### **REVIEW ARTICLE**



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# Open versus robotic partial nephrectomy: Systematic review and meta-analysis of contemporary studies

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#### Abstract

**Objectives:** To compare perioperative outcomes of robotic-assisted partial nephrectomy (RaPN) with open partial nephrectomy (OPN).

**Methods:** Systematically search through PubMed, Embase, ClinicalKey, Cochrane Library, ProQuest, ScienceDirect, Web of Science, and ClinicalTrials.gov for eligible studies was performed to April 11, 2018. A meta-analysis was conducted for studies comparing RaPN and OPN. Confounding variables were assessed by meta-regression or subgroup analysis.

**Results:** This study included 34 studies with 60 808 patients. Meta-analysis revealed less blood loss, less transfusion, longer operative time, less postoperative complications, lower readmission rate, shorter length of stay, and less estimated glomerular filtration rate (eGFR) decline in RaPN groups. The superiority of RaPN in blood loss was attenuated with highly complex renal masses. The superiority of RaPN in in intraoperative complications was strengthened with renal hilar control. The advantage of RaPN in surgical margin was increased in patient with body mass index (BMI) < 28.

**Conclusions:** Compared with OPN, RaPN provided lower morbidities and better renal function preservation.

### KEYWORDS

meta-analysis, open procedure, partial nephrectomy, reobotic surgical procedures

### 1 | INTRODUCTION

Partial nephrectomy (PN) is a preferred surgical approach for small renal masses.<sup>1-4</sup> Larger and more complex renal tumors are increasingly managed by PN with technical advancement.<sup>5</sup> While traditional open partial nephrectomy (OPN) has been the standard approach,

RaPN, first described by Gettman et al in 2004, provides magnified stereoscopic visualization and precise control of articulated robotic-assisted instruments.<sup>7</sup> The learning curve of RaPN is much shorter than LPN and only requires 25 cases as suggested by Pierorazio et al.<sup>8</sup> A population-based study showed widespread adoption of the robotic-assisted technique by 45.4% annual increase use in RaPN comparing with 7.9% in OPN.<sup>9</sup> RaPN is also feasible in dealing with large, complex, and hilar renal masses.<sup>10,11</sup> Rapid adoption and expanded indications of RaPN challenged the traditional

evolution of minimal invasive techniques led to the adoption of laparoscopic partial nephrectomy (LPN) and robotic-assisted partial nephrectomy (RaPN) and are becoming the standard of care.<sup>6</sup>

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### 2 | METHOD AND MATERIALS

The current meta-analysis that was conducted under rigorous guidelines as described in the preferred reporting items for systematic reviews and meta-analyses (PRISMA) recommendations (Figure 1).<sup>12</sup>

## 2.1 | Database searches and identification of eligible papers

A systematic literature review was performed by using PubMed, Embase, ClinicalKey, Cochrane Library, ProQuest, ScienceDirect, Web of Science, and ClinicalTrials.gov to April 11, 2018, with keyword of (open partial nephrectomy) AND (robotic assisted partial nephrectomy OR robotic partial nephrectomy). To include as many eligible articles as possible, we did not set any limitation term during literature search strategy except for only limitation of language of English written. To expand the potentially eligible articles, we searched for articles from the reference lists of specific review and original articles relevant to current topic.<sup>6,13,14</sup>

### 2.2 | Inclusion and exclusion criteria

Inclusion criteria included (a) articles investigating differences of demographic profiles and perioperative outcomes between RaPN and OPN; (b) articles that compare RaPN, OPN, and LPN where data between RaPN and OPN could be extracted; and (c) articles written in English. Exclusion criteria included (a) articles in which radical nephrectomy was performed as a comparator; (b) articles in which single-port or hand-assisted approach was performed; (c) not primary articles such as, review articles, letters, and commentaries; and (d) papers with abstract only. If two or more studies were presented in an overlapping time by the same authors and/or same institution, the study in which the largest number of patients and/or articles provided the more comprehensive information and/or the most recently published study were used.

### 2.3 | Assessment of study quality

The quality of enrolled studies was determined using the Newcastle-Ottawa scale (NOS) (www.ohri.ca/programs/clinical\_epidemiology/ oxford.asp). A NOS score of 5 or less was considered low, 6 to 7 was intermediate, and 8 to 9, high quality. The level of evidence of each study was also rated.

### 2.4 | Data analysis

Two independent authors reviewed the full texts of the included studies. Patient baseline demographics (age, sex, body mass index

### What is already known about this subject?

- Traditional open partial nephrectomy (OPN) has been the standard approach for larger and more complex renal tumors.
- Evolution of minimal invasive techniques led to the adoption of robotic-assisted partial nephrectomy (RaPN).
- Previous observational studies showed that RaPN is also feasible in dealing with large, complex, and hilar renal masses.

