

Robotic-Assisted Versus Conventional Open Partial Nephrectomy (Robocop): A Propensity Score-Matched Analysis of 249 Patients

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Keywords

Partial nephrectomy · Urological surgery · Robotic-assisted surgery · Renal neoplasm · Propensity score

Abstract

Objectives: The objective of this study was to compare open partial nephrectomy (OPN) and robotic-assisted PN (RAPN) based on a propensity score-matched sample and to test the Comprehensive Complication Index (CCI) as an end point for complications. **Methods:** Patients undergoing PN from 2010 to 2018 at a university care center were included. OPN and RAPN cases were matched in a 2:1 ratio using propensity score-matching with age, gender, BMI, RENAL score, and tumor size as confounders. The primary end point was complications measured with the CCI as continuous score (0–100, 100 indicating death). **Results:** Data of 570 patients were available. After matching, both cohorts (OPN = 166; RAPN = 83) showed no baseline differences. For the primary end point, CCI, RAPN was superior (RAPN 2.6 ± 7.9 vs. OPN 8.7 ± 13.9 ; $p < 0.001$). Additionally, RAPN was superior for length of stay (RAPN 6.5 ± 4.0 vs. OPN 7.4 ± 3.5 days; $p < 0.001$), hemoglobin drop (RAPN 2.8 ± 1.4 vs. OPN 3.8 ± 1.6 g/dL; $p < 0.001$), and drop of glomerular filtration rate (RAPN 11.4 ± 14.2 vs. OPN 19.5 ± 14.3 mL/min; $p < 0.001$). OPN had shorter

operating times (RAPN 157 ± 43 vs. OPN 143 ± 45 min; $p = 0.014$) and less ischemia (RAPN 13% vs. OPN 28%; $p = 0.016$).

Conclusions: RAPN provides superior short-term results regarding overall complications without compromising renal function for small and less complex tumors. However, OPN remains an important option for more complex and larger tumors.

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Introduction

Annually, 15,000 cases of renal cell carcinoma are diagnosed in Germany. This number accounts for 3% of all new cancer diagnoses and is the third most common cancer of the urogenital tract. At the moment of diagnosis, more than 60% are still of a localized pT1 tumor stage [1]. Partial nephrectomy (PN) is the method of choice for surgical treatment [2].

In Germany, open partial nephrectomy (OPN) is performed in about 63% of cases and therefore still considered as the current standard of care. In contrast, robotic-assisted partial nephrectomy (RAPN) is performed in approximately 22% of cases. In recent years, RAPN is gaining increasing importance, but with remarkable vari-

ances between the different countries. A study by Flegar et al. [3] showed an increase in RAPN cases in the United States from zero to 54.5% and in Germany from 0.2 to 8.6% between 2006 and 2014.

According to the 2013 EAU guidelines, robotic and conventional laparoscopic partial nephrectomy are equally recommended as OPN [4]. The potential advantages of minimally invasive surgery, including RAPN and laparoscopic PN, include a lower risk of bleeding [5], postoperative wound infection [6], less need for analgesia [7], and allows earlier mobilization of the patient and therefore a shorter hospital stay [8], leading to a faster recovery and return to daily life. In addition, Chatterjee et al. [9] reported a higher incidence of permanent flank bulges and durable flank pain for OPN. These assumptions were confirmed in recent meta-analyses by Cacciamani et al. [10] and Tsai et al. [11]. One of the limitations which was well discussed by the authors is the lack of appropriate statistical measures such as propensity score matching in the retrospective studies. This can account for baseline imbalances between OPN and RAPN cases to some extent [12, 13]. In addition, validated nephrometry scores such as RENAL or PADUA were not always used as matching variables to account for tumor complexity in those studies [14, 15].

Furthermore, both OPN and RAPN are safe procedures with generally low complications rates. The Clavien-Dindo Classification (CDC) has well-documented limitations in terms of sensitivity and interpretation. Therefore, the Comprehensive Complication Index (CCI), which is based on the CDC but summarizes the cumulative burden of complications on a continuous scale from zero (no complication) to 100 (death), was tested as an appropriate end point to compare complications between both groups [16, 17]. Furthermore, the CCI was validated of major uro-oncological procedures such as PN, radical prostatectomy, and radical cystectomy [18].

