REVIEW



Perioperative, functional, and oncologic outcomes of robot-assisted versus open partial nephrectomy for complex renal tumors (RENAL score \geq 7): an evidence-based analysis

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Abstract

This study aims to assess the efficacy and safety of robot-assisted partial nephrectomy (RAPN) compared with open partial nephrectomy (OPN) in the management of complex renal tumors (defined as RENAL score \geq 7). We conducted a comprehensive literature search in PubMed, Embase, Web of Science, and Cochrane Library to identify relevant comparative studies up to January 2023. This study was conducted with the Review Manager 5.4 software, and included RAPN and OPN-controlled trials for complex renal tumors. The prime outcomes were to assess the perioperative results, complications, renal function, and oncologic outcomes. A total of 1493 patients were included in seven studies. Compared to OPN, RAPN was associated with a significantly shorter hospital stay (weighted mean difference [WMD] – 1.53 days, 95% confidence interval [CI] – 2.44, -0.62; p = 0.001), less blood loss (WMD – 95.88 mL, 95% CI – 144.19, -47.56; p = 0.0001), lower transfusion rates (OR 0.33, 95% CI 0.15, 0.71; p = 0.005), fewer major complications (OR 0.63, 95% CI 0.39, 1.01; p = 0.05), and fewer overall complications (OR 0.49, 95% CI 0.36, 0.65; p < 0.00001). Nevertheless, no statistically significant differences were found between the two groups in operative time, warm ischemia time, estimated glomerular decline, intraoperative complications, positive surgical margins, local recurrence, overall survival, and recurrence-free survival. The study demonstrated that RAPN had superior perioperative parameters and fewer complications when compared to OPN for complex renal tumors. However, no significant differences were found in terms of renal function and oncologic outcomes.

Keywords Robotic surgery · Open surgery · Partial nephrectomy · Complex renal tumors

Introduction

By 2026, renal cell carcinoma is expected to ascend to the sixth and ninth most prevalent cancers in males and females, accounting for approximately 3% of the total cancer burden worldwide [1]. A growing body of research indicates that partial nephrectomy (PN) is associated with comparable cancer-specific survival and superior renal function in cases of localized renal tumors when compared to radical nephrectomy [2–4]. In accordance with consensus guide-lines, PN is strongly advocated as the optimal treatment for

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Li Yang ery_yangli@lzu.edu.cn T1 renal tumors [3]. Since the introduction of laparoscopy, several studies have demonstrated that there are comparable oncological outcomes and superior perioperative parameters between laparoscopic and open partial nephrectomy (OPN) [5, 6]. Furthermore, recent studies have shown that robot-assisted partial nephrectomy (RAPN) can lead to a shorter hospital stay, reduced blood loss, and equivalent oncological outcomes in comparison to OPN when treating non-complex renal tumors [7].

However, complex renal tumors are often profoundly embedded in the renal parenchyma near the middle portion of the kidney in the coronal plane, and located relatively close to the renal collecting system [8]. Several studies have shown that the efficacy of RAPN in managing complex renal tumors, yet they failed to use standardized scales to evaluate the complexity of masses, such as the RENAL and PADUA score [9, 10]. Due to the technical and ergonomic complexities associated with RAPN, it is not extensively utilized for treating complex tumors, thus OPN is still extensively used

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[11]. Research into these topics is still scarce, particularly with regard to RAPN for complex renal tumors (defined as RENAL score \geq 7). Moreover, the limited sample size from a single center restricts our ability to draw reliable generalizations, and the results are still controversial.

To assist clinicians in their clinical decision-making process, we conducted a comprehensive systematic review and meta-analysis to evaluate the efficacy and safety of RAPN and OPN in treating complex renal tumors.

Methods

This meta-analysis was rigorously conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 [12, 13], and was registered in the PROSPERO registry (ID: CRD42023392423).

Literature search strategy, study selection and data collection

We conducted an exhaustive search of relevant databases, such as PubMed, Embase, Web of Science, and Cochrane Library, to retrieve data up to January 2023. The search terms were as follows: ((Robotic partial nephrectomy OR Robot-assisted partial nephrectomy OR Robot-assisted nephron-sparing surgery) AND (Open partial nephrectomy OR Open nephron-sparing surgery) AND (Kidney cancer OR Renal carcinoma OR Renal tumor OR Renal mass) AND (Complex OR Complexity)). To ensure completeness, we additionally conducted a manual exploration of related references, minutes, and abstracts.

The PICOS approach was used to formulate inclusion criteria. P (patients): all the patients were diagnosed with complex renal tumors (defined as RENAL score \geq 7) [9]; I (intervention): undergoing RAPN; C (comparator): OPN was performed for comparison; O (outcome): perioperative outcomes, complications, renal functional and oncologic outcomes; S (study type): prospective studies, retrospective studies, as well as randomized controlled trials (RCTs). The exclusion criteria included: (1) non-comparative studies and duplicate studies; (2) case reports, comments, letters and unpublished studies; and (3) studies that lacked the requisite data for meta-analysis.

Two reviewers independently extracted the relevant data from each eligible literature. The following data were recorded: (1) first author, year of publication, country, center, propensity scoring analysis, and sample size. (2) Age, gender, body mass index (BMI), tumor site, tumor diameter, follow-up period, and RENAL score. (3) Perioperative outcomes, including hospital stay, operative time, blood loss, transfusion rates, warm ischemia time, estimated glomerular (eGFR) decline, intraoperative complications, major complications (Clavien grade \geq 3), and overall complications (Clavien grade \geq 1) [14]. (4) Oncologic outcomes, including positive surgical margin (PSM), overall survival (OS), recurrence-free survival (RFS), tumor stage, and tumor pathology. Any discrepancies and disagreements were reconciled through a collaborative approach involving a third reviewer to reach an agreement.

To evaluate the quality of the literature, two independent reviewers used the risk of bias in the non-randomized studies of interventions (ROBINS-I) tool [15]. In case of any discrepancies, they discussed and resolved them.

