



ORIGINAL RESEARCH ARTICLE

## Early and late surgical complications following living donor nephrectomy

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### ABSTRACT

**Objective:** To report early and late surgical complications following laparoscopic, open and hand-assisted laparoscopic living donor nephrectomy, including duration of sick leave, kidney function and potential risk factors for surgical complications.

**Material and methods:** Retrospective study on living kidney donors between September 2014 and June 2021 at Rigshospitalet, Copenhagen. Patient data included demographics, comorbidities, surgical information, and postoperative complications (early <30 days and late >30 days). Complications were graded according to Clavien Dindo (CD). Return to work and reasons for prolonged sick leave were recorded.

Multivariable logistic regression to identify risk factors for early complications CD  $\geq 2$  and time-dependent cause specific Cox regression to identify risk factors for late complications.

**Results:** A total of 223 living donors were included. Early complications were observed in 22% of donors. Early complications were often mild, and the most common complications were pneumonia, wound infection, and urinary retention. Of the 201 donors available for long-term follow-up, 10% experienced a late complication, including incisional port-site hernia and chronic post-surgical pain. 18% reported a prolonged sick leave beyond the planned 6 weeks.

**Conclusions:** Living donor nephrectomy is associated with a low risk of serious early surgical complications although many will experience minor related complications. As surgical safety has been confirmed in several studies the focus should be on the psychosocial and long-term aspects of living kidney donation to meet donor concerns pre-donation.

### ARTICLE HISTORY

Received 25 September 2024

Accepted 10 March 2025

Published 5 May 2025

### KEYWORDS

Laparoscopy; hand-assisted laparoscopy; nephrectomy; living kidney donor; surgical complications; renal transplantation

## Introduction

Living kidney donors are healthy individuals who, for the benefit of others, undergo surgery with the risk of short- and long-term complications. The potential donors undergo a thorough health screening to ensure optimal safety for the donor, and quality of the donated kidney, which in turn ensures recipient and graft survival [1, 2]. Previous studies show an overall low surgical complication rate in living donor nephrectomy [3], but the complication rates vary [4]. Risk factors for surgical complications are more elusive and vary significantly in published studies [4–6].

The risks of surgery may impair donor quality of life, and it is therefore crucial, that healthcare professionals and donors are aware of surgical risks, but also the psychological stress and fatigue associated with donation [7]. A qualitative study showed that the core outcomes for the donor pre-donation were surgical complications, long-term kidney function, and time to recovery including duration of sick leave [8]. However, a review on the studies reporting on the outcomes following living kidney donation states that 89% of the studies have follow-up less than a year which impairs reporting of late complications [9].

Thus, more studies with longer follow-up and a strict classification of surgical complications adherent to guidelines are still needed as well as studies on labor affiliation and kidney function following living kidney donation [10].

We aimed to describe early and late surgical complications following living donor nephrectomy and to identify donors at increased risk of surgical complications. Further, we describe return to work post donation and long-term kidney function.

## Patients and methods

All living kidney donors between September 2014 and June 2021 at Rigshospitalet, Copenhagen, Denmark were included. Data includes demographic data, information from the work-up before transplantation, and peri- and post-operative information. Comorbidities were graded according to the Charlson Comorbidity Index (CCI) [11]. Data was obtained from the donors' electronic health records from the first pre-donation visit until the loss to follow-up, death, or until the last date of follow-up 31st of December 2021, whichever

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Supplemental data for this article can be accessed online at <https://doi.org/10.2340/sju.v60.43346>

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occurred first. Loss to follow-up was registered if the donor was referred to follow-up in another region or the patient's general practitioner.

### **Work-up pre-donation**

The selection and work-up of possible living kidney donors follow the KDIGO (kidney disease improving global outcome) guidelines [2]. Potential donors have to be a minimum of 18 years of age to be considered as living donors. We have no strict upper age limit. A body mass index (BMI) > 35 is a relative contraindication, but it depends on body fat distribution as evaluated by the surgeon.

During the work-up, comorbidities, current medication, and family history of cardiovascular disease, diabetes, and cancer were recorded. The glomerular filtration rate was measured by <sup>51</sup>Cr-EDTA and adjusted for body surface area. The estimated Glomerular Filtration Rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation [2]. A CT scan was performed to evaluate kidney and vessel anatomy and a renography to evaluate the right/left division of kidney function. An experienced urologist evaluated the CT scan and renography to decide which kidney should be donated. In general, a single-vessel kidney was preferred.

