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Comparative analysis of perioperative outcomes between robot-assisted partial nephrectomy and open partial nephrectomy: a propensity-matched study

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Abstract

Aim: Partial nephrectomy is the standard treatment for small renal tumors; however, it remains unclear which surgical approach from among robot-assisted partial nephrectomy (RAPN) and open partial nephrectomy (OPN) is superior. This study aimed to compare perioperative outcomes of RAPN and OPN performed at a single institution after adjusting for preoperative patient and tumor characteristics using propensity score matching (PSM).

Methods: In this retrospective cohort study, patients who underwent RAPN or OPN for a renal mass of cT1-2 N0 M0 between 2005 and 2020 at our institution were recruited. The study outcomes were perioperative outcomes, complications, and pathological and functional outcomes. PSM was used to account for baseline covariates.

Results: Overall, 131 RAPN and 71 OPN cases were extracted; in addition, 58 cases of RAPN and OPN were selected via PSM. RAPN was superior to OPN in terms of estimated blood loss (10 g vs. 160 g, $P < 0.001$), ischemia time (23 min vs. 34 min, $P < 0.001$), and hospital duration (7 days vs. 12 days, $P < 0.001$). There were no significant differences in the incidence of perioperative complications or in the rate of positive surgical margins (both $P > 0.05$). With respect to functional outcomes, the rates of preservation of renal function at both 1 day and 3 months postoperatively were higher with RAPN than with OPN (85.3% vs. 69.1% and 93.3% vs. 85.6% respectively, both $P < 0.001$).



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Conclusion: In selected cases, RAPN with warm ischemia appears to preserve renal function equally well or better compared to OPN with cold ischemia.

Keywords: Partial nephrectomy, robot-assisted nephrectomy, open surgery, perioperative outcomes, renal function, propensity score matching

INTRODUCTION

Partial nephrectomy (PN) for localized renal cell carcinoma has been reported to have oncological outcomes equivalent to those achieved by radical nephrectomy, with preservation of postoperative renal function^[1,2]. As a result, PN has become the standard treatment for small renal cell carcinomas.

Robot-assisted partial nephrectomy (RAPN) is recognized as a minimally invasive surgical method. Its application as an alternative to open partial nephrectomy (OPN) is rapidly growing^[3,4]. This is largely due to RAPN's high-definition 3D optical system and flexible wristed instruments that allow surgeons to perform tumor excision and renorrhaphy with an accuracy equal to or greater than that achieved by OPN^[5].

Various studies have compared RAPN and OPN^[6-12]. However, because the outcomes of PN are influenced by several factors, including tumor location, anatomical complexity, patient renal function, and operator proficiency, there is some controversy over which surgical approach is superior. Current guidelines do not indicate a preference for one technique over the other, leading to decisions being predominantly made on the basis of the surgeons' expertise and skills^[13].

The present study aimed to comprehensively compare the perioperative outcomes of RAPN and OPN performed at a single institution after adjusting for preoperative patient and tumor characteristics using propensity score matching (PSM).

METHODS

Study population

This study was approved by the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine (R1581).

We retrospectively collected clinical data of 202 patients with renal masses of cT1-2 cN0 cM0 diagnosed via CT or MRI who underwent RAPN or OPN between 2005 and 2020 at Kyoto University Hospital. During this period, RAPN was performed by 10 experienced surgeons and OPN was performed by 15 experienced surgeons. The choice of the surgical method (RAPN or OPN) was determined on a case-by-case basis at a preoperative medical conference. However, due to insurance coverage changes that came into effect in 2016, RAPN became the preferred technique. As a general rule, OPN has been applied to patients with a single kidney or chronic kidney disease (CKD) grade 4 or higher (eGFR < 30) since 2016. Cases where preoperative imaging was not available were excluded from the study because the anatomic complexity of the tumors could not be accurately determined. Cases with multiple tumors were also excluded for the same reason. Cases in which other surgeries were simultaneously conducted with PN were excluded because perioperative outcomes of PN surgery could not be accurately evaluated.