The aim of this study was the comparison between OPN and RAPN based on a propensity score-matched sample and to test the CCI as a primary end point for complications in order to gain evidence for the preparation of future randomized controlled trials.

Material and Methods

Data Collection

Data were retrieved from a retrospectively (January 2010 until 2016) and prospectively (since 2016) maintained database from the Department of Urology at the University Medical Center Mannheim at Heidelberg University (institutional review board approval 2014-811R-MA). All consecutive patients undergoing ei-

ther OPN ($n = 809$) or RAPN ($n = 93$) until 2018 were screened, leading to a complete sample of 902 patients. Patients undergoing radical nephrectomy were not considered. Additionally, the RAPN program was introduced in 2014 at our institution. Patients with incomplete data or missing digital preoperative imaging were excluded from analysis.

Preoperative demographic and clinical information were used for propensity score matching (see Table 1). The assessment of tumor complexity was based on the RENAL nephrometry score as well as tumor size. Patients with missing data on BMI, tumor size, RENAL score or patients with multiple tumors, simultaneous cystoprostatectomies, imaging or inaccurate data were excluded, leading to a final sample of 570 patients (OPN: $n = 487$; RAPN: $n = 83$). Data are reported up to 30 days postoperatively.

Surgical Technique

OPN was performed as described previously [19]: A retroperitoneal approach with a 10- to 15-cm flank incision above the eleventh rib in order to access the retroperitoneal cavity was made. Complete exposure of the organ and the renal hilum allowed for identification and marking of the renal vessels and the ureter with vessel loops. Resection of the tumor was either performed by clamping of the renal vessels or in a zero ischemia technique. Afterward, bleeding vessels and defects of the urinary collecting system were sutured with monofilament sutures. Resection margins were adapted by secure renorrhaphy using 1 or 2 layers of monofilament sutures. Finally, the kidney was covered with the perirenal fat and the wound closed in layers.

RAPN was performed as described previously [20]: In detail, the patient was lying on the left or right site, respectively. First, a mini-laparotomy was performed to ensure an adhesion-free peritoneum. If the peritoneum was adhesion free, the optical trocar was placed and 3 trocars for robotic-assisted surgery as well as an assistant trocar were placed. After exposure of the kidney as well as the upper ureter, the tumor was excised. Resection of the tumor was either performed by clamping of the renal vessels or in zero ischemia technique. Defects of the urinary collecting system were closed using monofilament sutures, and bleeding vessels were secured by monofilament sutures. Resection margins were adapted by secure renorrhaphy using polyfilament sutures using the sliding knot technique with hem-o-loc clips. The kidney was covered with retroperitoneal fat again and the wounds were closed in layers.

For both approaches, retroperitoneal or abdominal standard drain placement was omitted but might have been placed on the surgeon's discretion. This approach has been shown to be safe in previous studies by the main [21].

Outcomes

The primary end point of the analysis was the CCI. The CCI was calculated based on CDC with the freely available calculator at www.assesssurgery.com. In contrast to the CDC, the CCI provides in general a continuous scale from 0 (no complication) to 100 (death of the patient), allowing an easier comparison between treatment groups [16, 17, 22, 23]. However, due to the low range and small values of the observed CCI in our sample, we additionally categorized the CCI into (a) CCI = 0 meaning no complications; (b) CCI >0 and <26.2 (which marks a IIIa complication on the CDC) reflecting minor complications; and (c) ≥ 26.2 as a measure of major complications.