Living donors visit the outpatient clinic 5 weeks post-transplantation, at 3 months and 1 year, and after that, donors are offered life-long follow-up with yearly visits. Financial coverage of loss of income and any expenses for transportation and other donation-related expenses is covered by the Danish Ministry of Health. The standard duration of planned sick leave was 6 weeks post-donation.

### **Surgical technique**

The surgical techniques were open donor nephrectomy (ODN), laparoscopic donor nephrectomy (LDN), and hand-assisted laparoscopic donor nephrectomy (HALDN). Five surgeons performed the procedures. Patients were placed in a left or right flank position with a slight break in the table according to the side of the nephrectomy.

With laparoscopy, the first port was placed according to the Hasson open technique, and the next three ports were placed under visual guidance (5- and 12-mm trocars). The right or left colonic flexure mobilization was conducted and the kidney was dissected as well as the ureter which was divided with surgical clips. Thereafter, the renal vessels were dissected and divided with endovascular GIA. The kidney was put in an endo-bag and removed by enlarging one of the port holes.

For the hand-assisted laparoscopy, a gel port was used. The port was inserted in an open incision in the right fossa. The next three ports were placed under visual guidance as with the laparoscopic approach. The fascia was closed with a synthetic, monofilament absorbable suture. The skin was closed with monofilament, synthetic resorbable suture intracutaneously, or a non-absorbable monofilament suture.

The open procedures were performed through an incision under the curvature or through a midline incision in a patient who had previous abdominal surgery.

The prophylactic antibiotics used perioperatively were cephalosporin and were administered as a single dose and thromboprophylaxis included low molecular weight heparin the night before donation and graduated compression stockings post-operatively.

### **Surgical complications and late outcomes**

Perioperative complications were defined as adverse events during surgery and were registered if perioperatively bleeding was >500 mL, an injury to a vessel, intestine, or another organ as well as perioperative conversion to open or hand-assisted approach.

Postoperative complications were divided into early (≤30 days) and late (>30 days). All complications were graded according to the Clavien Dindo (CD) classification [12].

The complications were subdivided into wound-related, vascular, infectious, and miscellaneous. Wound infection was defined as clinical signs of infections and/or culture-verified wound infection. Wound dehiscence was either partial or total dehiscence where parts of the incision had pulled apart requiring secondary suturing or application of sterile strips. Vascular complications were defined as bleeding or symptomatic hematomas. Infectious complications were urinary tract infections (UTIs) with symptoms and culture-verified infection. Pneumonia was defined as elevated infectious parameters, coughing, and either radiological or culture-verified pneumonia. Chronic post-surgical pain was defined as pain persisting >3 months following surgery where other causes of pathology were ruled out.

It was registered if the donor had returned to work within 6 weeks post-donation. If not, the reason for prolonged sick leave was recorded, and the duration in weeks of the prolonged sick leave.

Creatinine was registered 1-, 2- and 3 years post-donation, and it was registered if it was above the gender-specified threshold, 90 µmol/L for females and 105 µmol/L for men.

### **Statistical analysis**

Continuous variables are reported as median with interquartile range (IQR), full range or mean and standard deviation (sd). Categorical variables are reported as frequency accompanied by percentages of the total.

Multivariable logistics regression analysis was used to analyze the association between donor-related variables and early (≥CD2) complications. The results are presented by odds ratio (OR) with 95% confidence interval (95% CI). Model control was performed using the Box-Tidwell test.

The median time of follow-up was calculated using the reverse Kaplan-Meier method.

Multivariable time-dependent cause-specific Cox proportional-hazards regression was performed to analyze the risk of late surgical complications, with results presented as hazard ratio

(HR) and 95% CI. Independent samples t-test was used to compare the surgical procedures regarding WIT (warm ischemia time), intraoperative blood loss, and time of surgery.

All tests were two-sided, and p-values less than 0.05 were considered statistically significant. Statistical analysis was performed in SPSS and R-studio version 4.1.0.

## Results

A total of 223 living donor nephrectomies were performed in the inclusion period.

Background information is presented in Table 1. More than half of the patients were female, and 92% had a CCI of 0. Hypertension at the time of donation was present in 14% of the donors.

