Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Original article | Published 25 August 2017 | doi:10.4414/smw.2017.14497
Cite this as: Swiss Med Wkly. 2017;147:w14497

Early complications after living donor nephrectomy: analysis of the Swiss Organ Living Donor Health Registry

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Summary

BACKGROUND: We evaluated the prospectively collected data about the incidence of early peri- and postoperative complications, and potential risk factors for adverse outcomes after living kidney donation in Switzerland.

METHODS: Peri- and postoperative events were prospectively recorded on a questionnaire by the local transplant teams of all Swiss transplant centres and evaluated by the Swiss Organ Living Donor Health Registry. Complications were classified according to the Clavien grading system. A total of 1649 consecutive donors between 1998 and 2015 were included in the analysis.

RESULTS: There was no perioperative mortality observed. The overall complication rate was 13.5%. Major complications defined as Clavien ≥3 occurred in 2.1% of donors. Obesity was not associated with any complications. Donor age >70years was associated with major complications (odds ratio [OR] 3.99) and genitourinary complications (urinary tract infection OR 5.85; urinary retention OR 6.61). There were more major complications observed in donors with laparoscopic surgery versus open surgery (p = 0.048), but an equal overall complication rate (p = 0.094).

CONCLUSION: We found a low rate of major and minor complications, independent of surgical technique, after living donor nephrectomy. There was no elevated complication rate in obese donors. In contrast, elderly donors >70 years had an elevated risk for perioperative complications.

Key words: living donor nephrectomy, early complications, kidney transplantation, morbidity, donor registry

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Introduction

Kidney transplantation is considered the optimal treatment in patients with end-stage renal disease. Despite efforts to increase the number of deceased donors, the demand for renal transplantation exceeds the available organs by far. This shortage has led to an increase of kidney transplantations from living donors during the last decades. Living kidney donation (LKD) in Switzerland has been performed since the beginning of kidney transplantation in 1966. The percentage of kidney transplants from living donors has steadily increased and nowadays accounts for about one third of all donors in Switzerland [1, 2]. Living kidney donation has several advantages for the kidney recipient like improved long-term allograft survival, pre-emptive transplantation or shorter time on dialysis and therefore improved patient survival [3–5]. Ethical concerns about this procedure have existed since the very beginning of living kidney transplantation (LKT), as a healthy individual is exposed to the risk of a surgical procedure without a direct health benefit for him- or herself. In addition, selection criteria of living kidney donors have changed over time and nowadays some elderly, overweight or hypertensive donors are also accepted, with higher short- and long-term risks of complications [6, 7]. Therefore, detailed information about the risk of LKD is crucial to justify this procedure. Potential future donors must be better informed so that they fully understand the potential risk and long-term consequences associated with such a procedure. Despite the increase of LKD during past decades there are only a few articles reporting prospectively collected cohort data about perioperative, short-term and long-term complications after living donor nephrectomy [8–11]. Owing to the complete lack of such data in the early nineties, the Swiss Organ Living Donor Health Registry (SOL-DHR) was founded in 1993 with the aim to prospectively assess

the incidence of complications of LKD and to identify risk profiles associated with unfavourable outcomes [12]. We analysed the data from the SOL-DHR in terms of the incidence of early peri- and postoperative complications after LKD and potential risk factors for adverse outcome.

Materials and methods

Data collection

Since 1993, all living kidney donors in Switzerland have been registered in a national registry, the SOL-DHR. Initially, all six kidney transplantation centres agreed to include all donors in the SOL-DHR and since 2007 it has been mandatory in accordance with Swiss transplantation law to provide a lifelong follow-up of all living donors in Switzerland. Since 1998, all six Swiss transplant centres (Basel, Berne, Geneva, Lausanne, St Gallen, Zurich) report the peri- and postoperative surgical complications to the SOL-DHR by filling in a questionnaire. For this study all patients who are registered in the SOL-DHR database with available data on the peri- and postoperative surgical complications from January 1998 until December 2015 were included.

Preoperative data consisted of height, weight, blood pressure, body mass index (BMI), sex, age and any medication. Peri- and postoperative events were reported by the local transplant team and recorded in a questionnaire (appendix 1, available in a separate file for downloading) consisting of following data: surgical complications, wound infections, urinary tract infections (UTI), other infections, urinary retention, deep vein thrombosis, pulmonary embolism, psychological complications, arterial hypertension after surgery on at least 2 consecutive days, need for blood transfusion, length of hospital stay, analgesic medication at discharge, other complications, side of nephrectomy, surgical technique, re-operation during the first 3 months, overall pain perception on visual analogue scale. The questionnaire was completed at the time of the donor discharge after nephrectomy and sent to the SOL-DHR. In addition, early complications during the first 3 months after surgery, which were reported to the SOL-DHR by the donors' general practitioners or by the donors themselves, were included after evaluation and confirmation by the medical staff of the SOL-DHR.

