with surgeon 3 (S3), who took over the operation after participating in 20 cases. S2 had experience with 20 MIDNs, S3 had no experience with living kidney donation. All surgeons are certified general and visceral surgeons with specialization in visceral transplantation, but without extensive experience in laparoscopic surgery. At the end of this evaluation, S1 had performed 52 RPDNs, S2 34, and S3 14 RPDNs.

Fig. 1a shows the actual operation times of both surgeons S1 and S2, with a continuous decline in operation time when individual operations were ordered chronologically. Fig. 1b shows operation times visualized with the CUSUM method. For both surgeons, an initial learning phase is observed between case one and eight. After a short plateau, the descending slope of the curve after about 15 cases marks the end of the learning phase. All adverse events related to the donor operation (bleeding, parenchymal lesion of the kidney, short ureter) occurred after the end of the initial learning phase (at case 19, 32, and 40).

Due to the low number of RPDNs performed by S3 ( $n = 14$ ), learning was not completed by the end of the analysis, therefore the learning curve of S3 is not shown.

### 3.6. Donors' rating of the consequences of donation

Three months after living kidney donation, RPDN patients retrospectively rated the physical burden of the donation significantly lower than MIDN patients did (mean: 1.11 vs. 1.69,  $p = 0.01$ ; Fig. 2). No significant difference was found regarding the psychological burden of living kidney donation (mean: 0.92 vs. 0.88,  $p = 0.88$ ; Fig. 2). RPDN patients retrospectively rated their postoperative pain as lower than MIDN patients (mean: 1.66 vs. 2.54,  $p < 0.001$ ; Fig. 3). They also felt less bothered by the surgical scar compared to MIDN patients three months (mean: 0.26 vs. 0.62,  $p = 0.03$ ; Fig. 3) as well as one year (mean: 0.21 vs. 0.58,  $p = 0.02$ ) after living donation.

The percentage of donors reporting current problems they attributed to the donation did not differ between the groups (Table 5). Most frequently reported physical problems were pain/discomfort in the scar area and physical weakness/fatigue. Impaired activities mostly were sporting activities. Mental problems particularly were persistent worries regarding the recipient/graft function, impaired mental well-being,

and emotional fatigue. Other problems concerned financial, vocational, insurance-related, and social issues.

## 4. Discussion

As reviewed recently by Özdemir-van Brunschot, there are several studies demonstrating the safety of different key-hole techniques for living donor nephrectomy. Hand assistance and a retroperitoneal approach seem to reduce surgical complications, operation times and first warm ischemia times [6]. Our center has very little experience with laparoscopic donor nephrectomy, but with MIDN, which was also carried out with a complete retroperitoneal approach. Considering the anatomy of the kidney, our own experience with a retroperitoneal approach, and the promising literature on RPDN [9,14–16], a retroperitoneoscopic approach appeared to be the logical consequence to further reduce the physical burden of the donor nephrectomy for both right and left sided living kidney donations.

There are still concerns about right sided nephrectomies [7,25], but other studies show the feasibility of right sided living donor nephrectomies [26,27]. More than half of the donations in our study were right kidneys, and there was never a need for venous reconstruction, and no venous thrombosis occurred in the grafts. Importantly, there was no difference in graft function or survival between MIDN and RPDN, ensuring safety of the procedure for the recipient.

Beyond recipient outcome, establishing a new technique in living donation is delicate, since the safety of the donor is the main concern. It has been shown in laparoscopic donor nephrectomy, that experienced and fixed teams reduce not only operative times but also complications [28]. Therefore, we aimed to perform RPDN in fixed teams. This might have contributed to the short operation times in RPDN compared to MIDN (where no fixed teams were established) at our own center and compared to laparoscopic donor nephrectomies reported by others [7,9,25,27].

Our learning curves were very short with 8–15 cases compared to laparoscopic approaches [25,29] and comparable between the surgeons despite different experience with living kidney donation. The learning of S2 was faster compared to S1, which might be explained by the fact that S2 had assisted nearly all cases of S1. This is in accordance with data demonstrating a clear center difference in learning effects of hand assisted RPDN [30], which might be attributed to different team structures or experiences. Hollenbeck et al. proposed that participating in at least 13 laparoscopic donor nephrectomies or performing at least six, significantly reduced operative times [31], while Serrano et al. found that transplant surgery fellows need 35 to 38 cases to become proficient, with a tipping point of learning at 24 to 28 cases [29]. For hand assisted RPDN, Wahba et al. demonstrated a continuous decrease in operation time for the first 30 operations [32].

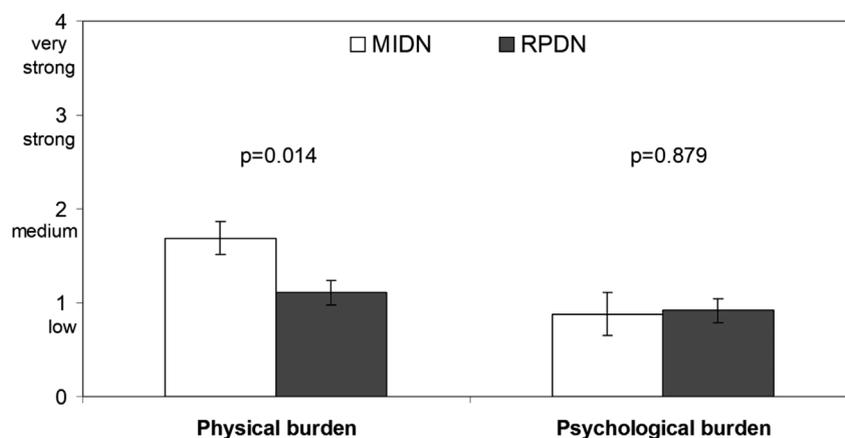


Fig. 2. Physical and psychological burden of living kidney donation (donors' rating three months after donation) after mini incision donor nephrectomy (MIDN) and retroperitoneoscopic donor nephrectomy (RPDN).