Fifteen donors (7%) were lost to follow-up within the first months as they were from Greenland, the Faroe Islands, or another region in Denmark.

### Peri- and post-operative outcomes

Table 2 shows the perioperative characteristics and early complications. The left kidney was chosen in 66% of the cases. The technique used for the right kidney was HALDN except for one right kidney that was removed laparoscopically as per surgeon preference. The use of HALDN and LDN was the same during the included time period.

The ODN procedures occurred in the beginning of the included period, because the specific surgeon could not perform LDN.

When comparing LDN and HALDN, there was significantly shorter WIT and time of surgery in the HALDN group ( $p < 0.001$ ). Blood loss and length of stay (LOS) were comparable between the three groups (Appendix 1).

One or more perioperative complications occurred in 19 donors with the most frequent being lesion of a vein ( $n = 5$ ). Overall, complications were mild and there was no perioperative mortality. Two laparoscopic procedures were converted to open procedures, and five laparoscopic procedures were converted to hand-ports due to complications.

Early complications occurred in 22% of the cases. The most frequent early complications were urinary retention (6%), pneumonia (4%), wound infection (2.6%), and other (3.5%) which includes subcutaneous emphysema, dyspnoea requiring continuous positive airway pressure (CPAP) and haematuria. Half of the early complications were CD grade 1. Four donors required reoperation within the first 30 days. One patient who underwent ODN was reoperated three times, the first time due to fascia rupture and the following two reoperations were caused by suspicion of fascia rupture but turned out to be collections of fluid in the subcutaneous space that were drained. One patient had severe postoperative pain, and a CT scan of the abdomen revealed free air in the abdomen. The patient was reoperated, no perforations were found; however, a fluid collection was treated with drainage. The remaining two patients that were reoperated had hematomas that were drained surgically.

In multivariable modeling, we found an interaction between former smokers and increasing age for the risk of early  $\geq$ CD 2

**Table 1.** Baseline characteristics of the living donor population (2014–2021) including demographic variables and donor medical history.

| Preoperative characteristics                       | N = 223           |
|----------------------------------------------------|-------------------|
| <b>Age, Median (min;max)</b>                       | 54 (23; 76)       |
| <b>BMI, Median (IQR) (missing 7)</b>               | 26.5 (23.8; 28.9) |
| <b>BMI groups N (%)</b>                            |                   |
| Normal weight <25                                  | 77 (34.5)         |
| Overweight 25–30                                   | 93 (41.7)         |
| Obese > 30                                         | 46 (20.6)         |
| <b>Female, n (%)</b>                               | 123 (55.2 %)      |
| <b>Charlson Comorbidity Index</b>                  |                   |
| - 0                                                | 204 (91.5%)       |
| - 1                                                | 15 (6.7%)         |
| - 2                                                | 4 (1.8%)          |
| <b>Familiar disposition diabetes</b>               | 21 (9.4%)         |
| <b>Familiar disposition cardiovascular disease</b> | 21 (9.4%)         |
| <b>Previous kidney stones</b>                      | 7 (3.1%)          |
| <b>Hypertension</b>                                | 30 (13.5%)        |
| <b>Smoking status</b>                              |                   |
| - Never smoker                                     | 93 (41.7%)        |
| - Former smoker                                    | 85 (38.1%)        |
| - Current smoker                                   | 45 (20.2%)        |
| <b>mGFR/clearance</b>                              |                   |
| <b>Median (IQR)</b>                                | 105 (89; 120)     |
| <b>Adjusted for body surface</b>                   | 93.5 (84; 106)    |
| <b>Medication</b>                                  |                   |
| - No medication                                    | 120 (53.8%)       |
| - Cholesterol lowering                             | 18 (8.1%)         |
| - Thyroid medication                               | 10 (4.5%)         |
| - Antidepressant                                   | 10 (4.5%)         |
| - Antihypertensive                                 | 22 (9.9%)         |
| - Diuretics                                        | 14 (6.3%)         |
| - Betablocker                                      | 2 (0.9%)          |
| - Astma inhalation                                 | 10 (4.5%)         |
| - Other medication                                 | 69 (30.9%)        |
| <b>Social status</b>                               |                   |
| <b>Living alone</b>                                | 41 (18.4%)        |
| <b>Blood related to recipient</b>                  | 121 (54.3%)       |

BMI: body mass index; eGFR: estimated glomerular filtration rate; IQR: Interquartile range; SSRI: selective serotonin reuptake inhibitors.