Table 1. Overview of baseline data before and after propensity score matching

| | Pre-matching | | | Post-matching | | | Totals N = 570 |
|------------------------------|-------------------|-------------------|---------------------|-------------------|-------------------|--------------------|-------------------|
| | OPN N = 487 | RAPN N = 83 | p value | OPN N = 166 | RAPN N = 83 | p value | |
| <i>Age, years</i> | | | | | | | |
| Mean ± SD | 63.0±12.7 | 63.5±11.6 | 0.700 ^a | 64.4±11.9 | 63.5±11.6 | 0.557 ^a | 63.0±12.6 |
| Median (Q1, Q3) | 64.0 (55.0, 73.0) | 63.0 (56.0, 72.0) | | 66.0 (56.2, 74.0) | 63 (56.0, 72.0) | | 64 (55.0, 73.0) |
| <i>Gender</i> | | | | | | | |
| Male | 325 (66.7%) | 55 (66.3%) | 1.000 ^b | 108 (65.1%) | 55 (66.3%) | 0.962 ^b | 380 (66.7%) |
| Female | 162 (33.3%) | 28 (33.7%) | | 58 (34.9%) | 28 (33.7%) | | 190 (33.3%) |
| <i>BMI, kg/m²</i> | | | | | | | |
| Mean ± SD | 27.4±5.0 | 27.6±5.6 | 0.852 ^a | 27.6±5.2 | 27.6±5.6 | 0.939 ^a | 27.5±5.0 |
| Median (Q1, Q3) | 26.6 (24.2, 30.0) | 27.4 (23.6, 30.4) | | 26.5 (24.1, 30.1) | 27.4 (23.6, 30.4) | | 26.7 (24.2–30.0) |
| <i>RENAL score</i> | | | | | | | |
| Mean ± SD | 7.5±1.8 | 6.2±1.8 | <0.001 ^a | 6.3±1.8 | 6.2±1.8 | 0.846 ^a | 7.3±1.9 |
| Median (Q1, Q3) | 8.0 (6.0, 9.0) | 6.0 (5.0, 8.0) | | 6.0 (5.0, 7.0) | 6.0 (5.0, 8.0) | | 7.0 (6.0, 9.0) |
| <i>Tumor size, cm</i> | | | | | | | |
| Mean ± SD | 3.6±1.9 | 2.8±1.1 | <0.001 ^a | 2.7±1.2 | 2.8±1.1 | 0.978 ^a | 3.5±1.8 |
| Median (Q1, Q3) | 3.2 (2.4, 4.5) | 2.5 (2.0, 3.0) | | 2.5 (2.0, 3.2) | 2.5 (2.0, 3.0) | | 3 (2.3, 4.4) |
| <i>Histology</i> | | | | | | | |
| Clear cell | 240 (49.4%) | 47 (56.6%) | 0.110 ^b | 72 (43.4%) | 47 (56.6%) | 0.108 ^b | 287 |
| Papillary 1 & 2 | 82 (16.9%) | 20 (24.1%) | | 32 (19.3%) | 20 (24.1%) | | 102 |
| Oncocytoma | 40 (8.2%) | 5 (6.0%) | | 19 (11.4%) | 5 (6.0%) | | 45 |
| Chromophobe | 33 (6.8%) | 5 (6.0%) | | 14 (8.4%) | 5 (6.0%) | | 38 |
| Other | 91 (18.7%) | 6 (7.3%) | | 28 (16.9%) | 6 (7.3%) | | 97 |
| Missing | 1 | 0 | | 1 | 0 | | 1 |

OPN, open partial nephrectomy; RAPN, robotic-assisted partial nephrectomy. ^a *p* values were derived by *t* test. ^b *p* values were derived by χ^2 test.

Secondary end points included resection status (R1/R0), blood loss, ischemia (yes/no and time), blood transfusion (yes/no), drop in hemoglobin, length of hospital stay (LOS), operating time, and drop in glomerular filtration rate (GFR).