Statistical analysis

The statistical analysis of this study was performed using Cochrane Collaborative RevMan5.4 software. The odds ratio (OR) was calculated for dichotomous variables, and the weighted mean difference (WMD) was calculated for continuous variables, with 95% confidence intervals (CI) presented for the outcomes. Moreover, the heterogeneity of each indicator was measured by the I^2 test [16], and statistical significance was determined by a *p* value of less than 0.05. Furthermore, we used a funnel plot to evaluate the publication bias.

Subgroup analysis

A subgroup analysis was performed according to age, sample size, country/region, and RENAL score.

Results

Baseline characteristics

A total of 132 studies were initially identified through electronic search, and 13 were retained after the removal of duplicates. A preliminary review of the titles and abstracts revealed that seven studies involving 1493 patients (804 RAPN vs. 689 OPN) were selected for inclusion in the metaanalysis (Fig. 1) [17–23]. All seven of the non-RCTs were retrospective comparisons, with four of them being multiinstitutional [20-23] and two involving propensity scoring analysis [18, 21]. These studies were conducted in various countries, such as the United States, Korea, Japan, and China, with a follow-up period ranging from 4 to 53 months. Tables 1 and 2 provide a summary of the main characteristics of the patients (country, center, propensity scoring analysis, sample size, age, gender, BMI, tumor site, tumor diameter, follow-up period, and RENAL score). Table 3 displays the tumor stage and pathology.



Fig. 1 PRISMA flow diagram for the systematic review

No significant difference was found in age (p = 0.07), gender (p=0.5), left side (p=0.37), BMI (p=0.58), preoperative eGFR (p = 0.79), and tumor diameter (p = 0.96) (Table S1).

Assessment of quality

All the studies performed comparative analysis, most of which were published between 2017 and 2022, with an intermediate level of evidence. The included studies exhibited a moderate risk of bias, with the exception of one study that demonstrated a low risk of bias (Table S2) [18].

Outcome analysis

Perioperative effectiveness

The pooled results demonstrated no difference in operative time between the two groups (six studies; p = 0.18) [17–22]. In terms of length of hospital stay, the RAPN had a significantly shorter length of hospital stay compared with the OPN (WMD -1.53 days, 95% CI -2.44, -0.62; p = 0.001); seven studies (Fig. 2) [17–23]. The data on blood loss were extracted from seven studies [17-23]. The combined results demonstrated that RAPN was associated with less blood loss than OPN (WMD - 95.88 mL, 95% CI – 144.19, – 47.56; *p* = 0.0001). Moreover, transfusion rates were reported in six studies. The results of the

Reference	Year	Country	Center	Propensity scor-	Patients		Age(y)		Male/Fema	ale	BMI (kg/m ²)	
				ing analysis	RAPN	OPN	RAPN	OPN	RAPN	OPN	RAPN	OPN
Hori	2022	Japan	Single-center	No	77	43	68 (11.11)	65 (10.37)	51/26	30/13	23.3 (3.48)	23.3 (3.48)
Abedali	2020	USA	Single-center	Yes	148	74	60.3(13.1)	58.2 (12.7)	87/61	42/32	31.2 (6.9)	31.3 (8.4)
Kim	2019	Korea	Single-center	No	85	64	53 (13.33)	52 (14.82)	55/30	42/22	24.7 (3.41)	24.8 (2.67)
Garisto	2018	USA	Multi-institutional	No	203	76	59.8 (12.1)	60.7 (11.2)	125/78	44/32	31 (6.8)	31.2 (6.1)
Wang	2017	China	Multi-institutional	Yes	190	190	61.8 (12.3)	59.8 (11.8)	139/51	132/58	25.4 (5.2)	24.6 (4.5)
Zargar	2014	USA	Multi-institutional	No	10	52	61.3 (10.7)	61.5 (11.4)	NA		30(5.4)	31.7 (6.6)
Simhan	2012	USA	Multi-institutional	No	91	190	58.1 (11.7)		178/103		NA	

Table 2 The trials included in the systemic review

Reference	Tumor s Rt)	site (Lt/	Tumor diam	eter (cm)	RENAL score	Preoperative min/1.73 m)	eGFR (ml/	Follow-up durati	on (month)
	RAPN	OPN	RAPN	OPN		RAPN	OPN	RAPN	OPN
Hori	44/33	20/23	2.5 (0.89)	2.9(1.19)	RENAL score > 7	NA		29–110 months	29-110 months
Abedali	66/82	30/44	4.06 (1.85)	4.69 (2.46)	RENAL score > 7	76.4 (25.2)	83.3 (28.2)	1 months	1 months
Kim	49/36	36/28	4.3 (1.7)	3.1 (1.85)	RENAL score ≥ 10	87.1 (17.78)	83.3 (18)	15-53 months	15-53 months
Garisto	86/117	38/38	5 (1.81)	5.2 (2)	RENAL score > 9	81 (22.96)	77 (30.37)	25 months	25 months
Wang	119/71	107/83	3.8 (2.4)	3.6 (2.1)	RENAL score \geq 7	78.3 (18.3)	81.6 (20.8)	49-52 months	49-52 months
Zargar	NA		4.15 (2.15)	4.3 (1.56)	RENAL score 9-12	NA		4-19.6 months	4-19.6 months
Simhan	NA		3.7 (2.4)		RENAL score > 7	NA		21.3 months	21.3 months

RAPN robot-assisted partial nephrectomy, OPN Open partial nephrectomy; mean (SD)

meta-analysis revealed that RAPN had significantly lower transfusion rates compared to OPN (OR 0.33, 95% CI 0.15, 0.71; p = 0.005) (Fig. 3). No statistically significant difference in warm ischemia time was observed between the two groups (six studies; p = 0.29) (Fig. 4) [17–22].