Surgical technique

The surgeons at our hospital have received adequate surgical training, have performed many operations at our hospital and other institutions, and are qualified practitioners in Japan. The RAPN procedure employed at our hospital was relatively similar to that reported by Kaouk *et al.*^[14] and was performed using the da

Vinci S or Xi surgical system (Intuitive, CA, USA). In many cases, the renal artery was clamped using a bulldog clamp. However, when the tumor was superficial and peripheral, the zero ischemia technique was performed, in which the renal artery was not clamped^[15]. The tumor was then resected along its outline, as confirmed by ultrasonography beforehand. The resection margin was 3-5 mm. If the renal pelvis was open, a central suture was performed to ensure that there was no urine leak before renorrhaphy. The renal artery was declamped after renorrhaphy to check for bleeding from the cut surface.

OPN was performed using the subcostal or flank approach. In most cases, the retroperitoneal approach was used, and OPN under cold ischemia was performed. The renal artery was clamped, and the entire kidney was surrounded by ice slush for 5-10 min before tumor resection^[16]. Open calyces and bleeding sites were carefully repaired and renorrhaphy was performed. The renal artery was declamped after renorrhaphy.

Outcomes of interest

The primary and secondary outcomes were examined and compared as evaluation points between RAPN and OPN.

The primary outcomes were perioperative outcomes, namely estimated blood loss (EBL), operative time, ischemia time, and hospital stay. All intraoperative and postoperative complications were also evaluated based on the Clavien-Dindo (CD) classification^[17].

The secondary outcomes were pathological and functional outcomes, namely the rates of malignancy, positive surgical margins in malignancy, and pathological stage. Renal function was measured at baseline and at 1 day and 3 months postoperatively based on the estimated glomerular filtration rate (eGFR). The ratio of eGFR at both 1 day and 3 months postoperatively to the baseline eGFR (% preservation of eGFR) was used as an index to evaluate the postoperative residual renal function.

Covariates

Patients' preoperative variables were analyzed as covariates, including age at treatment, sex, body mass index (BMI), Charlson comorbidity index (CCI)^[18], preoperative eGFR, clinical stage, clinical tumor size (the maximum diameter at preoperative imaging), and tumor side (left or right). Tumor complexity and anatomical characteristics were determined by the urologist and defined using the total "RENAL" nephrometry score^[19], namely Radius (tumor size as maximal diameter), Exophytic/endophytic properties of the tumor, Nearness of tumor's deepest portion to the collecting system or sinus, Anterior/posterior descriptor, and the Location relative to the polar line.

Statistical analyses

Statistical analyses and interpretation of the results were performed according to established guidelines^[20]. Continuous variables are presented as median and interquartile range (IQR) or mean and standard deviation. Categorical variables are presented as frequency and proportion. Differences in the distribution of continuous and categorical variables between the RAPN and OPN groups were compared using the Mann-Whitney and chi-square tests, respectively.

Adjustments were made using 1:1 nearest-neighbor PSM to account for possible baseline differences between patients who underwent OPN and RAPN^[21]. Propensity scores were calculated using a logistic regression model with odds of receiving RAPN as a dependent variable and age at treatment, sex, BMI, CCI, preoperative eGFR, clinical stage, clinical tumor size, tumor side (right or left), individual RENAL score item, and total RENAL nephrometry score as independent variables. After balanced matching of covariates, the effects of the surgical procedures on outcomes were estimated using the Mann-Whitney and chi-square tests for continuous and categorical variables, respectively.

All statistical tests were performed using JMP Pro 15.1.0. For all statistical analyses, $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

As shown in [Table 1](#), a total of 202 patients (131 RAPN and 71 OPN) were included in this study. Prior to PSM, the patients in the cohort who underwent RAPN had a significantly higher BMI ($P = 0.006$) than those who underwent OPN. Furthermore, they had significantly lower RENAL nephrometry scores than those who underwent OPN (6.8 ± 1.61 vs. 7.5 ± 1.56 , respectively; $P = 0.003$). A total of 116 cases were compared, comprising 58 RAPN cases and 58 OPN cases that were matched by PSM. In the post-PSM cohort, there were no differences between the RAPN and OPN groups for any of the covariates assessed (all $P > 0.05$) [[Figure 1](#)].