Statistical Analysis

Statistical analysis was performed by the Institute of Medical Biometry and Informatics, University of Heidelberg, which was otherwise not involved in the study. In order to receive comparable individuals from both groups in terms of age, gender, BMI, RENAL score, and tumor size (confounders), a 2:1 propensity score matching including all 5 confounders was applied to the final sample. The confounders were described and evaluated descriptively for the unmatched and matched sample. Group comparisons between RAPN and OPN were conducted for all confounders using the *t* test or the χ^2 test. The analysis of the primary end point between the RAPN and OPN group was assessed by the Wilcoxon rank-sum test. The secondary end points were compared between RAPN and OPN using the *t*-test, the Wilcoxon rank-sum test, or the χ^2 test. The primary and the secondary end points were analyzed based on the matched and the unmatched sample. Additionally, we analyzed the categorized CCI within an ordinal logistic

regression model considering the surgical approach (OPN/RAPN), all 5 confounders and of the procedure by the respective surgeon as fixed effects and the surgeon and the propensity score matching ID (only for the matched sample) as random effects. A *p* value of ≤ 0.05 was considered statistically significant. All analyses were performed in an explorative manner using R version 3.5.2 (R project, R Foundation for Statistical Computing).

Results

Overall, a total of 902 PNs were performed of which data of 570 patients (OPN 487; RAPN 83) were eligible for propensity matching and statistical analysis (see flow-chart in Fig. 1). After matching, there were no differences between the 2 groups for the described cofounders (Table 1). All procedures were performed by a total of 19 primary surgeons.

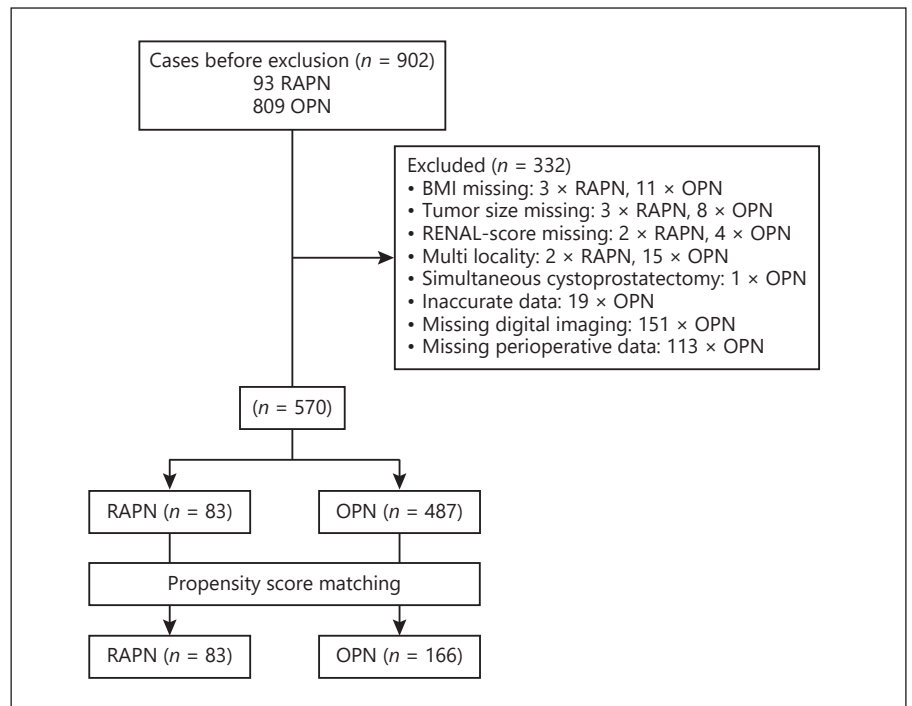


Fig. 1. Flowchart of the study.

Primary End Point

The CCI values were significantly lower for the RAPN group $\{2.6 \pm 7.9$ (mean \pm SD); 0 (0, 0) (median [Q1, Q3])} compared to the OPN group $\{9.7 \pm 14.9$; 0 [0, 20.9]) for both the unmatched ($p < 0.001$) and the matched cohort {RAPN: $\{2.6 \pm 7.9$ [mean \pm SD]; 0 [0, 0] (median [Q1, Q3])} versus OPN $\{8.7 \pm 13.9$ (mean \pm SD); 0 (0, 20.9) (median [Q1, Q3]); $p < 0.001$ } (also see Table 2), indicating less complications for RAPN. Additionally, CDC grades were summarized in Table 3.