Complications

It was observed that RAPN and OPN groups had comparable intraoperative complication rates (four studies; p=0.55) [19–22]. Major complications occurred in 7.7% (49 of 636 cases) of RAPN and 12.1% (55 of 456 cases) of OPN. Patients undergoing RAPN had a lower incidence of major complications than those undergoing OPN (five studies; OR 0.63, 95% CI 0.39, 1.01; p=0.05) [18–22]. A pooled analysis of five studies revealed that, in comparison with OPN, RAPN had a significantly lower rate of overall complications (OR 0.49, 95% CI 0.36, 0.65; p < 0.00001). Specifically, RAPN had an overall complication rate of 23.0% (130 out of 565 cases), whereas OPN had a higher rate of 36.2% (154 out of 425 cases) (Fig. 5) [17, 19–22].

Renal functional and oncologic outcomes

In terms of eGFR decline, no significant difference was observed between the two groups (four studies; p = 0.11) (Fig. 4) [18–21]. There is no statistical significance in the PSM between RAPN and OPN (six studies; p = 0.13) [17–22]. No significant differences were also found in terms of local recurrence between RAPN and OPN groups (four studies; p = 0.78) [19–21, 23]. Furthermore, the cumulative analysis revealed no significant difference in OS between the two groups (three studies; p = 0.34) [17, 19, 21]. Similarly, the pooled results revealed no difference between the two groups in RFS (three studies; p = 0.63) (Fig. 6) [17–22].

Subgroup analysis

The subgroup analysis revealed that age, sample size, region, and RENAL score all played a part in producing heterogeneity between studies to varying extents (Table 4).

Age and region were major factors driving the heterogeneity in length of stay. In patients aged below 60 years, RAPN was associated with a significantly shortened hospital stay compared to OPN (p < 0.00001). Conversely, no significant difference was observed in patients aged 60 years and above (p = 0.14). Moreover, in the Non-Asian subgroup, patients undergoing RAPN had a significantly shorter lengths of hospital stay compared to OPN (p < 0.00001), while no significant difference was found in the Asian subgroup (p = 0.41).

The heterogeneity for blood loss was influenced by sample size and RENAL score. A significantly lower blood loss was observed in the RAPN group compared to the OPN group in the subgroup with a sample size ≥ 200 (p = 0.005), while no significant difference was found between the two groups in the subgroup with a sample size < 200 (p = 0.21). Furthermore, in the RENAL score ≥ 7 subgroup, RAPN was associated with a significantly reduced amount of blood loss when compared to OPN (p = 0.01). Conversely, no significant difference was observed in the RENAL score ≥ 9 group (p = 0.18).

In terms of transfusion rates, age was a major factor driving the heterogeneity. Among patients aged ≥ 60 years, RAPN was associated with significantly lower transfusion rates compared to OPN (p = 0.01). Conversely, no significant difference was observed in the subgroup of patients aged < 60 years (p = 0.28). Furthermore, the region exhibited a considerable degree of heterogeneity in terms of warm ischemia time. The warm ischemia time was shorter for RAPN in the Non-Asian subgroup (p = 0.02), but no significant difference was observed in the Asian subgroup (p = 0.41).

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	Tumor stage		Tumor nathology	
	1 UIII01 Stage			
	RAPN	OPN	RAPN	NAO
Hori	pTla:71; pTlb:5; pT3a:1	pT1a:32; pT1b:10; pT3a:1	Clear cell: 99; papillary: 14; chromophobe: 8, unclassified: 3; translocation: 1; other: 5	Clear cell: 48; papillary: 7; chromophobe: 2; unclassified: 5; translocation: 0; other: 1
Abedali	pT1a:97; pT1b:26; pT2a:0; pT2b:0; pT3a:7	pT1a:44; pT1b:12; pT2a:2; pT2b:1; pT3a:4	Clear cell: 58; others: 19	Clear cell: 36; others: 7
Kim	cTla:36; cT1b:35; cT2a:14	cT1a:42; cT1b:16; cT2a:6	Clear cell: 65; papillary: 1; chromophobe: 10; collecting duct: 0; unclassified: 2; benign: 0	Clear cell: 50; papillary: 3; chromophobe: 3; collecting duct: 0; unclassified: 0; benign: 8
Garisto	cT1a:67; cT1b:112; cT2a:20; cT2b:4	cTla:18; cTlb:42; cT2a:11; cT2b:5	Clear cell: 128; papillary: 23; chromo- phobe: 14; others: 14	Clear cell: 46; papillary: 11; chromophobe: 7; others: 3
Wang	pT1a:101; pT1b:27; pT2a:20; pT3a:16	pT1a:102; pT1b:30; pT2a:15; pT3a:12	Clear cell: 107; papillary: 28; chromo- phobe: 24; others: 5; benign: 26	Clear cell: 99; papillary: 31; chromophobe: 26; others: 3; benign: 26
Zargar	All are cT1 and cT2		NA	
Simhan	All are cT1 and cT2		NA	

Heterogeneity

Most outcomes demonstrated a low to moderate degree of heterogeneity between the included studies; however, considerable heterogeneity was observed in operative time, length of the hospital, blood loss, warm ischemia time, and eGFR decline.

Sensitivity analysis

To assess the reliability of our results, we conducted a sensitivity analysis using the leave-one-out test for operative time, length of the hospital, blood loss, warm ischemia time, and eGFR decline based on the limited number of literatures included in the study. No significant change was observed in the pooled WMD and OR, which unequivocally confirms the validity of our results.

Publication bias

We conducted a funnel plot analysis to evaluate the potential for publication bias among the indices of operative time, length of the hospital, blood loss, and PSM. Though our findings indicated that the distribution of studies was nearly symmetric, there remains some evidence of publication bias (Fig. S1).

Discussion

The present study provides a comprehensive assessment of the existing evidence regarding the perioperative results, complications, renal functional and oncologic outcomes between RAPN and OPN for complex renal tumors. Furthermore, certain significant findings drawn from this study require further discussion.