Perioperative outcomes and complications

EBL was significantly higher and hospital stay longer in the OPN group than in the RAPN group [[Table 2](#)]. Ischemia time was significantly longer in the OPN group than in the RAPN group; however, cold ischemia time accounted for the majority of the ischemia time in the OPN group.

There were no intraoperative complications in any of the 116 cases selected by PSM. However, postoperative complications occurred in 11 patients who underwent OPN and 8 patients who underwent RAPN.

In both patients who underwent RAPN and OPN, postoperative complications of CD grade 3 or higher included urinomas requiring ureteral stenting and pseudoaneurysms requiring embolization. There was no significant difference in the incidence of postoperative complications between OPN and RAPN [[Table 2](#)].

Pathological outcomes

After PSM, one case of pT2a and one case of pT3a were observed in patients who underwent OPN. There was no difference between the OPN and RAPN groups in terms of positive surgical margins [[Table 3](#)].

Functional outcomes

In the post-PSM cohort, the % preservation of eGFR at both 1 day and 3 months postoperatively was significantly better in the RAPN group than in the OPN group, although the eGFR at 3 months was not significantly different between the two groups. There were fewer cases with upstaged CKD grades in the RAPN group than in the OPN group (30 cases with OPN vs. 17 cases with RAPN; $P = 0.014$) [[Table 3](#)]. The changes in eGFR for all cases, imperative cases, and elective cases are shown in [Figure 2](#).

Multivariate analysis

In the pre-PSM cohort, RAPN was found to be a good predictor of EBL ($P < 0.0001$), ischemia time ($P < 0.0001$), transfusion rate ($P = 0.019$), hospital stay ($P < 0.0001$), eGFR ($P < 0.0001$) and % preservation of eGFR ($P < 0.0001$) at the 3rd postoperative month (POM), and CKD upstaging ($P = 0.001$) via multivariate analysis [[Figure 3](#)].

DISCUSSION

Previous studies have shown mixed results when comparing the outcomes of RAPN and OPN. Simhan *et al.*^[11] compared perioperative outcomes of 281 patients with moderately and highly complex renal lesions. The results showed that RAPN yielded perioperative and functional outcomes similar to OPN, with the additional benefit of shorter hospital stays. Garisto *et al.*^[6] compared perioperative, functional, and

Table 1. Descriptive characteristics of the study population and tumor characteristics