\*Disposition: first degree relative with diabetes. Cardiovascular disease: first degree relative with cardiovascular disease before the age of 55 (men) and 65 years (women).

complications (OR: 1.11, CI: 1.01; 1.22,  $p = 0.03$ ) (Table 2). This effect could not be detected for current smokers.

Late complications and outcomes are presented in Table 3. A total of 201 donors had available long-term follow-up of which 10% experienced late complications which included port-site incisional hernias ( $n = 8$ ) and chronic post-surgical pain ( $n = 8$ ). Seven donors were reoperated >30 days after donation, of which five were due to port-site incisional hernia.

We did not find an association between the included variables (BMI, age, use of tobacco, and surgical technique) and the risk for late complications (Table 3). Most late complications occurred within the first 2 years post-donation and were comparable between the LDN and HALDN groups (Appendix 2).

### Late outcomes

Forty-four percent of the donors returned to work within the planned 6-week sick leave (Table 3). Of the donors who had a job

**Table 2.** Perioperative characteristics for living donor nephrectomy procedures, early complications and risk factors for early complications > Clavien Dindo 2 (< 30 days).

| Early complications                                                                            |                             |
|------------------------------------------------------------------------------------------------|-----------------------------|
| Perioperative characteristics, % (N)                                                           | N = 223                     |
| Left kidney                                                                                    | 66.4% (148)                 |
| ODN                                                                                            | 1.8% (4)                    |
| LDN                                                                                            | 65.5% (146)                 |
| HALDN                                                                                          | 32.7 (73)                   |
| Multiple veins                                                                                 | 5.3% (12)                   |
| Multiple arteries                                                                              | 19.2% (43)                  |
| Perioperative complication                                                                     | 8.5% (19)                   |
| - Bleeding > 500 mL                                                                            | 1.8% (4)                    |
| - Lesion of intestine                                                                          | 0.9% (2)                    |
| - Lesion of spleen                                                                             | 0.9% (2)                    |
| - Injury to a vein*                                                                            | 2.2% (5)                    |
| - Injury to an artery                                                                          | 1.7% (4)                    |
| - Conversion to hand-port**                                                                    | 2.2% (5)                    |
| - Conversion to open                                                                           | 0.9% (2)                    |
| - other***                                                                                     | 0.4% (1)                    |
| Time of surgery (min)                                                                          | 114.17±26.68 <sup>a</sup>   |
| Blood loss (mL), mean ± sd                                                                     | 51.04 ± 187.67 <sup>b</sup> |
| WIT (min) mean ± sd                                                                            | 2.42 ± 1.41 <sup>c</sup>    |
| Length of stay (days), median (IQR)                                                            | 4 (3; 5)                    |
| Early complications                                                                            |                             |
| Early complications % (N)                                                                      | 21.5% (48)                  |
| Wound-related                                                                                  |                             |
| Wound infection                                                                                | 2.6 % (6)                   |
| Neuropathic pain                                                                               | 1.3% (3)                    |
| Wound dehiscence                                                                               | 0.4% (1)                    |
| Vascular                                                                                       |                             |
| Hematoma                                                                                       | 1.7% (4)                    |
| Infectious                                                                                     |                             |
| UTI                                                                                            | 1.8% (4)                    |
| Pneumonia                                                                                      | 4.0% (9)                    |
| Sepsis                                                                                         | 0.4% (1)                    |
| Miscellaneous                                                                                  |                             |
| Fascia rupture                                                                                 | 0.9% (2)                    |
| Collection                                                                                     | 1.3% (3)                    |
| Testicular pain/swelling                                                                       | 0.4% (1)                    |
| Urinary retention                                                                              | 5.8% (13)                   |
| Other                                                                                          | 3.5% (8)                    |
| Clavien Dindo                                                                                  |                             |
| Clavien Dindo 1                                                                                | 12.5% (28)                  |
| Clavien Dindo 2                                                                                | 9.4% (21)                   |
| Clavien Dindo 3b                                                                               | 2.7% (6)                    |
| Reoperations <30 days****                                                                      |                             |
| Hematoma                                                                                       | 0.8% (2)                    |
| Fascia rupture                                                                                 | 0.8% (2)                    |
| Collection                                                                                     | 1.2% (3)                    |
| Multivariable logistic regression analysis for early complications >Clavien Dindo 2 (<30 days) |                             |
| Variable                                                                                       | OR (95% CI)                 |
| Age at time of donation (per year increase)                                                    | 0.95 (0.88; 1.02)           |
| BMI normal weight (<25)                                                                        | Reference                   |
| BMI overweight (BMI 25–30)                                                                     | 2.07 (0.71; 6.00)           |