Every early complication observed in a donor was classified by the medical board of the SOL-DHR according to the Dindo-Clavien grading system for surgical complications [13]. Grade 1 is any deviation from the normal postoperative course that requires no treatment other than antiemetic, antipyretic, diuretic or analgesic medication, electrolytes or physiotherapy. Grade 2 requires medical therapy other than that allowed for in Grade 1. Grade 3 requires endoscopic, surgical or radiological interventions under local (3a) or general anaesthesia (3b). Grade 4 signifies failure in at least one organ system and is life threatening, requiring intensive care. Grade 5 equals death of the patient. Each complication was counted separately: one donor could present with several complications independent of each other, so each donor could contribute several times to a complication subtype.

During the study period, five different surgical techniques for LKD were performed. Classic open nephrectomy (OLDN) was used in the early period, fully laparoscopic nephrectomy (LDN) was introduced in 1997, hand-assisted laparoscopic nephrectomy (HLDN) in 1998, mini-incision pararectal nephrectomy (MLDN) in 1999 and retroperitoneoscopic nephrectomy (RLDN) in 2001. For the analysis of the influence of surgical technique on complications, two surgical categories were defined, either open (OLDN + MLDN) or laparoscopic (LDN, HLDN and RLDN).

The protocol was approved by the institutional ethics committees of the University of Basel, University of Berne, University of Geneva, University of Lausanne, Kantonsspital St. Gallen and University of Zurich, Switzerland.

Statistical analysis

We used JMP software version 12 (SAS Institute Inc., Cary, NC) for statistical analysis. Categorical data as given as count (percentage) and analysed with Pearson's chi-square or Fisher's exact test. Continuous data are given as median (interquartile range [IQR]) and were analysed with the Wilcoxon or Student's t-test as appropriate. Odds ratios were calculated by comparing the frequency of the investigated outcome between two groups. As only three comparisons for each outcome were made, no correction for multiple testing was considered necessary. A p-value <0.05 was taken to indicate statistical significance.

Results

Donor characteristics

From January 1998 to December 2015, 1694 living kidney donors were registered in the SOL-DHR. Data on peri- and postsurgical complications were available in 1649 of kidney donors (97.4%). Baseline characteristic are summarised in table 1. Duration of the hospital stay changed significantly over time, from a median of 10 days (IQR 8.25–11.75) in 1998 to 5 days (IQR 4–6) after 2012 (p <0.0001). During the study period, there were five different surgical types of donor nephrectomy performed (table 2). No perioperative mortality was observed during the study period. Overall there were 254 complications in 222 patients (13.5%) reported to the SOL-DHR and summarised in table 3. The overall rate of donors with severe complications (Clavien 3 and 4) was 2.1% (n = 34). Twenty donors needed a reoperation, 17 during the early postoperative period and 3 donors after discharge and within the first 3 months after nephrectomy. In eight donors reoperation was due to bleeding complications (seven with severe retroperitoneal hematoma and one with a lesion of the internal iliac artery). Other reasons for reoperation were hernia (n = 2), bowel perforation (n = 2) and mechanical ileus (n = 2). Conversion to OLDN was necessary in ten donors (seven LDN, one HLDN and in two RLDN). The incidence of severe complications (Clavien 3 and 4) was more frequent in donors undergoing laparoscopic techniques for nephrectomy than with open surgery (p = 0.048), but the overall complication rate, as well as the incidence of reoperation, were similar between the two surgical categories (p = 0.094 and p = 0.15 respectively). Age was significantly associated with severe complications (Clavien 3 and 4) when comparing donors aged >70 years with donors aged <50 years (OR 3.99, 95% CI 1.37 -11.67) (table 4). There was no association for donors with higher BMI (BMI <30 kg/m^2 vs 30–35 kg/m^2, p = 0.41; BMI <30 kg/m^2 vs BMI

>35 kg/m^2, p = 0.52). In total, 17 donors (1.03%) received blood transfusions because of significant blood loss.