Variables	Cohort before PSM			Cohort after PSM			
	OPN (n = 71)	RAPN (n = 131)	P value	OPN (n = 58)	RAPN (n = 58)	P value	SMD
Age (yr)			0.065			0.36	0.173
Mean (SD)	59.4 (14.1)	63.0 (12.7)		59.3 (13.4)	61.7 (14.3)		
Sex, n (%)			0.56			0.83	
Male	51 (71.8)	99 (75.6)		43 (74.1)	44 (75.9)		
Female	20 (28.2)	32 (24.4)		15 (25.9)	14 (24.1)		
BMI, kg/m ²			0.006			0.78	0.052
Mean (SD)	23.2 (4.1)	24.8 (3.8)		23.8 (4.2)	23.6 (3.5)		
Charlson comorbidity index, n (%)			0.36			0.90	
0	35 (49.3)	76 (58.0)		30 (51.7)	29 (50.0)		
1	11 (15.5)	28 (21.4)		11 (19.0)	11 (19.0)		
2	19 (26.8)	20 (15.3)		15 (25.9)	14 (24.1)		
≥ 3	6 (8.4)	7 (5.3)		2 (3.4)	4 (6.9)		
eGFR (mL/min/1.73 m ²)			0.35			0.51	0.275
Median (IQR)	64.1 (45.1-86.0)	66.3 (56.6-77.0)		64.7 (47.1-86.0)	62.1 (54.9-73.3)		
Imperative case, n (%)	34 (47.9)	44 (33.6)	0.046	24 (41.3)	25 (43.1)	0.85	
Clinical stage, n (%)			0.19			1.00	
cT1a	55 (77.5)	111 (84.7)		49 (84.5)	49 (84.5)		
cT1b	13 (18.3)	20 (15.3)		9 (15.5)	9 (15.5)		
cT2a-b	2 (2.8)	0 (0)		0 (0)	0 (0)		
Tumor size (cm)			0.26			0.63	0.089
Median	3.0	2.7		2.5	3.0		
IQR	2.1-3.9	2.0-3.5		1.8-3.6	2.0-3.7		
Tumor side, n (%)			0.45			1.00	
Left	37 (52.1)	61 (46.6)		28 (48.3)	28 (48.3)		
Right	34 (47.9)	70 (53.4)		30 (51.7)	30 (51.7)		
RENAL nephrometry score			0.08			0.80	
Radius, n (%)							
≤ 4 cm	54 (76.1)	111 (84.7)		49 (84.5)	48 (82.8)		
4-7 cm	15 (21.1)	20 (15.3)		9 (15.5)	10 (17.2)		
≥ 7 cm	2 (2.8)	0 (0)		0 (0)	0 (0)		
Exophytic/endophytic			0.17			0.71	
≥ 50% Exophytic	25 (35.2)	53 (40.5)		20 (34.5)	23 (39.7)		
< 50% Exophytic	33 (46.5)	66 (50.4)		27 (46.6)	27 (46.4)		
Endophytic	13 (18.3)	12 (9.1)		11 (19.0)	8 (13.8)		
Nearness to the collecting system			0.25			0.90	
≥ 7 mm	15 (21.1)	42 (32.1)		14 (24.1)	12 (20.7)		
4-7 mm	16 (22.5)	24 (19.8)		11 (19.0)	11 (19.0)		
≤ 7 mm	40 (56.3)	65 (49.6)		33 (56.9)	35 (60.3)		
Anterior/posterior, n (%)			0.52			0.23	
Anterior	37 (52.1)	60 (45.8)		30 (51.2)	28 (26)		
Posterior	29 (40.9)	56 (42.3)		24 (41.4)	31 (53.5)		
Location relative to the polar lines			0.02			1.00	
Above or below the polar line	16 (22.5)	56 (42.8)		16 (27.6)	16 (27.6)		
Lesion crosses the polar line	33 (46.5)	44 (33.6)		23 (39.7)	23 (39.7)		
> 50% is across the polar line and crosses the axial midline entirely between the polar lines	22 (31.0)	31 (23.7)		19 (32.8)	19 (32.8)		
Total score, mean (SD)	7.5 (1.56)	6.8 (1.61)	0.003	7.4 (1.58)	7.4 (1.51)	0.95	0

RAPN: Robot-assisted partial nephrectomy; OPN: open partial nephrectomy; PSM: propensity score matching; eGFR: estimated glomerular filtration rate; SD: standard deviation; IQR: interquartile range; SMD: standardized mean difference; Imperative case: single kidney, bilateral tumors, or chronic kidney disease (eGFR < 60).