**Table 2.** (continued)

| Variable                                   | OR (95% CI)       |
|--------------------------------------------|-------------------|
| BMI obese (BMI > 30)                       | 1.57 (0.43; 5.73) |
| Per year increasing age and never smoker   | Reference         |
| Per year increasing age and former smoker  | 1.11 (1.01; 1.22) |
| Per year increasing age and current smoker | 1.11 (0.96; 1.29) |

\*The lesions of veins intraoperatively were primarily lesions to the lumbar veins (*n* = 3) and were handled by the insertion of clips.

\*\* Laparoscopic procedures where hand-port was inserted intraoperatively.

\*\*\*Lesion of low diaphragm, clips.

\*\*\*\* four patients had seven reoperations.

<sup>a</sup>Available data for 141 donors.

<sup>b</sup>Data available on 208 donors.

<sup>c</sup>Data available on 105 donors.

BMI: Body mass index; CI: Confidence Interval; HALDN: hand-assisted laparoscopic donor nephrectomy; IQR: Interquartile range ; LDN: Laparoscopic donor nephrectomy; ODN: open donor nephrectomy; OR: Odds ratio; SD: Standard deviation; UTI: Urinary tract infection; WIT: Warm ischemia time

pre-donation, 29% (*n* = 40) prolonged their sick leave exceeding the planned 6 weeks. The reasons for prolonged sick leave were predominantly pain after surgery (*n* = 12), fatigue (*n* = 6), or because the donor had a physically challenging occupation that they could not maintain within the first 6 weeks post-donation.

Out of the 165 donors with available 1-year follow-up data, the median creatinine was 104 (IQR: 92; 115). Above-threshold creatinine was found in 70% of the donors, and 30% had creatinine within the gender-specified threshold.

In the follow-up period, only one donor died (6 years post-donation), and the cause of death was cancer. Median follow-up was 3.51 years (IQR: 1.30; 5.22).

The cumulative incidences of graft loss after 1 and 5 years were 1.4% (95% CI: 0; 2.9) and 9.4% (95% CI: 4.5; 14.3) respectively.

## Discussion

In this study, we found that most living kidney donors had mild postoperative complications and identified risk factors for early complications ≥CD2 being a history of tobacco use in combination with increasing age.

Over the years, there have been several improvements in surgical techniques for living donor nephrectomy, most importantly the shift from open to laparoscopic surgery [13]. Moreover, improvements in anesthesia and post-operative surgical care should make donor nephrectomy safe, but this should be consistently documented for tertiary specialized centers that operate a kidney transplantation program. The considerations before living donation entail the surgeon's reflections on surgical approaches and laterality of the kidney, aspects regarding the recipient, as well as the donor's concerns about the potential consequences.

Early complications following nephrectomy for kidney cancer are reported to be 12–30% [14, 15]. In living kidney donors, this is reported to be 7–18% [3, 16, 17]. The healthy screening bias between cancer patients and healthy donors likely explains the difference. Most of the complications for living donors are mild (CD 1 or 2) as is the case in our study. The somewhat higher