Some studies have indicated that, due to the requirement of reverting to docking or re-positioning the patient, the utilization of a robotic platform would extend the duration of the surgical procedure [24]. Interestingly, the pooled results demonstrated no difference in operative time between the two groups in our study. The positive result can be attributed to the doctors' experience with other robotic surgeries, such as robotic radical prostatectomy and cystectomy, as well as the studies conducted by large medical institutions. Moreover, several factors, such as the assistant's proficiency, BMI, and intraoperative complications, other than tumor characteristics, may influence the duration of the operation [25]. In terms of length of the hospital, the RAPN had a significantly shorter length of hospital stay compared with the OPN. Minimally invasive surgery offers a range of benefits, such as decreased blood loss during the surgical procedure, improved visibility for the surgeon, and reduced tissue

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	I	RAPN			OPN			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Abedali 2020	226.5	65.4	148	200.5	74.8	74	17.0%	26.00 [5.96, 46.04]	
Garisto 2018	208	68.15	203	213.5	48.89	76	18.5%	-5.50 [-19.95, 8.95]	
Hori 2022	276	55.56	77	215	54.07	43	16.9%	61.00 [40.62, 81.38]	
Kim 2019	150	59.26	85	145	55.56	64	17.4%	5.00 [-13.55, 23.55]	
Wang 2017	141.7	38.1	190	148.5	42.5	190	19.7%	-6.80 [-14.92, 1.32]	
Zargar 2014	250.8	66	10	244.1	59.3	52	10.5%	6.70 [-37.27, 50.67]	
Total (95% CI)			713			499	100.0%	13.96 [-6.46, 34.39]	
Heterogeneity: Tau ² =	: 533.82;	Chi ² =	43.16,	df = 5 (F	< 0.00	1001); P	²= 88%		
Test for overall effect:	Z=1.34	(P = 0.	18)						-100 -50 0 50 100
		•	,						shorter in RAPN shorter in OPN
			,						shorter in RAPN shorter in OPN
В			,						shorter in RAPN shorter in OPN
В	F	RAPN	,		OPN			Mean Difference	shorter in RAPN shorter in OPN Mean Difference
B Study or Subgroup	F Mean	RAPN SD	Total	Mean	opn Sd	Total	Weight	Mean Difference IV, Random, 95% Cl	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% Cl
B Study or Subgroup Abedali 2020	F <u>Mean</u> 3	RAPN SD 1.6	<u>Total</u> 148	Mean 5.3	DPN SD 4.2	<u>Total</u> 74	Weight 13.1%	Mean Difference IV, Random, 95% CL -2.30 [-3.29, -1.31]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% CI
B Study or Subgroup Abedali 2020 Garisto 2018	F <u>Mean</u> 3 3	RAPN SD 1.6 0.74	<u>Total</u> 148 203	Mean 5.3 5	DPN <u>SD</u> 4.2 1.11	<u>Total</u> 74 76	<u>Weight</u> 13.1% 15.4%	Mean Difference IV, Random, 95% CI -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.73]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% Cl
B Study or Subgroup Abedali 2020 Garisto 2018 Hori 2022	F <u>Mean</u> 3 3 9	RAPN SD 1.6 0.74 1.48	<u>Total</u> 148 203 77	<u>Mean</u> 5.3 5 8	DPN SD 4.2 1.11 1.48	<u>Total</u> 74 76 43	Weight 13.1% 15.4% 14.7%	Mean Difference <u>IV, Random, 95% Cl</u> -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.73] 1.00 [0.45, 1.55]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% CI
B Abedali 2020 Garisto 2018 Hori 2022 Kim 2019	F <u>Mean</u> 3 3 9 5	RAPN 5D 1.6 0.74 1.48 1.48	Total 148 203 77 85	<u>Mean</u> 5.3 5 8 7	DPN 5D 4.2 1.11 1.48 2.96	Total 74 76 43 64	Weight 13.1% 15.4% 14.7% 13.9%	Mean Difference <u>IV, Random, 95% Cl</u> -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.73] 1.00 [0.45, 1.55] -2.00 [-2.79, -1.21]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% CI
B Abedali 2020 Garisto 2018 Hori 2022 Kim 2019 Simhan 2012	F <u>Mean</u> 3 3 9 5 3.61	RAPN 5D 1.6 0.74 1.48 1.48 1.6	<u>Total</u> 148 203 77 85 91	Mean 5.3 5 8 7 5.74	DPN 5D 4.2 1.11 1.48 2.96 3.95	Total 74 76 43 64 190	Weight 13.1% 15.4% 14.7% 13.9% 14.4%	Mean Difference IV, Random, 95% CI -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.31] 1.00 [0.45, 1.73] -2.00 [-2.79, -1.21] -2.13 [-2.78, -1.48]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% CI
B Study or Subgroup Abedali 2020 Garisto 2018 Hori 2022 Kim 2019 Simhan 2012 Wang 2017	F <u>Mean</u> 3 9 5 3.61 7.8	RAPN 5D 1.6 0.74 1.48 1.48 1.48 1.6 2.1	<u>Total</u> 148 203 77 85 91 190	Mean 5.3 5 8 7 5.74 9.2	DPN <u>SD</u> 4.2 1.11 1.48 2.96 3.95 3.8	Total 74 76 43 64 190 190	Weight 13.1% 15.4% 14.7% 13.9% 14.4% 14.5%	Mean Difference IV, Random, 95% CI -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.73] 1.00 [0.45, 1.55] -2.00 [-2.79, -1.21] -2.13 [-2.78, -1.48] -1.40 [-2.02, -0.78]	shorter in RAPN shorter in OPN Mean Difference IV. Random, 95% Cl
B Study or Subgroup Abedali 2020 Garisto 2018 Hori 2022 Kim 2019 Simhan 2012 Wang 2017 Zargar 2014	F <u>Mean</u> 3 3 9 5 3.61 7.8 4	RAPN 5D 1.6 0.74 1.48 1.48 1.48 1.6 2.1 1.11	Total 148 203 77 85 91 190 10	Mean 5.3 5 8 7 5.74 9.2 6	DPN <u>SD</u> 4.2 1.11 1.48 2.96 3.95 3.8 1.48	Total 74 76 43 64 190 190 52	Weight 13.1% 15.4% 14.7% 13.9% 14.4% 14.5% 13.9%	Mean Difference IV, Random, 95% CI -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.73] 1.00 [0.45, 1.55] -2.00 [-2.79, -1.21] -2.13 [-2.78, -1.48] -1.40 [-2.02, -0.78] -2.00 [-2.80, -1.20]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% CI
B Study or Subgroup Abedali 2020 Garisto 2018 Hori 2022 Kim 2019 Simhan 2012 Wang 2017 Zargar 2014	F <u>Mean</u> 3 3 9 5 5 3.61 7.8 4	RAPN 5D 1.6 0.74 1.48 1.48 1.48 1.6 2.1 1.11	Total 148 203 77 85 91 190 10	Mean 5.3 5 8 7 5.74 9.2 6	DPN 4.2 1.11 1.48 2.96 3.95 3.8 1.48	Total 74 76 43 64 190 190 52	Weight 13.1% 15.4% 14.7% 13.9% 14.4% 13.9%	Mean Difference IV, Random, 95% CI -2.30 [-3.29, -1.31] -2.00 [-2.27, -1.73] 1.00 [0.45, 1.55] -2.00 [-2.79, -1.21] -2.13 [-2.78, -1.48] -1.40 [-2.02, -0.78] -2.00 [-2.80, -1.20]	shorter in RAPN shorter in OPN Mean Difference IV, Random, 95% CI