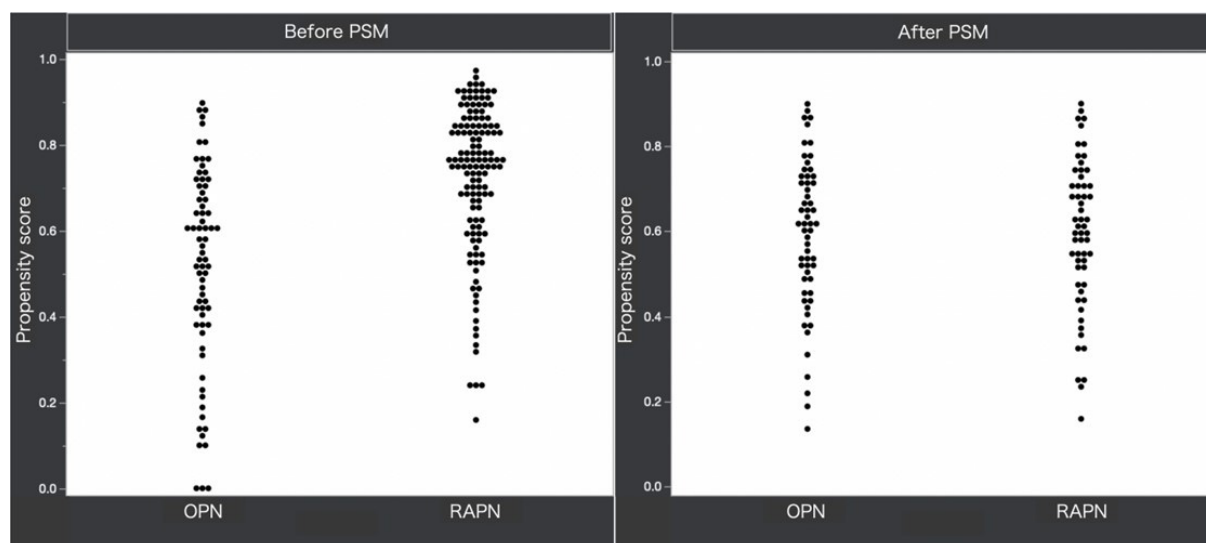


Figure 1. Distribution of the propensity scores. Before PSM (left) and after PSM (right). PSM: propensity score matching; OPN: open partial nephrectomy; RAPN: robot-assisted partial nephrectomy.

Table 2. Comparison of perioperative outcomes between patients treated with RAPN and those treated with OPN after propensity score matching for clinical characteristics

Variables	OPN (n = 58)	RAPN (n = 58)	P value
EBL (mL)			< 0.001
Median (IQR)	160 (90-300)	10 (0-60)	
Operative time (min)			0.003
Median (IQR)	232 (200-260)	258 (223-297)	
Renal artery clamping, n (%)			0.31
Main artery clamping	55 (94.8)	57 (98.3)	
Zero ischemia	3 (5.2)	1 (1.7)	
Ischemia time (min)			< 0.001
Median (IQR)	34 (26-44)	23 (18-28)	
Cold ischemia time	27 (21-36)	0	
Transfusion, n (%) (including autologous blood transfusions)	4 (6.9)	1 (1.7)	0.17
Hospital stay, days			< 0.001
Median (IQR)	12 (9-14)	7 (7-9)	
Conversion to radical nephrectomy, n (%)	2 (3.5)	2 (3.5)	1.0
Overall postoperative complications, n (%)	11 (19.0)	8 (13.8)	0.64
Clavien-Dindo complication ≤ 2	8 (13.8)	3 (5.2)	0.11
Clavien-Dindo complication ≥ 3	3 (5.2)	5 (8.6)	0.46

EBL: estimated blood losses, IQR: interquartile range; OPN: open partial nephrectomy; RAPN: robot-assisted partial nephrectomy.

oncological outcomes of RAPN and OPN for the treatment of highly complex renal tumors of 279 cases. Their results indicated that RAPN presents a safe and effective alternative to OPN for highly complex renal tumors, with advantages of reduced blood loss, shorter ischemia time, and shorter length of hospital stay. Other original studies comparing RAPN with OPN have reported that the advantages of RAPN include lower rates of complications^[8,22-24]. Although, there are many retrospective studies comparing OPN and RAPN, few have compared these surgical approaches in a single-institutional setting using PSM. Because our study analyzed RAPN and OPN from a single institution and matched the patients' backgrounds and tumor complexities using PSM, we believe that our results provide a higher level of evidence. In fact, the use of PSM for all preoperative factors, including the RENAL score, in both groups, which are thought to play important roles in determining the indications and outcomes of RAPN and OPN, resulted in no significant differences between the two groups.