Secondary End points

There were no differences between the 2 surgical approaches for resection status (positive margins) and blood loss. OPN had significantly fewer cases where ischemia was applied and a significantly shorter operating time. However, RAPN resulted in a shorter LOS and smaller Hb and GFR drop values (see Table 2).

In addition, regression analyses were performed for the primary outcome CCI (Table 4). Table 4 depicts confounders for the occurrence of complications measured with the CCI. After matching, the surgical approach remained the only significant factor associated with the outcome. RAPN was associated with lower CCI compared to OPN in the pre-matching and the post-matching sample.

Discussion

The presented propensity score-matched analysis compared OPN versus RAPN. RAPN showed superior outcomes compared to OPN in terms of complications, LOS, GFR, and hemoglobin drop. While RAPN was also superior in terms of ischemia time in the unmatched cohort, after matching, there were no significant differences between both groups. In addition, more patients in the OPN group were operated without ischemia after matching. Furthermore, OPN showed shorter procedure times while there were no differences for blood loss and resection status.

The aforementioned findings are in line with recent systematic reviews and meta-analyses [10, 11]. While these meta-analyses included more than 30 studies, only a few of these studies used statistical methods to adjust for baseline differences such as matching. The importance to account for baseline differences becomes apparent as an open approach is usually preferred for more complex tumors which would bias unadjusted outcome analysis. In the presented analysis, OPN cases were more complex and had larger tumors before matching. After matching, groups became similar for baseline characteristics. In addition, while for the unmatched cohort ischemia time was significantly longer for the OPN group, ischemia time did not differ after matching. However, the significance of