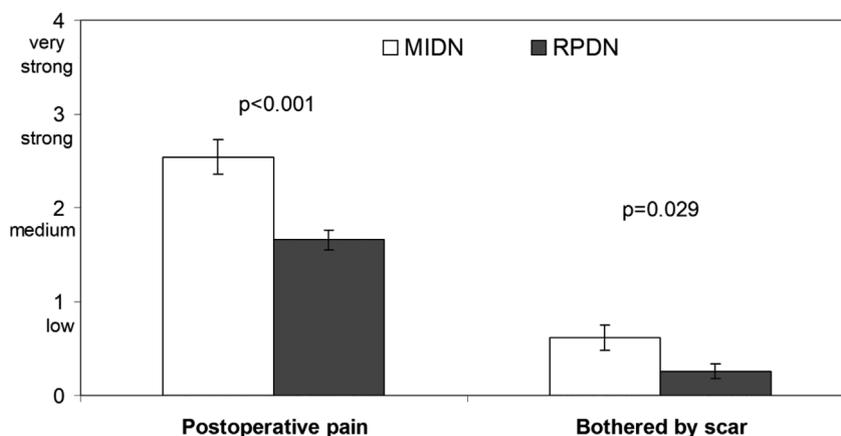


Fig. 3. Postoperative pain and bothered by scar (donors' rating three months after donation) after mini incision donor nephrectomy (MIDN) and retroperitoneoscopic donor nephrectomy (RPDN).

Fortunately, in our study, very short learning curves and operative times come with a low complication rate. We had to perform only one extension of the gridiron incision. No blood transfusions, no reoperations, and no other severe complications occurred in the RPDN group. There were two graft-related complications, both without consequences for the donor. Remarkably, all three events happened in another team constellation than our standard team.

The percentage of donors reporting current problems and impairments in the follow-up questionnaires did not differ between RPDN and MIDN, but RPDN donors perceived the physical burden of the operation and the postoperative pain as lower than MIDN donors, and they felt less bothered by the surgical scar. This can be seen as a benefit experienced by the donors themselves.

Limitations of the study: Due to the retrospective evaluation of complications in the MIDN group and the less consequent follow-up, mild complications might have been missed in MIDN and could possibly be recorded more accurately in the RPDN group, since patients were explicitly asked for complaints during follow-up four weeks after donation. Furthermore, patients were informed about the new operation technique and might have expected a shorter hospital stay, which might have influenced the day of discharge, along with the expectations of the discharging physicians. The donors' own rating of the surgical burden could also be influenced by the preoperative information about the less invasive surgical technique.

In summary, RPDN can be adopted easily and safely, even in a medium size transplant center. We recommend to establish fixed teams and a structured training program. By changing our donor operation from MIDN to RPDN, we did not see any negative impact on donor and recipient outcome. Donors themselves actually reported a lower physical burden of RPDN compared to MIDN donors. By introducing RPDN, the donor can profit from earlier discharge and lower physical burden, even during the learning curve. The results underline not only the need but also the opportunity to minimize donor's burden of living donation.

Table 5  
Current problems reported by donors after living kidney donation (LKD).

	3 months after LKD			1 year after LKD		
	MIDN n = 26	RPDN n = 65	P	MIDN n = 27	RPDN n = 67	P
Donors with physical symptoms	6 (23%)	19 (29%)	n.s.	6 (22%)	16 (24%)	n.s.
Donors with mental symptoms	1 (4%)	5 (8%)	n.s.	4 (15%)	10 (15%)	n.s.
Donors with impaired activities	6 (23%)	10 (15%)	n.s.	3 (11%)	8 (12%)	n.s.
Donors with other problems	0 (0%)	3 (5%)	n.s.	0 (0%)	2 (3%)	n.s.
Donors with any problems	9 (35%)	22 (34%)	n.s.	9 (33%)	20 (30%)	n.s.

MIDN: mini incision donor nephrectomy, RPDN: retroperitoneoscopic donor nephrectomy; n.s.: not significant.

**Declaration of interest**

None.

**Provenance and peer review**

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**Ethical approval**

None.

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**Author contribution**

MK: wrote the manuscript, designed and performed study, analyzed data; SK: wrote the manuscript, designed and performed study, analyzed data; JL: performed study, reviewed manuscript; CW: analyzed data; BN: reviewed the manuscript, designed and performed study.

**Research registry number**

DRKS - German Clinical Trials Register.  
 DRKS00016730.  
[https://www.drks.de/drks\\_web/navigate.do?navigationId=trial.HTML&TRIAL\\_ID=DRKS00016730.](https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00016730)

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## CRedit authorship contribution statement

**Martina Koch:** Conceptualization, Formal analysis, Writing - original draft. **Sylvia Kroencke:** Conceptualization, Formal analysis, Writing - review & editing. **Jun Li:** Formal analysis, Writing - review & editing. **Christian Wiessner:** Formal analysis, Writing - review & editing. **Björn Nashan:** Conceptualization, Formal analysis, Writing - review & editing. **Acknowledgements**

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## Conflicts of interest

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijso.2019.07.038>.

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