Table 3. Pathological and functional outcomes

Variables	OPN (n = 58)	RAPN (n = 58)	P value
Pathological outcomes			
Malignancy, n (%)	55 (94.8)	52 (89.7)	0.30
Positive surgical margins, n (%)	0/55 (0)	1/52 (1.9)	0.50
Stage at final pathology			0.30
pT1a	50 (86.2)	45 (77.6)	
pT1b	3 (5.2)	6 (10.3)	
pT2a-b	1 (1.7)	0 (0)	
pT3a	1 (1.7)	0 (0)	
uncertain	3 (5.2)	7 (12.1)	
Functional outcomes			
eGFR at POD 1, mL/min/1.73 m ²			
Median (IQR)	44.4 (32.3-64.1)	53.1 (40.8-66.6)	0.047
% preservation of eGFR at POD 1 compared with baseline, (%)	69.1 (40.8-66.6)	85.3 (72.0-95.4)	< 0.001
eGFR at 3rd POM, mL/min/1.73 m ²			
Median (IQR)	56.5 (41.9-72.7)	58.3 (48.9-72.0)	0.19
% preservation of eGFR at 3rd POM compared with baseline, (%)	85.6 (78.6-88.6)	93.3 (83.4-100.9)	< 0.001
CKD upstaging at 3rd POM, n (%)	30 (51.7)	17 (29.3)	0.014

RAPN: Robot-assisted partial nephrectomy; OPN: open partial nephrectomy; eGFR: estimated glomerular filtration rate; IQR: interquartile range; POD: postoperative day; POM: postoperative month; CKD: chronic kidney disease.

The results of our study indicate that RAPN is superior to OPN in terms of EBL, ischemia time, and length of hospital stay. In OPN, cases with long ischemia time of more than 40 min were observed, which were caused by difficulty in suturing and hemostasis owing to difficulty in visualizing the site of the opening of the renal pelvis and bleeding point. We found no significant differences in the incidence of perioperative complications or in the rate of positive surgical margins. With respect to functional outcomes, the rates of preservation of renal function at both 1 day and 3 months postoperatively were higher and the rates of CKD grade upstaging were lower for patients who underwent RAPN than for those who underwent OPN.

There are two possible explanations for the higher rate of preserved renal function in patients who underwent RAPN. One is the difference in the volume of nephron loss during PN. The high-definition 3D optical system and flexible wristed instruments used in RAPN result in lower levels of nephron loss in the resection margin compared with OPN. However, this is merely a predictive interpretation because it is not possible to retrospectively and accurately measure the safety margin in all cases.

Another explanation is the difference in the length of ischemia time. It is known that cold ischemia suppresses damage to the remaining kidney even after 30 min^[25,26]. However, although there is clear evidence regarding the protective role of renal cooling in the context of impaired renal function, some studies have suggested that prolonged cold ischemia times and short warm ischemia times also cause nephron damage^[27,28]. Considering the results of this study, even when cold ischemia using ice slush was performed, it appears that if the ischemia time becomes longer, a shorter period of warm ischemia may be more advantageous for preserving renal function than a longer period of cold ischemia. A previous retrospective study found similar results; the OPN group with cold ischemia had a longer ischemia time, and no significant eGFR advantage was found in favor of OPN. In addition, the trend toward GFR recovery was better in the RAPN group, although it did not reach statistical significance^[6].

In studies comparing the effects of cold and warm ischemia and ischemia time on renal function, results showed that when ischemia lasted for 30 min or longer, renal function was better preserved with cold ischemia. This is because cold ischemia reduces the diffuse and irreversible damage to parenchyma