Heterogeneity: Tau² = 1.37; Chi² = 100.42, df = 6 (P < 0.00001); l² = 94%Test for overall effect: Z = 3.30 (P = 0.0010)

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-4 -2 0 2 4 shorter in RAPN shorter in OPN



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		RAPN			OPN			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95	6 CI IV, Random, 95% CI
Abedali 2020	210.5	208.9	148	368.5	308.7	74	13.1%	-158.00 [-235.97, -80	.03]
Garisto 2018	200	185.19	203	300	222.2	76	15.7%	-100.00 [-156.08, -43	.92]
Hori 2022	10	29.63	77	234	327.41	43	11.0%	-224.00 [-322.08, -125	.92]
Kim 2019	200	148.15	85	200	148.15	64	16.7%	0.00 [-48.06, 48	.06]
Simhan 2012	131.3	127.8	91	256.5	291.3	190	16.6%	-125.20 [-174.24, -76	.16]
Wang 2017	196.8	64.3	190	240.8	73.6	190	19.6%	-44.00 [-57.90, -30	.10]
Zargar 2014	225	213.33	10	300	194.81	52	7.3%	-75.00 [-217.43, 67	.43]
Total (95% CI)			804			689	100.0%	-95.88 [-144.19, -47	561 🔶
Heterogeneity: Tau ² =	= 3043.5	3: Chi ² =	35.97.	df = 6 (P	< 0.000	01); I ² =	83%		
Test for overall effect	Z = 3.89	P = 0.0	0001)						-500 -250 0 250 500
									less in RAPN Less in OPN
B									
D		RAPN		OP	N I			Odds Ratio	Odds Ratio
Study or Subgrou	p Ev	ents T	otal I	Events	Total	Weigh	nt M-H.	Random, 95% CI	M-H, Random, 95% Cl
Abedali 2020		2	148	10	74	14.4	%	0.09 [0.02, 0.41]	
Garisto 2018		6	203	12	76	21.39	%	0.16 [0.06, 0.45]	
Hori 2022		2	77	4	43	12.5	%	0.26 [0.05, 1.48]	
Kim 2019		8	85	7	64	20.69	%	0.85 [0.29, 2.47]	
Wang 2017		12	190	17	190	25.49	%	0.69 [0.32, 1.48]	
Zargar 2014		0	10	8	52	5.89	%	0.25 [0.01, 4.67]	
Total (95% CI)			713		499	100.0	%	0 33 (0 15 0 71)	
Total quanta					455	100.0		0.00 [0.10, 0.11]	-
		20		60					
Hotorogonoite To:	- 0 4	30 8: Ohiz-	- 10.01	58 0 df = 5	D = 0	063-12-	E 4 04	F	
Heterogeneity: Tai	u² = 0.41	30 6; Chi² =	= 10.82	58 2, df = 5	(P = 0.	06); I² =	= 54%	H O	
Heterogeneity: Tai Test for overall effe	u² = 0.4) ect: Z =	30 6; Chiᢪ⊧ 2.83 (P	= 10.82 = 0.00	58 2, df = 5 5)	(P = 0.	06); I² =	54%	H O	.01 0.1 1 10 100 less in RAPN less in OPN

Fig. 3 Forest plots of perioperative outcomes for RAPN versus OPN. A blood loss, B transfusion rates

trauma. Moreover, minimally invasive surgery has been shown to expedite recovery, reduce the risks associated with prolonged bed rest, and shorten hospital stays [26]. However, no significant difference was observed in the Asian subgroup in terms of length of stay. This result may be attributable to several factors. First, the hospital stay in minimally invasive surgeries is contingent upon a variety of factors, including hospital capacity, the expertise of the surgeon, and the surgical procedure. Second, recovery after surgery protocols may be strengthened to further reduce the length of the hospital stay following minimally invasive surgery [27]. Third, the rapid advancement of anesthesiology and perioperative

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Fig. 4 Forest plots of perioperative outcomes and complication for RAPN versus OPN. A Warm ischemia time, B eGFR decline

care administration could potentially facilitate a reduction in hospital stay [28]. Therefore, to confirm the validity of outcomes, more compelling evidence is essential.

The results of a meta-analysis revealed that RAPN was associated with reduced blood loss compared to RAPN. Blood loss is an important measure of surgical quality. Robotic vision imaging systems can greatly expand the surgical field, enabling surgeons to closely observe blood vessels, quickly recognize sites of bleeding, and promptly arrest the loss of blood with the use of electric coagulation forceps, thus effectively reducing the amount of blood loss. Moreover, the pneumoperitoneum setup through minimally invasive surgery assists in stanching venous bleeding during dissection [29]. Similarly, the results of the meta-analysis revealed that RAPN had significantly lower transfusion rates compared to OPN. However, the doctor's degree of experience and the organization's guidelines on blood transfusion are also correlated to the transfusion rate.