Grade 2 complications were mainly infectious diseases (see table 3). UTI was significantly associated with older age (table 5). There were no associations between the incidence of wound infections and a higher BMI (BMI <30 kg/m^2 vs BMI >30 kg/m^2, p = 0.54) or between open versus laparoscopic nephrectomy (p = 0.76). Urinary retention was more frequently observed in male than in female donors (17/559 vs 11/1062, p = 0.008) and in donors aged >70 years compared to donors aged <50 years (OR 6.61, 95% CI 2.29–19.11) (table 6). At the day of discharge 66.8% of donors still took some analgesic drugs.

During the postoperative phase 73 donors (4.4%) had hypertensive blood pressure readings (>140/90 mm Hg) on at least two consecutive days. Of these, 49 donors were already treated for hypertension. For 11 donors, blood pressure normalised during follow-up; 13 donors had persistent hypertension and had to start antihypertensive medication.

Psychological disorders (depression, anxiety) were observed in 44 donors (2.7%). There was no centre effect for

Table 3: Donor complications.

Complication	Comment	n
Clavien 4b		
Pulmonary embolism	Reanimation with ICU admission with full recovery	1
Clavien 4a		
Myocardial infarction	NSTEMI with ICU admission	1
Aortical lesion	life threatening intraoperative bleeding	1
Clavien 3b		
Retroperitoneal haematoma	Reoperation	7
Chylous leakage	Reoperation	3
Hernia	Reoperation (1 inguinal, 1 incisional)	2
Small bowel perforation	Reoperation	2
Mechanical ileus	Reoperation (1 ileum resection)	2
Testicular torsion	Reoperation with orchiectomy	1
Benign prostatic hyperplasia with recurrent urinary retention	Reoperation with TURP	1
Arterial lesion	Renal arterial branch (intraoperative), internal iliac artery (reoperation)	2
Carotid dissection	Reoperation	1
Clavien 3a		
Pneumothorax	Chest drain	5
Chylous leakage	Percutaneous drainage	4
Pulmonary oedema	ICU admission and loop diuretics	1
Clavien 2		
Urinary tract infection		43
Wound infection		17
Pneumonia		14
Epididymitis	Requiring antibiotics	5
Septicaemia	Venous line associated	3
Other infections	Requiring antibiotics	15
Acute hepatitis	Drug related	1
Paralytic ileus	Prolonged ileus > 2 days	6
Severe gastritis	Gastroscopy	3
Haematoma	Requiring blood transfusion	12
Allergic reaction	2 antibiotic associated, 3 unknown reasons	5
Thrombosis	Right arm	1
Bronchospasm post-surgery	Known asthma	2
Cardiac arrhythmia	1 atrial fibrillation, 1 AV re-entry tachycardia	2
Clavien 1		
Urinary retention		28
Other genitourinary disorders	3 hydrocele, 1 macrohaematuria, 1 penis ulcer	5
Chylous leakage	Without further intervention	7
Pneumothorax	Without chest drain	6
Severe haematoma	No blood transfusion or intervention	10
Secondary wound healing	Bedside wound opening day 2	1
Severe vomitus	≥ 2 days	10
Intraoperative positioning related complication	6 rhabdomyolysis, 1 severe shoulder pain, 3 nerve lesion, 1 costal fracture	11
Anaesthesia related complication	1 teeth damage, 1 glottis lesion, 1 keratitis, 3 venous line related phlebitis	6
Allergic skin reaction	No treatment	5
Severe skin emphysema	After retroperitoneoscopic nephrectomy	1
Retained needle	No further intervention as asymptomatic	1
Overall total n		**254**

AV = atrioventricular; ICU = intensive care unit; NSTEMI = non-ST elevation myocardial infarction; TURP = transurethral resection of the prostate

the overall rate of all the different categories of complications (p = 0.24).

Discussion

During the study period, there was no perioperative mortality in 1694 consecutive living donor nephrectomies. Historically, not a single donor has died as a consequence of the nephrectomy since the beginning of LKD in Switzerland in 1966 [14]. In the literature the overall LKD specific mortality is known to be between 0.03% and 0.04% [11, 15]. Overall, there were 254 complications in 222 donors (13.5%) observed during the study period. This complication rate is similar to those reported in the literature, with a rate of 7.9 to 20.9% [8, 16–19]. Severe postoperative complications (Clavien 3 and 4) were seen in 2.1% of donors compared with 2.9% to 7.3% in previous publications [8, 17, 18]. We found a significant association between severe complications (Clavien 3 and 4) and donor age (>70 years vs <50 years) and the laparoscopic surgical approaches. Similar findings were reported by Lentine and co-workers, who found a higher incidence of all grades of complications with increasing age at donation (adjusted OR 1.01, 95% CI 1.01–1.02) [17] and by the Norwegian Registry [8], which showed a significant association between laparoscopic nephrectomy and major complications with an OR of 2.01. This result might be explained by a learning curve after introduction of the new laparoscopic surgical techniques, as has been reported by several groups [8, 20]. But after analysing the overall complication rates by surgical technique, we could not find any difference between open and laparoscopic nephrectomy (p = 0.094).