**Table 3.** Late outcomes for living kidney donation and risk factors for late surgical complications (> 30 days).

| Variable                                                                              | N (%)              |
|---------------------------------------------------------------------------------------|--------------------|
| Late complications <sup>a</sup> (N = 201)                                             | 23 (10.3%)         |
| Port-site incisional hernia <sup>b</sup>                                              | 8 (3.6%)           |
| Chronic post-surgical pain                                                            | 8 (3.6%)           |
| Unsatisfied with cosmetic results of wound                                            | 3 (1.3%)           |
| - Need for revision of wound                                                          | 1 (0.4%)           |
| Abscess/infection in wound                                                            | 1 (0.4%)           |
| Testicular pain/swelling                                                              | 2 (0.9%)           |
| Clavien Dindo                                                                         |                    |
| Clavien Dindo 1                                                                       | 13 (5.8%)          |
| Clavien Dindo 2                                                                       | 3 (1.3%)           |
| Clavien Dindo 3b                                                                      | 7 (3.1%)           |
| Reoperations > 30 days                                                                |                    |
| Collections                                                                           | 2 (1%)             |
| Port-site incisional hernia                                                           | 5 (2.5%)           |
| eGFR values 1-year post-donation (mL/min/1.73m <sup>2</sup> ) (n = 181) <sup>c</sup>  |                    |
| - < 45                                                                                | 13 (7.2%)          |
| - 46–59                                                                               | 61 (33.7%)         |
| - 60–90                                                                               | 75 (41.4%)         |
| - > 90                                                                                | 0                  |
| - Missing                                                                             | 32 (17.7%)         |
| Status 6 weeks post-donation, N (%)                                                   |                    |
| Return to work within 6 weeks                                                         | 98 (43.9%)         |
| Prolonged sick leave                                                                  | 40 (17.9%)         |
| Retired pre-donation                                                                  | 49 (22.0%)         |
| Unemployed pre-donation                                                               | 9 (4.0%)           |
| Unknown                                                                               | 27 (12.1%)         |
| Weeks of prolonged sick leave (after the first 6 weeks)                               |                    |
| 1–6 weeks                                                                             | N = 30             |
| 7–12 weeks                                                                            | N = 6              |
| 13–20 weeks                                                                           | N = 2              |
| Unknown                                                                               | N = 2              |
| Reason for prolonged sick leave                                                       |                    |
| Pain                                                                                  | N = 12             |
| Fatigue                                                                               | N = 6              |
| Physical work                                                                         | N = 7              |
| Psychological distress                                                                | N = 4              |
| Other (i.e. taking care of recipient)                                                 | N = 3              |
| Unknown                                                                               | N = 2              |
| Multivariable cause-specific Cox proportional hazards of late complications > 30 days |                    |
| Variable                                                                              | HR (95% CI)        |
| Age per year difference                                                               | 1.00 (0.97; 1.03)  |
| Surgical technique LDN                                                                | Reference          |
| Surgical technique HALDN                                                              | 0.93 (0.37; 2.3)   |
| Surgical technique ODN                                                                | 3.75 (0.47; 29.82) |
| Never smoker                                                                          | Reference          |
| Former smoker                                                                         | 1.10 (0.42; 2.87)  |
| Current smoker                                                                        | 1.51 (0.51; 4.43)  |
| Normal BMI < 25                                                                       | Reference          |
| BMI overweight (25–30)                                                                | 1.67 (0.44; 3.57)  |
| BMI obese (> 30)                                                                      | 2.35 (0.80; 6.93)  |

<sup>a</sup>22 donors were lost to follow-up due to follow-up in another region or country (Faroe Islands or Greenland).

<sup>b</sup>Five donors were operated for port-site incisional hernia. The remaining three donors who experienced port-site incisional hernia were not operated on as the hernia was not symptomatic and the physician and donor agreed on an observational strategy.

<sup>c</sup>Data included for patients with follow-up ≥12 months. The missing data is due to missing laboratory values before 2016 when the electronic chart system changed.

BMI: Body mass index; CI: Confidence Interval; eGFR: estimated glomerular filtration rate; HALDN: hand-assisted laparoscopic donor nephrectomy; LDN: Laparoscopic donor nephrectomy; ODN: open donor nephrectomy; OR: Odds ratio.

overall complication rate in our center possibly reflects our systematic grading of all complications as well as the high rate of CD 1 complications (13%) and our reporting of previously underreported complications such as testicular pain and chronic post-surgical pain [18, 19].

The rapid development of surgical approaches for living donor nephrectomy offers a wide array of possibilities. The EAU guideline recommendations for living donor nephrectomy are either LDN or HALDN which are the methods used in this study in 98% of the cases [20]. HALDN offers tactile feedback as the surgeon's hand is in the abdominal cavity during the procedure whereas the scars are smaller in LDN as no hand-port is inserted. Our results align with the findings of previous studies that found LDN and HALDN to have comparable results in terms of early complications, long-term outcomes, and graft survival. The choice of procedure should thus be determined by the expertise of the surgeon and the surgical center [21].