The combined results demonstrated that there was no statistically significant difference in warm ischemia time between the RAPN and OPN. However, certain aspects require our attention. Several studies have suggested that warm ischemia time should be kept below 25 or 30 min to avoid potential damage to renal function [30, 31]. Interestingly, five studies have reported that the ischemia time in the RAPN group is less than 25 min, with another study having a mean warm ischemia time of 28 min. Considering the above, the ischemia time of the RAPN is acceptable for complex renal tumors. Nevertheless, warm ischemia time was shorter for RAPN in the Non-Asian subgroup. The

duration of the operation was related to a variety of factors, including the surgeon's level of experience and the location or size of the tumour [28]. Therefore, further studies with larger sample sizes and long-term follow-ups are necessary to validate the results more conclusively.

We assessed the complications based on the Clavien-Dindo grade [14]. There was no statistically significant difference in intraoperative complications between the RAPN and OPN groups. Nevertheless, patients undergoing RAPN had fewer major complications than patients undergoing OPN. Furthermore, the meta-analysis also revealed that RAPN was associated with fewer overall complications than OPN. Given that the incision is done at the 11th or 12th rib to accomplish partial nephrectomy in open surgery, its trauma is quite severe, leading to a high physiological load on the body, which may result in severe complications and impede postoperative recovery. Furthermore, robotic surgery offers several advantages, including a smaller incision and limited anatomical exposure, which can reduce the risk of damage to adjacent organs and, consequently, postoperative complications [32]. Tsai et al. [33] performed a metaanalysis showing that RAPN is also associated with fewer complications than OPN for non-complex renal tumors.

No statistically significant difference in eGFR decline was observed between the RAPN and OPN groups. Moreover, other significant factors should be taken into consideration. Several studies have suggested that preoperative renal function and the retained number of nephrons are the primary determinants of long-term renal function, while warm ischemia time is of minor consequence [34, 35].

10

200

100

100

10

10

Odds Ratio

M-H, Random, 95% Cl

Total events 34 32 Heterogeneity: Tau² = 0.29; Chi² = 5.75, df = 3 (P = 0.12); I² = 48% 0.005 0.1 Test for overall effect: Z = 0.60 (P = 0.55) less in RAPN less in OPN B RAPN OPN Odds Ratio Odds Ratio M-H, Random, 95% Cl M-H, Random, 95% Cl Events Weight Study or Subgroup Total Events Total Abedali 2020 16 148 15 74 28.9% 0.48 [0.22, 1.03] Garisto 2018 0.55 [0.23, 1.33] 203 76 23.3% 14 9 Kim 2019 10 85 12 64 22.1% 0.58 [0.23, 1.44] Wang 2017 5 190 9 190 15.8% 0.54 [0.18, 1.65] Zargar 2014 2.80 [0.66, 11.83] 4 10 10 52 9.9% Total (95% CI) 636 456 100.0% 0.63 [0.39, 1.01] 55 Total events 49 Heterogeneity: Tau² = 0.05; Chi² = 4.80, df = 4 (P = 0.31); l² = 17% 0.01 0.1 Test for overall effect: Z = 1.93 (P = 0.05) less in RAPN less in OPN C RAPN OPN Odds Ratio Odds Ratio Study or Subgroup Events Total ents Total Weight M , Random, 95% Cl M-H, Random, 95% CI Garisto 2018 203 29.2% 0.54 [0.31, 0.93] 57 32 76 Hori 2022 11 77 17 43 11.3% 0.25 [0.11, 0.62] Kim 2019 85 0.56 [0.29, 1.09] 28 30 64 19.7% Wang 2017 30 190 55 190 35.2% 0.46 [0.28. 0.76] Zargar 2014 4 10 20 52 4.6% 1.07 [0.27, 4.25] Total (95% CI) 100.0% 0.49 [0.36, 0.65] 565 425 Total events 130 154 Heterogeneity: Tau² = 0.00; Chi² = 3.62, df = 4 (P = 0.46); I² = 0% 0.01 0.1 Test for overall effect: Z = 4.77 (P < 0.00001) less in RAPN less in OPN Fig. 5 Forest plots of complication for RAPN versus OPN. A Intraoperative complications, B major complications, C overall complication

Additionally, age is an essential factor for the restoration of postoperative long-term renal function. Furthermore, no considerable difference was observed in the age, preoperative eGFR in the included studies, this further confirms that RAPN can effectively preserve renal function. However, further research utilizing a larger sample size and long-term observation is necessary to validate renal function.

Patton et al. [36] reported that the PSM rate of RAPN for complex renal tumors (RENAL score > 9) ranges from 0 to 3.7%. Nevertheless, Marszalek et al. [37] showed that PSM may not be an accurate predictor of local recurrence. Other factors such as tumor diameter, surgical approach, and tumor stage could potentially affect PSM [38]. Our study revealed that the PSM rate of RAPN was 4.30% (28 out of 656 cases), while that of OPN was 5.52% (34 out of 615 cases). However, further studies must be carried out to validate these results. No significant differences were also found regarding local recurrence between RAPN and OPN groups. Similarly, there is also no statistically significant difference between the two groups in OS and RFS. When assessing the oncologic outcomes between RAPN and OPN, several pivotal factors must be taken into account. First, due to the limited duration of the follow-up period in the majority of studies (4-53 months) and the insufficient number of studies, it is impossible to draw firm conclusions. Second, due to the scantiness of the literature, we cannot ascertain the metastatic recurrence and cancer-specific survival between the two groups. Therefore, further research with a longer follow-up period and a more substantial sample size are essential to verify the oncologic results.