Twenty donors needed a reoperation. The most common reasons were bleeding complications (n = 8) and bowel complications (n = 5). In 10 donors, the laparoscopic surgical approach was converted to OLDN, in two of these patients because of severe intraoperative bleeding. Mjoen et al reported intraoperative bleeding complications in 14/1022 donors, with necessary conversion to open surgery in 3/14 [8]; even fatal haemorrhage has occurred [21, 22].

Chylous leakage was observed in 13 donors (0.8%), three of whom needed reoperation and four an intervention with percutaneous drainage of the chyle, with our without a low fat medium-chain triglyceride diet and octreotide application for resolving of the chylous leakage. The highest rate of chylous drainage after LDN in the literature was reported by Capocasale et al., at 3.8% of donor [23]. The chylous leakage in their series was solely observed in donors with left sided LDN, which was also the case in our series. This complication is left-side dependent because of the root of the mesentery and the presence of the left ascending lumbar trunk in the area of surgical dissection. We could not find a relation between the occurrence of chylous leakage and nephrectomy techniques (open vs laparoscopic) (p = 0.31).

There are a large number of publications comparing the complication rate of different kinds of surgical techniques. In two large systematic reviews and one meta-analysis the authors could not find a significant difference between the different surgical techniques with regard to the overall early intra- and perioperative complication rates [24–26]. These data suggest that there is no substantial difference between the applied surgical techniques in terms of early complication rate. In general, laparoscopic nephrectomy is more often used nowadays because it is associated with less pain after surgery, shorter hospital stay and faster return to work [27–29].

Donor obesity is always a concern, not only in terms of onset of metabolic syndrome after kidney donation with its risk of end-stage renal disease, but also in terms of perioperative complication rates. During past decades more and more obese donors were accepted for donation [19]. In our study, we did not find an association between obese

Table 1: Baseline characteristics.

	data available (n)	
BMI (kg/m^2), median (IQR)	1637	25.0 (22.8–27.8)
BMI 30–35 kg/m^2, n (%)		168 (10.3)
BMI >35 kg/m^2, n (%)		19 (1.2)
Age (years), median (range)	1649	52.3 (21.6–80.0)
21–30 years, n (%)		63 (3.8)
31–40 years, n (%)		238 (14.4)
41–50 years, n (%)		453 (27.5)
51–60 years, n (%)		508 (30.8)
61–70 years, n (%)		329 (20.0)
71–80 years, n (%)		58 (3.5)
Female (%)	1649	65.1%
Right kidney (%)	1252	30.9%
Creatinine (µmol/l), median (IQR)	1620	67 (58–77)
GFR (ml/min/1.73m^2), median (IQR)	1620	115.5 (99.0–134.3)
Arterial hypertension (%)	1386	18.3%

BMI = body mass index; GFR = glomerular filtration rate; IQR = interquartile range

Table 2: Surgical method.

	n	Frequency
Open nephrectomy	210	12.7%
Pararectal mini-incision nephrectomy	121	7.4%
Pure laparoscopy	208	12.6%
Hand assisted laparoscopic nephrectomy	569	34.5%
Retroperitoneoscopic	541	32.8%

Table 4: Odds ratios for Clavien ≥3 complications by age groups.

Age group	Odds ratio	95% confidence interval	p-value
<50 yrs	Reference		
50–60 yrs	0.81	0.32–2.06	0.816
60–70 yrs	1.64	0.70–3.82	0.26
>70 yrs	3.99	1.37–11.67	**0.0197**

Table 5: Odds ratios for urinary tract infection by age group.

Age group	Odds ratio	95% confidence interval	p-value
<50 yrs	Reference		
50–60 yrs	1.82	0.79–4.19	0.199
60–70 yrs	2.79	1.23–6.34	**0.0154**
>70 yrs	5.86	2.01–16.56	**0.0027**

Table 6: Odds ratio for urinary retention by age groups.