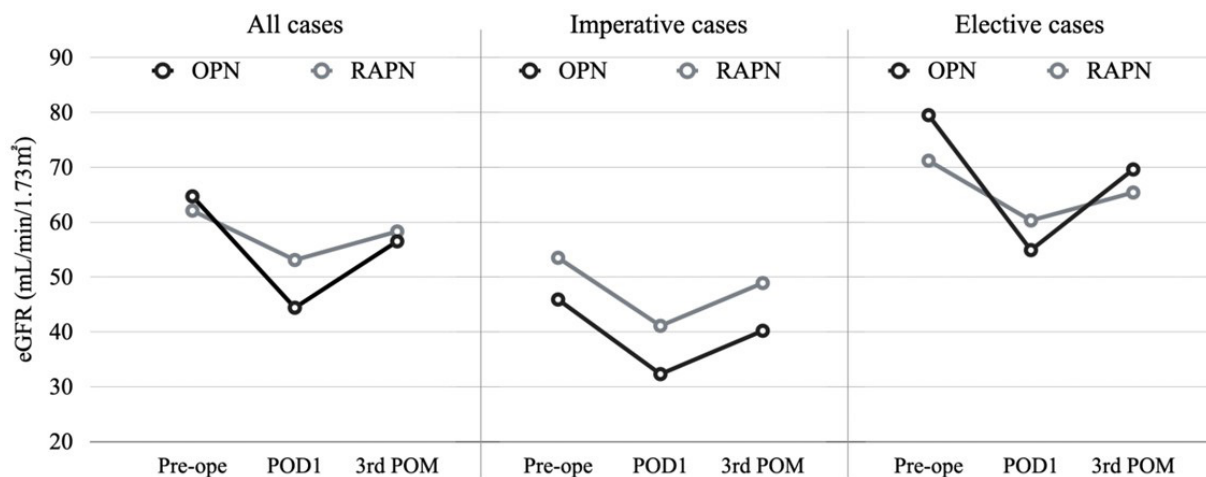


Figure 2. Pre- and post-operative changes in median eGFR in OPN and RAPN for all, imperative, and elective cases. eGFR: Estimated glomerular filtration rate; OPN: open partial nephrectomy; RAPN: robot-assisted partial nephrectomy; Imperative case: single kidney, bilateral tumors, or chronic kidney disease (eGFR < 60).

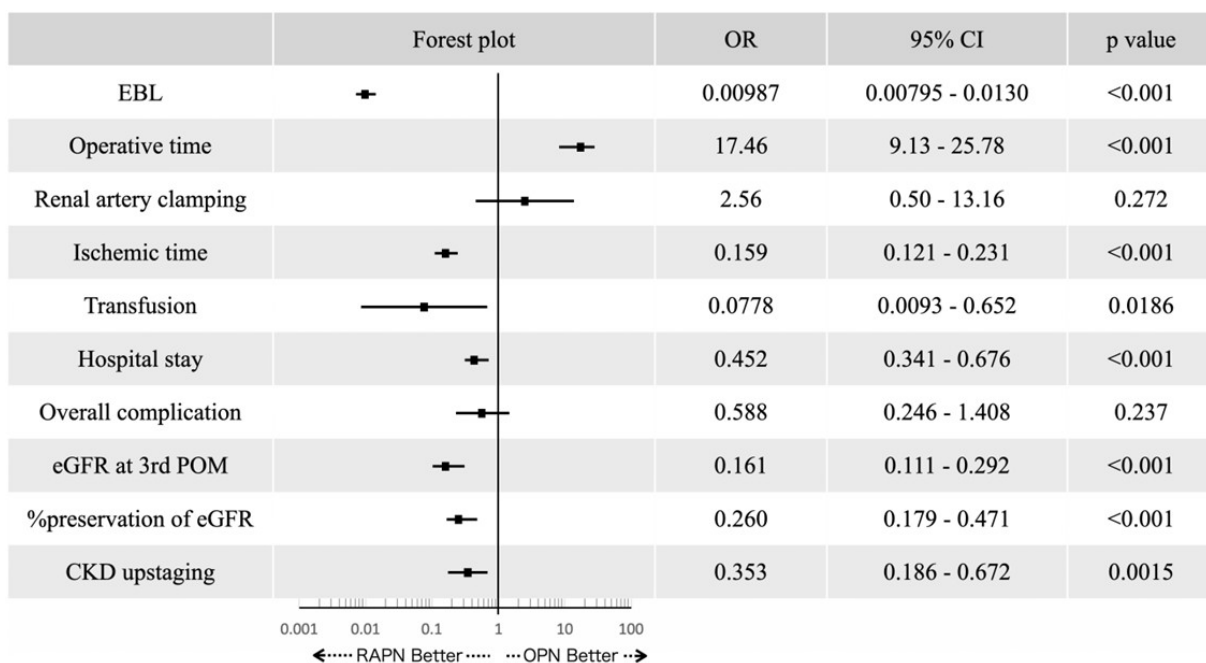


Figure 3. Multivariate logistic regression tests the impact of RAPN vs. OPN on each perioperative outcome according to each OPN and RPN group before matching.