The included studies performed the different surgical methods (transperitoneal or retroperitoneal) for PN, leading to certain heterogeneity. The retroperitoneal approach offers several advantages, such as facilitating ligation of the renal artery, thereby reducing blood loss during renal tumor separation, as well as minimizing interference with the intestine, thus diminishing the risk of complications. However, this approach is associated with certain drawbacks, such

А

Study or Subgroup

Garisto 2018

Kim 2019

Wang 2017

Zargar 2014

Total (95% CI)

RAPN

15

8 85

10 190

> 1 10

Total

203

488

Events

OPN

13

4

14 190

1 52

Events Total

76

64

382

Weight

35.6%

23.4%

34.3%

100.0%

6.7%

M-F

Odds Ratio

Random, 95% Cl

0.39 [0.17, 0.86]

1.56 [0.45.5.42]

0.70 (0.30, 1.61)

5.67 [0.32, 99.04]

0.79 [0.36, 1.73]

A

		RAP	U.	OPN	i i		Odds Ratio		Odds Batio	
	Study or Subaroup	Events	Total	Events	Total	Weight	M-H. Random, 95% (CI	M-H. Random, 95% Cl	
-	Garisto 2018	18	203	10	76	45.2%	0.64 [0.28, 1.4]	61		
	Hori 2022	1	77	3	43	5.8%	0.18 (0.02, 1.7	41		
	Kim 2019	0	85	1	64	3.0%	0.25 [0.01, 6.1]	81		
	Simhan 2012	5	91	8	190	23.3%	1.32 [0.42, 4.1]	61		
	Wang 2017	3	190	8	190	17.0%	0.36 [0.10, 1.4]	01		
	Zargar 2014	1	10	4	52	5.8%	1.33 [0.13, 13.3	5]		
	Total (95% CI)		656		615	100.0%	0.65 [0.37, 1.13	3]	•	
	Total events	28		34						
	Heterogeneity: Tau ² =	0.00; Chi	² = 4.17	', df = 5 (l	P = 0.5	3); l² = 09	6	+		600
	Test for overall effect: 2	Z = 1.53 (P = 0.1	3)				0.002		500
	-								1633 111 10-14 1633 11 0-14	
	В									
		RAPN	N I	OPN	1		Odds Ratio		Odds Ratio	
2	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% (CI	M-H, Random, 95% Cl	
	Garisto 2018	9	203	3	76	35.2%	1.13 [0.30, 4.2	9]		
	Kim 2019	4	85	3	64	26.6%	1.00 [0.22, 4.6	5]	+	
	Simhan 2012	0	91	0	190		Not estimable	le		
	Wang 2017	4	190	6	190	38.2%	0.66 [0.18, 2.3	8]		
	Total (95% CI)		569		520	100.0%	0.89 [0.40, 1.97	7]		
	Total events	17		12						
	Heterogeneity: Tau ² =	0.00; Chi	² = 0.38	i, df = 2 (i	P = 0.8	4); l² = 09	6	0.01	0.1 1 10	100
	Test for overall effect: 1	Z = 0.28 (P = 0.7	8)				0.01	less in RAPN less in OPN	
	C									
	C									
	~				~		Hazard Ratio		Hazard Ratio	
-	Study or Subgroup	log[Ha	zard R	atio	SE M	leight N	V, Random, 95% Cl		IV, Random, 95% Cl	
	Hori 2022			-0.01 0.	.36 6	64.6%	0.99 [0.49, 2.00]			
	Kim 2019			-1.28 0.	.68 3	33.5%	0.28 [0.07, 1.05]			
	Wang 2017		ं	-1.26 3.	.48	1.9%	0.28 [0.00, 260.00]	•		_
	T									
	Total (95% CI)				1	00.0%	0.63 [0.25, 1.62]			
	Heterogeneity: Tau* =	= 0.23; C	$hi^{*} = 2.$	80, df = 1	2 (P =	0.25); 1*=	= 29%	0.001	0,1 1 10	1000
	Test for overall effect	: Z = 0.95	6 (P = 0)	1.34)					lower in RAPN lower in OPN	
	D									
	D						Hanard Datia		Userand Datis	
	Chuche an Cucharrown	le eff le	nord D	atia 1	CF 14	lainht B	Hazard Ratio		Hazard Ratio	
-	Study of Subgroup	logiHa	Zara R	atio	SE W		V, Random, 95% CI			
	Hori 2022		9	1.28 1.	25 3	50.0%	0.28 [0.02, 3.22]			
	Kim 2019			3.91 0.	.91 3	33.1% 4	9.90 [8.38, 296.95]			
	wang 2017			0.51 0.	32 3	30.9%	0.60 [0.32, 1.12]		-	
	Total (05% CI)					00.0%	2 06 10 40 40 501			
	Total (95% CI)				10	0.0%	2.06 [0.10, 40.56]			
	Heterogeneity: Tau* =	= 6.16; C	ni= 2'	1.95, df =	: 2 (P «	< 0.0001)); if = 91%	0.002	0.1 1 10	500
	lest for overall effect	: Z = 0.48	3 (P = 0	.63)					lower in RAPN lower in OPN	

Fig. 6 Forest plots of mortality rates for RAPN versus OPN. A PSM, B local recurrence, C overall survival, D recurrence-free survival

as restricted operative space [39]. Therefore, further highquality research is required to determine which surgical approach (transperitoneal or retroperitoneal) is more suitable for complex renal tumors. The RENAL score performs a standardized anatomical classification to facilitate surgical decision-making and categorize the complexity of renal tumors. According to the score, lesions with a RENAL score range of 4–6, 7–9, and 10–12 are deemed of low, moderate, and high complexity, respectively (9). Although we have a conducted subgroup analysis based on the RENAL score (RENAL score \geq 7 and RENAL score \geq 9 subgroup), there is still a degree of heterogeneity, thus necessitating further exploration to validate the outcomes. Nevertheless, certain limitations of our study are noteworthy. First, all the included studies were retrospective with most of them having intermediate quality, potentially introducing selection and blindness bias. Second, no subgroup analysis was conducted based on the surgical approach (transperitoneal or retroperitoneal), which may have resulted in some heterogeneity in outcomes. Third, the follow-up period of some studies was limited, making it difficult to compare the renal function and oncological outcomes between the two groups. Fourth, given that all of the included studies were conducted in large, high-volume institutions by experienced robotic surgeons, it is necessary to interpret the results with caution, as they may not be generalizable to other institutions. Finally, the small Table 4Subgroup analysis ofperioperative and oncologicoutcomes for RAPN and OPN