Table 2. Perioperative outcomes stratified by surgical approach

| Outcomes | Pre-matching | | | Post-matching | | |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|-----------------------|
| | OPN N = 487 | RAPN N = 83 | <i>p</i> value | OPN N = 166 | RAPN N = 83 | <i>p</i> value |
| <i>CCI</i> | | | | | | |
| Mean ± SD | 9.7±14.9 | 2.6±7.9 | <0.001 ^a | 8.7±13.9 | 2.6±7.9 | <0.001 ^a |
| Median (Q1, Q3) | 0.0 (0.0, 20.9) | 0.0 (0.0, 0.0) | | 0.0 (0.0, 20.9) | 0.0 (0.0, 0.0) | |
| Missing | 2 | 0 | | 1 | 0 | |
| <i>R status, n (%)</i> | | | | | | |
| R0 | 416 (97.9) | 70 (95.9) | 0.354 ^{b,*} | 136 (97.8) | 70 (95.9) | 0.464 ^{b,*} |
| R1 | 7 (1.6) | 3 (4.1) | | 2 (1.4) | 3 (4.1) | |
| Not determined | 2 (0.5) | 0 (0.0) | | 1 (0.7) | 0 (0.0) | |
| Missing | 62 | 10 | | 27 | 10 | |
| <i>LOS, d</i> | | | | | | |
| Mean ± SD | 7.7±4.3 | 6.5±4.0 | <0.001 ^a | 7.4±3.5 | 6.5±4.0 | <0.001 ^a |
| Median (Q1, Q3) | 7.0 (6.0, 8.0) | 6.0 (5.0, 6.0) | | 6.0 (6.0, 8.0) | 6.0 (5.0, 6.0) | |
| Missing | 0 | 0 | | 0 | 0 | |
| <i>OP duration, min</i> | | | | | | |
| Mean ± SD | 145.6±49.4 | 157.0±42.6 | 0.029 ^c | 142.5±45.3 | 157.0±42.6 | 0.014 ^c |
| Median (Q1, Q3) | 139.5 (113.0, 173.0) | 150.0 (128.0, 179.5) | | 136.0 (110.0, 172.0) | 150.0 (128.0, 179.5) | |
| Missing | 1 | 0 | | 1 | 0 | |
| <i>Blood loss, mL</i> | | | | | | |
| Mean ± SD | 311.8±367.3 | 372.2±762.7 | 0.635 ^a | 306.0±345.7 | 372.2±762.7 | 0.948 ^a |
| Median (Q1, Q3) | 200.0 (100.0, 400.0) | 200.0 (100.0, 300.0) | | 200.0 (100.0, 400.0) | 200.0 (100.0, 300.0) | |
| Missing | 47 | 60 | | 16 | 60 | |
| <i>Ischemia, n (%)</i> | | | | | | |
| No | 94 (19.3) | 11 (13.3) | 0.246 ^b | 46 (27.7) | 11 (13.3) | 0.016 ^b |
| Yes | 393 (80.7) | 72 (86.7) | | 120 (72.3) | 72 (86.7) | |
| Missing | 0 | 0 | | 0 | 0 | |
| <i>Ischemia time,** min</i> | | | | | | |
| Mean ± SD | 18.9±8.2 | 16.6±5.1 | 0.002 ^c | 18.5±8.8 | 16.6±5.1 | 0.059 ^{c,**} |
| Median (Q1, Q3) | 18.0 (13.0, 22.0) | 16.0 (13.0, 20.0) | | 17.0 (13.0, 20.0) | 16.0 (13.0, 20.0) | |
| Missing | 2 | 0 | | 11 | 5 | |
| <i>Transfusion, n (%)</i> | | | | | | |
| No | 295 (85.3) | 40 (100.0) | – | 101 (84.2) | 40 (100.0) | – |
| Yes | 51 (14.7) | 0 (0.0) | | 19 (15.8) | 0 (0.0) | |
| Missing | 141 | 43 | | 46 | 43 | |
| <i>Hb drop</i> | | | | | | |
| Mean ± SD | 3.8±1.5 | 2.8±1.4 | <0.001 ^c | 3.8±1.6 | 2.8±1.4 | <0.001 ^c |
| Median (Q1, Q3) | 3.6 (2.7, 4.7) | 2.6 (2.0, 3.4) | | 3.6 (2.6, 4.5) | 2.6 (2.0, 3.4) | |
| Missing | 5 | 0 | | 2 | 0 | |
| <i>GFR drop</i> | | | | | | |
| Mean ± SD | 22.9±16.1 | 11.4±14.2 | <0.001 ^c | 19.5±14.3 | 11.4±14.2 | <0.001 ^c |
| Median (Q1, Q3) | 22.0 (12.7, 32.0) | 8 (2.0, 17.1) | | 18 (9.3, 29.1) | 8.0 (2.0, 17.1) | |
| Missing | 47 | 19 | | 17 | 19 | |

OPN, open partial nephrectomy; RAPN, robotic-assisted partial nephrectomy; CCI, Comprehensive Complication Index; LOS, length of hospital stay; GFR, glomerular filtration rate. ^a *p* values were derived by Wilcoxon rank-sum test. ^b *p* values were derived by χ^2 test. ^c *p* values were derived by *t* test. * Category “not determined” was not considered in the statistical test. ** Only patients with ischemia = “yes” are considered.