caused by prolonged warm ischemia^[29-35]. However, when ischemia time was less than 20 min, the preservation of renal function was excellent and no significant difference was observed between cold and warm ischemia^[25-28]. In light of our results, even in cases where renal function preservation is strongly desired, RAPN with warm ischemia presents a good option if ischemia time is expected to be short. This is evidenced by the equal or greater postoperative renal function achieved with RAPN over OPN. Furthermore, RAPN seems to have some advantages over OPN in terms of other perioperative outcomes. In fact, a study comparing RAPN and OPN for patients with a solitary kidney also concluded that RAPN may offer comparable perioperative and short-term functional outcomes compared with OPN, assuming careful patient selection and adequate surgical experience^[36].

In contrast, cold ischemia should be selected in cases where the tumor is anatomically complex and when the ischemia time is expected to be prolonged. The shorter the cold ischemia period, the better the postoperative renal function is. Considering this, OPN should be prioritized when it can ensure a faster and more accurate resection and renorrhaphy in cases with complex tumors.

In this study, 73 cases in RAPN and 13 cases in OPN were excluded by PSM. Excluded cases included patients in the RAPN group who were relatively older and had a higher BMI and lower RENAL score, and those in the OPN group who were relatively younger and had larger tumor diameters. Therefore, the results of this study may not necessarily apply to such excluded cases.

In recent years, there has been an increasing number of reports confirming that RAPN can be safely used for the resection of complex or large tumors^[6,37-39]. In this study and other reports, RAPN was shown to have equivalent or better outcomes compared with OPN in many aspects of the perioperative results. This suggests that RAPN is a viable surgical option for the resection of complex and large tumors in the future. However, this hypothesis is based on the premise that the surgeon has sufficient technical proficiency in robotic surgery. Therefore, it is necessary to select an appropriate surgical method according to the surgeon's and the institution's level of proficiency in robotic surgery, taking into consideration the complexity of the tumor and patient factors.

This study had several limitations. First, the sample size of the study was relatively small. Furthermore, it was nonrandomized and retrospective in nature; thus, it was subject to the inherent limitations of a retrospective analysis of observational data, possibly making it difficult to obtain original results. Second, the results of the PSM in this study may be generalized only among those within the propensity score range included in the paired analysis and may not be applicable to those outside this range. Third, different surgeons were involved in this study, which might be seen as a source of biases because different phases of different learning curves were included and might have influenced the results. Fourth, the timing of the surgery (i.e., pre- or post- 2016) was another limitation because more recent cases underwent RAPN and older cases predominantly underwent OPN, as RAPN has been covered by insurance in Japan since 2016. Finally, this study used data collected from a single center with a high incidence of kidney cancer and cannot be generalized to providers with different characteristics.

In conclusion, this study compares the perioperative outcomes of RAPN and OPN performed at a single institution. Our results indicate that RAPN with warm ischemia preserves renal function equally well or better than does OPN with cold ischemia in selected cases with short ischemic times.

DECLARATIONS

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Authors' contributions

Made substantial contributions to the conception and design of the study and performed data analysis and interpretation: Sawada A

Performed data acquisition as well as provided administrative, technical, and material support: Takahashi T, Kono J, Masui K, Sato T, Sano T, Goto T

Drafted the article or revised it for critically important intellectual content and approved the final version: Kobayashi T, Akamatsu S, Ogawa O

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declare that there are no conflicts of interest.

Ethical approval and consent to participate

This study was approved by the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine (reference number: R1581).

Consent for publication

Not applicable.

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