Regardless of the choice of procedure, the time to recovery and continuation of daily life post-donation with as little surgical morbidity is crucial. A Danish study showed post-donation fatigue was the primary reason for prolonged sick leave in living kidney donors and other qualitative studies have shown that fatigue predominantly affected female donors [22, 23]. The extended sick leave in 17.9% of the donors in our study aligns with other cohorts, and the main reasons were fatigue and pain [23, 24]. As the sick leave and financial coverage vary between countries the return to work and sick leave period is difficult to compare internationally.

In the last 50 years, the background population has increased BMI, age, and comorbidities and this shift in demographics is also the case for living donors [25]. These parameters should therefore be considered for living donors and in the analysis for risk factors. We found no increased risk of postoperative complications in donors with BMI > 25. This might be because the donors are a highly selected group with few comorbidities, and therefore increased BMI does not impose a significant risk. Other anthropometric measures such as hip/waist circumference could substitute BMI; however, Westenberg et al. found no association between peri- and postoperative complication and higher pre-nephrectomy BMI or other anthropometric measure of body composition. Westenberg et al found no association between peri- and postoperative complications and higher pre-nephrectomy BMI or other anthropometric measures of body composition [26]. Another study by Sterkenburg et al. found in a cohort of 496 living donors that in multivariate analysis male sex was associated with higher overall perioperative complication rate and male sex and higher BMI increased the risk of late complications [4]. We did not identify these risk factors in the current paper. However, we found that a history of smoking in donors with increasing age to be a significant risk factor for complications ≥CD2. A systematic review and meta-analysis on the effects of preoperative smoking in different types of surgery showed that patients with a history of smoking had a significantly increased risk of post-operative general morbidity, wound complications, and general infections [27]. Our findings are confirmed by another Nordic study where

tobacco smoking was shown to be a risk factor for surgical complications in living kidney donors [28]. We did not find that current smokers were at increased risk of surgical complications. This is possibly explained by the number of patients included, and due to the low number of complications  $\geq$ CD2, our study is underpowered to detect a potential increased risk in current smokers. Furthermore, another potential bias is that we have no detailed knowledge on the exact consumption of tobacco. Although potential living donors are recommended to stop smoking 6 weeks before surgery, the potential harmful effects of smoking should be underlined for the donors and smoking cessation initiatives implemented.

Smoking is not only a risk factor for surgical complications but has also been shown to impact long-term kidney function post-nephrectomy [29]. The risk of end-stage kidney disease (ESKD) for living donors was increased in a study by Muzaale et al. compared to the background population with an estimated cumulative incidence at 15 years post-donation of 30.8 per 10.000 (95% CI: 24.3–38.5) [30]. The risk was increasing with age at the time of donation. In our study, no patients progressed to ESKD in the included follow-up period.

The limitations of this study include the retrospective nature of the study with the risk of reporting bias, and that 6% of donors were lost to follow-up within the first month as they came from the Faroe Islands, Greenland, and other regions of Denmark. Furthermore, we have missing data on WIT and time of operation, predominantly in the years from 2014 to 2016, as the electronic health record changed to a new system in 2016. As postoperative complications are not common in this healthy population, this study is potentially underpowered to detect other risk factors for postoperative complications. This is indicated by some of the wide confidence intervals in the regression analysis for late complications such as surgical technique ODN (0.47; 0.29.8) and BMI > 30 (0.80; 6.9).

The strengths include the systematic reporting and grading of surgical complications as well as long follow-up and available recipient data. The long follow-up allows us to report core outcomes such as long-term complications, psychosocial factors such as return to work and prolonged sick leave as well as kidney function in the years following donation.

## Conclusion

In conclusion, this large cohort of living donor nephrectomy provides an in-depth overview of early and late complications and late outcomes. Our results support previous findings of the safety of living donor nephrectomy and the current work-up standards ensure that the donors are healthy with an overall low risk of surgical complications. However, it also emphasizes the need for stringent reporting of complications and use of grading systems so complication rates can be compared between centers. The high proportion of donors with extended sick leave further reinforces the importance of studies with long-term follow-up including long-term surgical outcomes and potential psychosocial consequences for living donors.

## Disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We thank Hein Vincent Stroomberg, MSc, Ph.D. for the statistical support for this paper.

## Funding and ethics

This work was partially supported by the Novo Nordisk Foundation (grant number NNF210C0072224) and by The Danish Kidney Association (Nyreforeningen).

The study was approved by the Danish Data Protection Agency (P-2019-661).

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