Table 3. CDC before and after matching

| | OPN (n = 487) | RAPN (n = 83) | Total (n = 570) | p value |
|------------------------------|---------------|---------------|-----------------|---------------------|
| <i>Before matching</i> | | | | |
| CDC grade, n (%) | | | | |
| 0 | 280 (57.7) | 73 (88) | 353 (62.1) | – |
| I | 74 (15.3) | 3 (3.6) | 77 (13.6) | |
| II | 62 (12.8) | 4 (4.8) | 66 (11.6) | |
| IIIa | 48 (9.9) | 2 (2.4) | 50 (8.8) | |
| IIIb | 12 (2.5) | 1 (1.2) | 13 (2.3) | |
| IVa | 7 (1.4) | 0 (0) | 7 (1.2) | |
| V | 2 (0.4) | 0 (0) | 2 (0.4) | |
| Missing | 2 | 0 | 2 | |
| CDC grade categorized, n (%) | | | | <0.001 ^a |
| 0 | 280 (57.7) | 73 (88) | 353 (62.1) | |
| I,II | 136 (28) | 7 (8.4) | 143 (25.2) | |
| IIIa, IIIb, IVa, V | 69 (14.2) | 3 (3.6) | 72 (12.7) | |
| Missing | 2 | 0 | 2 | |
| | | | | |
| | OPN (n = 166) | RAPN (n = 83) | Total (n = 249) | p value |
| <i>After matching</i> | | | | |
| CDC grade, n (%) | | | | |
| 0 | 96 (58.2) | 73 (88) | 169 (68.1) | – |
| I | 27 (16.4) | 3 (3.6) | 30 (12.1) | |
| II | 27 (16.4) | 4 (4.8) | 31 (12.5) | |
| IIIa | 10 (6.1) | 2 (2.4) | 12 (4.8) | |
| IIIb | 3 (1.8) | 1 (1.2) | 4 (1.6) | |
| IVa | 1 (0.6) | 0 (0) | 1 (0.4) | |
| V | 1 (0.6) | 0 (0) | 1 (0.4) | |
| Missing | 1 | 0 | 1 | |
| CDC grade categorized, n (%) | | | | <0.001 ^a |
| 0 | 96 (58.2) | 73 (88) | 169 (68.1) | |
| I, II | 54 (32.7) | 7 (8.4) | 61 (24.6) | |
| IIIa, IIIb, IVa, V | 15 (9.1) | 3 (3.6) | 18 (7.3) | |
| Missing | 1 | 0 | 1 | |

CDC, Clavien-Dindo Classification; OPN, open partial nephrectomy; RAPN, robotic-assisted partial nephrectomy. ^a p values were derived by χ^2 test.

zero ischemia is discussed controversial. A recent RCT by Anderson et al. [24] found that the off-clamp approach resulted in significantly longer operating times with no differences in any other parameter including kidney function at 3 months after surgery. Additionally, the CLOCK RCT also found no differences between the on- and off-clamp approach for the per-protocol analysis with regard to functional outcomes, while it has to be acknowledged that 40% of patients originally assigned to the off-clamp group were switched to the on-clamp group [25, 26]. Therefore, coming back to the current study, the better feasibility of off-clamp PN for OPN should not be considered as argument to prefer the open approach over the robotic-assisted approach. Remarkably, the complex-

ity of the tumors did not impact the occurrence of complications in the presented cohort (Table 4). This is reasonable since most of cases had low-risk tumors as measured with the RENAL nephrometry system.

In line with the aforementioned meta-analyses, RAPN was associated with a reduction in complications, before and after matching. On the other side, the largest tumor in the RAPN group was 6 cm which is considerably lower than the largest tumor on the OPN group for the unmatched (15 cm) and matched cohort (7.2 cm). Therefore, OPN remains a valuable option for large and complex tumors as it was shown by Oh et al. [27]. They found that an endophytic location of the tumor can be a predictor for an open surgical approach. In addition, OPN

Table 4. Results of ordinal logistic regression analysis with complications measured with the CCI as outcome variable

| Confounder | Pre-matching ^a | | | Post-matching ^b | | |
|--|---------------------------|------------------|------------------|----------------------------|------------------|------------------|
| | odds ratio N = 487 | 95% CI N = 83 | p value | odds ratio N = 166 | 95% CI N = 83 | p value |
| Surgical approach (RAPN) | 0.198 | [0.094, 0.418] | <0.001 | 0.215 | [0.095, 0.488] | <0.001 |
| Surgeon's number of PN at respective procedure | 1 | [0.998, 1.002] | 0.885 | 1 | [0.997, 1.002] | 0.703 |
| Gender (female) | 1.473 | [1.026, 2.113] | 0.038 | 1.642 | [0.916, 2.944] | 0.096 |
| Age | 1.001 | [0.988, 1.015] | 0.895 | 1.018 | [0.993, 1.044] | 0.166 |
| BMI | 0.996 | [0.961, 1.031] | 0.821 | 1.042 | [0.987, 1.100] | 0.134 |
| Tumor size | 1.087 | [0.987, 1.197] | 0.097 | 1.186 | [0.917, 1.534] | 0.193 |
| RENAL score | 0.964 | [0.871, 1.066] | 0.495 | 1.009 | [0.858, 1.187] | 0.964 |