Group	Subgroups	Studies (n)	MD/OR (95% CI)	$I^{2}(\%)$	р
Operative time					
Age	Mean age < 60 years	2	15.14 (-5.42, 35.71)	56	0.15
	Mean age \geq 60 years	4	13.49 (-16.22, 43.19)	92	0.37
Sample size	Sample size < 200	3	25.63 (-16.23, 67.49)	88	0.23
	Sample size \geq 200	3	2.49 (-14.30, 19.29)	78	0.77
Country/region	Asian	3	18.93 (-19.07, 56.94)	95	0.33
	Non-Asian	3	8.68 (-14.81, 32.18)	68	0.47
RENAL score	RENAL≥score 7	3	25.97 (-15.68, 67.61)	95	0.22
	RENAL≥score 9	3	-1.02 (-12.05, 10.02)	0	0.86
Length of stay					
Age	Mean age < 60 years	3	-2.12 (-2.57, -1.67)	0	< 0.00001
	Mean age $60 \ge$ years	4	-1.10 (-2.54, 0.34)	97	0.14
Sample size	Sample size < 200	3	-0.98 (-3.14, 1.17)	96	0.37
	Sample size \geq 200	4	-1.93 (-2.24, -1.63)	24	< 0.00001
Country/region	Asian	3	-0.79 (-2.26, 1.08)	96	0.41
	Non-Asian	4	-2.03 (-2.26, -1.08)	0	< 0.00001
RENAL score	RENAL≥score 7	4	-1.19 (-2.80, 0.43)	96	0.15
	RENAL≥score 9	3	-2.00(-2.24, -1.76)	0	< 0.00001
Blood loss					
Age	Mean age < 60 years	3	-91.67 (-188.98, 5.64)	89	0.06
0	Mean age ≥ 60 years	4	-103.23 (-175.20, -31.25)	81	0.005
Sample size	Sample size < 200	3	-96.78(-248.15, 54.58)	88	0.21
1	Sample size ≥ 200	4	-100.55 (-157.15, -43.95)	85	0.005
Country/region	Asian	3	-72.53 (-149.04, 3.98)	88	0.06
, ,	Non-Asian	4	-119.82 (-152.31, -87.34)	0	< 0.00001
RENAL score	RENAL score \geq 7	4	-128.73 (-206.68, -50.78)	89	0.01
	RENAL score ≥ 9	3	-53.48 (-130.85, 23.89)	72	0.18
Transfusion rate					
Age	Mean age < 60 years	2	0.29 (0.03, 2.73)	82	0.28
e	Mean age ≥ 60 years	4	0.33 (0.14, 0.79)	42	0.01
Sample size	Sample size < 200	3	0.57 (0.24, 1.35)	0	0.2
1	Sample size ≥ 200	3	0.24 (0.07, 0.84)	76	0.03
Country/region	Asian	3	0.65 (0.36, 1.18)	0	0.16
, ,	Non-Asian	3	0.14 (0.06, 0.32)	0	< 0.00001
RENAL score	RENAL score≥7	3	0.29 (0.08, 1.06)	66	0.06
	RENAL score ≥ 9	3	0.35 (0.10, 1.23)	59	0.1
Warm ischemia ti	me				
Age	Mean age < 60 year	2	-1.31 (-9.93, 7.31)	91	0.77
e	Mean age ≥ 60 years	4	-2.04(-6.04, 1.96)	85	0.32
Sample size	Sample size < 200	3	1.77(-0.57, 4.10)	25	0.14
I I I I	Sample size 200	3	-5.03(-10.24, 0.18)	88	0.06
Country/region	Asian	3	1.21(-1.65, 4.07)	71	0.41
, ,	Non-Asian	3	-5.39(-9.80, -0.98)	72	0.02
RENAL score	RENAL score > 7	3	-0.04 (-2.30, 2.22)	47	0.97
	RENAL score > 9	3	-2.35(-9.50, 4.81)	91	0.52
PSM		-			
Age	Mean age < 60 years	2	1.10 (0.37, 3.22)	0	0.87
0-	Mean age > 60 years	4	0.54 (0.28, 1.03)	0	0.06
Sample size	Sample size < 200	3	0.42 (0.10, 1.80)	0	0.24
r	Sample size > 200	3	0.70 (0.37, 1.30)	0	0.26

Table 4 (continued)

Group	Subgroups	Studies (n)	MD/OR (95% CI)	$I^{2}(\%)$	р
Country/region	Asian	3	0.30 (0.10, 0.88)	0	0.03
	Non-Asian	3	0.85 (0.45, 1.62)	0	0.63
RENAL score	RENAL \geq score 7	3	0.56 (0.18, 1.74)	0	0.32
	RENAL \geq score 9	3	0.66 (0.31, 1.40)	0	0.28

sample size of the studies impeded the reliability of outcomes such as OS and RFS, for which data were only available from three studies.

Conclusions

Compared to OPN, RAPN has been found to be advantageous for treating complex renal tumors (RENAL score \geq 7), with a shorter hospital stay, less blood loss and fewer complications. Moreover, the oncologic outcomes and renal function of RAPN are comparable to those of OPN. However, due to the majority of the included studies being of intermediate quality and retrospective in nature, further higher-quality research with long-term follow-ups is necessary to draw reliable conclusions regarding the comparison between the two techniques.

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Availability of data and material Raw data are available at request.

Declarations

Conflict of interest All the Authors have nothing to declare.

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