Age group	Odds ratio	95% confidence interval	p–value
<50 yrs	Reference		
50–60 yrs	1.08	0.40–2.92	0.88
60–70 yrs	1.30	0.46–3.68	0.62
>70 yrs	6.61	2.29–19.11	**0.0017**

donors (BMI >30 kg/m^2; 11.5% of the study population) and early complications of any kind. Whether this holds true for very obese donors (BMI >35 or >40 kg/m^2) is unclear as only 1.2% of our study population had a BMI >35 kg/m^2. Mjoen also found no association with perioperative bleeding and/or intraoperative incidents in their 8.3% obese donors with a BMI >30 kg/m^2 [8]. O'Brien reported an overall equal early complication rate in obese patients (25.6% of their study population) in a series of 383 donor nephrectomies, but a higher incidence of respiratory complications in a subgroup analysis of patient with a BMI >40 kg/m^2 [30]. Schold et al., in a large US registry study, did not find any association between obesity and procedure-related complications in more than 69 000 donor nephrectomies [19]. These data are in contrast to the registry-based studies from Friedman et al. and Patel et al., who reported a higher incidence of donor complications in obese patients with ORs of 1.76 and 1.92, respectively [16, 18]. Overall, the available data and our experience suggest an acceptable safety of nephrectomy in obese patient, with low levels of severe early complications across all BMI categories, but long-term surveillance of new onset of arterial hypertension or diabetes is mandatory when obese patients are accepted for donation.

Infectious diseases after donation were the most frequent Grade 2 complication, with a high rate of clinical UTI (2.6%). In contrast, Mjoen et al [8] found a much higher incidence of UTI (10.1%). But in their study, donors were systematically screened postoperatively with urine culture for UTI without differentiation between asymptomatic bacteriuria and clinical UTI. So there might be an overestimation of UTI in their study. We assume that the higher rate of urinary retention observed in male elderly donors is due to an underlying prostatic hyperplasia. We observed some complications associated with intraoperative positioning of the donor in 0.7%, as well as anaesthesia-related complication in 0.4% of donors. Data about the incidence of such complications in living donor nephrectomy are very rare in the literature, with only a few case reports of rhabdomyolysis after donor nephrectomy [31, 32]; this suggests an underreporting of such incidents.

Eighteen per cent of donors had a history of hypertension at the time of donation, which is comparable to other registries [7, 8]. During the hospitalisation, new onset hypertension was diagnosed in another 0.9% of donors. Previously published data from the SOL-DHR have shown that kidney donation increases the risk of hypertension after 1 year 3.64-fold [33] underlining the importance of close blood pressure surveillance after kidney donation.

The strengths of the current study are the prospective nature, standardisation, consistency and completeness of the data collected over 18 years on a nationwide basis, i.e., including every single consecutive donor within one country and resulting in a high number of donors included in the analysis. Data collection was very detailed and regular queries were made. In addition, each complication was confirmed by the medical staff of the SOL-DHR. Underreporting was further minimised by including complications reported to the SOL-DHR by the donors or their general practitioner. After confirmation these complication were included in the analysis.

However, there are also several limitations. Despite the very careful prospective collection of the complications on a standardised questionnaire, there remains a risk of underreporting of early complications and a lack of systematic review of donor charts and surgical reports. Secondly, the low frequency of major complications and intraoperative incidents limits multivariate analysis of several risk factors. Thirdly, there might be other risk factors not known and therefore not collected specifically by the SOL-DHR. However, patients had the possibility to mention any complication as free text on the form. Up to now, no clear complication or problem could be identified. Last, but not least, caution is necessary in extrapolating the low complication rates seen in our study to other cohorts without considering a potentially overall lower risk profile of our Swiss donor population.

In summary, our data confirm that living donor nephrectomy is a safe procedure with a low rate of major and minor complications, independent of surgical technique. We did not find a higher incidence of any complication in obese donors, which supports the policy of acceptance of obese individuals for donation. In contrast, we found a higher incidence of severe complications (Clavien 3 and 4) and genitourinary complications (UTI, urinary retention) in donors aged >70 years. It is mandatory to carefully inform older donors about their elevated perioperative risks. Furthermore, continuous prospective evaluation of donor complications by donor registries is crucial, to improve peri- and postoperative management and to detect any increase in risks, as donors with more comorbidities are accepted nowadays. Our results have prompted our Swiss working group for living donors to renew the documents for donors` general information accordingly.

Acknowledgement

We would like to thank the medical/surgical team of the Swiss Transplant centres for collecting the data. We would also like to thank Daniela Garzoni from the SOL-DHR for her help and support.

Financial disclosure

The study was sponsored by Viollier AG, Allschwil, Switzerland.

Competing interests

No potential conflict of interest relevant to this article was reported.

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Appendix 1: Questionnaire for reporting surgical complications to the SOL-DHR

The questionnaire is available as a separate file at https://smw.ch/en/article/doi/smw.2017.14497/