CCI, Comprehensive Complication Index; RAPN, robotic-assisted partial nephrectomy; PN, partial nephrectomy. Values in bold (<0.05) represent statistical significance. ^a Surgeon was considered as random effect. ^b Surgeon and propensity score matching ID were considered as random effects.

might be advantageous for nonstandard cases including but not limited to multifocal kidney tumors, cystic tumors, and adherent perirenal fat. For example, Khene et al. [28] found that adherent perirenal fat during RAPN is associated with increased blood loss and a higher risk of conversion to OPN or radical nephrectomy. On the other side, in experienced hands, trifecta achievement is comparable between RAPN and OPN even for completely endophytic tumors [27]. Looking at tumors \geq T1b tumors, Sprenke et al. [29] reported comparable results in terms of kidney function and overall complications in a cohort of 271 patients undergoing OPN or minimally invasive PN. Therefore, RAPN and OPN are both suitable options, especially for more complex tumors, and the experience of the operating surgeon seems to be a main contributor to the choice of the surgical approach.

Moreover, despite the use of statistical methods, the importance of randomized data cannot be replaced. Currently, there is the OpeRa trial (NCT03849820) which is designed as a multicenter RCT in Germany. OpeRa aims at comparing perioperative parameters with the number of complications being the primary outcome. A full study protocol and the first results are yet to be reported and urgently needed in order to plan additional confirmatory trials that are powered of oncological outcomes as well. Furthermore, the experience of the primary investigators is certainly a strength of the study while it needs to be considered that OpeRa is an industry-funded trial warranting careful interpretation. Besides the OpeRa trial, there is the CONVERT study (NCT04011891) planned as a feasibility study in Canada which might also contribute to a better understanding of patient recruitment and planning for upcoming trials. In summary, despite the

fact that the first RCTs are being initiated, further independent RCTs comparing OPN and RAPN are needed to assess the safety of RAPN. Currently, the ROBOCP feasibility RCT (NCT04534998) is conducted at our department in preparation for a confirmative phase III trial.

Limitations

First of all, this study comes with the known limitations of a retrospective study design. While baseline differences were adjusted by matching, this could not account for drawbacks resulting from review of patients' charts. For example, especially smaller complications that did not require medical or surgical treatment might not have been captured. However, this counts for both groups, OPN and RAPN, thus it is unlikely that this would have a significant impact on the overall results. Furthermore, surgical experience itself might be a significant contributor to outcomes. This is important to consider in future trials to avoid early learning curve effects. Finally, this is a single-institution analysis and warrants further validation in multicenter trials.

Conclusions

RAPN provides superior short-term results with regard to overall complications without compromising renal function at least for small and noncomplex tumors. However, OPN is used for more complex and larger tumors, thus remaining an important option for these patients. No randomized data are available but urgently needed for short-term, oncological, and functional endpoints with appropriate power.

Statement of Ethics

The study was approved by the institutional review board of Heidelberg University, Medical Faculty Mannheim (2014-811R-MA).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors met all of the following criteria: (1) substantial contributions to conception and design, and/or acquisition of data, and/or analysis, and interpretation of data; (2) authors participated in drafting the article or revising it critically for important intellectual content; and (3) authors gave final approval of the version to be published.

In detail, authors contributed to the following parts of the study: study conception and design: Kowalewski, Kriegmair, and Michel; acquisition of data: Müller, Walach, Mühlbauer, and Sidoti Abate; analysis: Brinster, Kirchner, and Kowalewski; analysis and interpretation of data: Kowalewski, Brinster, Kirchner, Honeck, Nuhn, Michel, and Kriegmair; drafting of manuscript: Kowalewski, Müller, Walach, Mühlbauer, and Sidoti Abate; critical revision: Nuhn, Honeck, Michel, and Kriegmair.

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