### What are the new findings?

- Compared with OPN, RaPN carried the advantage not only of decreased blood loss, less blood transfusion, lower postoperative complication rate, and shorter length of hospital stay but also lower readmission rate and less eGFR decline.
- The superiority of RaPN in estimated blood loss was attenuated with highly complex renal masses (RENAL score > 9).
- The superiority of RaPN in intraoperative complication rate was strengthened with renal hilar control.
- The advantage of RaPN in positive surgical margin was increased in patient with BMI < 28.

## How might these results change the focus of research or clinical practice?

RaPN provided lower perioperative and postoperative complications and a favorable postoperative eGFR impact. Renal parenchyma, a pivotal role on renal function preservation, would be better preserved with robotic technologies. Further prospective randomized clinical studies with adequate follow-up is needed.

[BMI], American Society of Anesthesiologists [ASA] physical status classification, tumor size, baseline renal function, and tumor complexity), perioperative outcomes (operative time, ischemic time, estimate blood loss [EBL], blood transfusion rate, conversion rate, complications, marginal status, and hospital stay), and postoperative outcomes (postoperative renal function, decline in estimated glomerular filtration rate [eGFR], readmission, positive surgical margin [PSM], and tumor recurrence rate) were extracted from each eligible study whenever available.

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FIGURE 1 Flowchart of the selection strategy for the current meta-analysis

Random-effects meta-analysis models were applied with the Comprehensive Meta-Analysis software, version 3 (Biostat, Englewood, New Jersey) for the presumed heterogeneity among the recruited studies.<sup>15</sup> Effect sizes (ESs) of the analyses were investigated by odds ratio (OR) for binary data and Hedges' g for continuous data. The Cochrane Q statistic and  $I^2$  statistic were used for evaluating heterogeneity among studies.<sup>16,17</sup> Funnel plots<sup>18</sup> and Egger's regression analysis<sup>19</sup> were used to assess publication bias. Besides, Duval and Tweedie's trim and fill test was used to adjust the ESs for data with significant publication bias.<sup>20</sup> The one study removal method for detecting outliers was used for sensitivity analyses.<sup>21</sup>

Meta-regression and/or subgroup analysis was used in datasets over five articles to assess for potential sources of heterogeneity among extracted variables including age, sex, BMI, ASA score, tumor size, RENAL nephrometry score,<sup>22</sup> and renal hilar control status. Two-tailed tests were used for all comparisons and a P value of <0.05 was considered statistically significant.

#### 3 | RESULTS

### 3.1 | Study selection

Figure 1 shows the PRISMA flowchart for study selection in this systematic review. At eligibility stage, 48 studies entered the full-text evaluation, and 14 studies were excluded because eligibility criteria were not met. The reasons for exclusion included not formally published articles, duplicated database from our recruited studies, mixed with other surgical methods, not English-written articles, and not clinical trials.

Thirty-four eligible studies<sup>9,23-55</sup> included 60 808 patients who underwent PN, of whom 19 638 underwent RaPN with mean age 58.9 years and 41 170 underwent OPN with mean age 58.5 years. Table 1 presents the baseline patient demographics of all enrolled studies.

### 3.2 | Perioperative outcomes

### 3.2.1 | Main result

There were no differences in ischemic time (Hedges' g = 0.095, 95%confidence intervals (95% CI, -0.058 to 0.248, P = 0.248), intraoperative complication rate (OR = 0.792, 95%Cl, 0.498-1.262, P = 0.327), and percentage of conversion to radical nephrectomy (OR = 1.171, 95% CI, 0.363-3.783, P = 0.792). In comparison with OPN, RaPN associated with decreased EBL (Hedges' g = -0.452, 95% CI, -0.546 to -0.358, P < 0.001, difference in means -104.295 c.c. 95% CI, -128.130 to -80.461) (Figure 2A) and blood transfusion rate (OR = 0.518, 95% CI, 0.427-0.628, P < 0.001) (Figure 2B) but longer operative time (Hedges' g = 0.264, 95% CI, 0.-0.406, P < 0.001, difference in means 14.557 min, 95% CI, 7.943-21.171) (Figure 2C).

### 3.2.2 | Heterogeneity, publication bias, sensitivity test, meta-regression, and subgroup meta-analysis

Significant heterogeneity (Q value = 83.366, df = 27,  $I^2 = 67.613\%$ , P < 0.001) and publication bias (t value = 5.560, df = 26, P < 0.001) were noted in terms of EBL. The trim and fill test still favored RaPN after adjustment by publication bias (Hedges' g = -0.329, 95% CI, -0.420 to -0.238). The sensitive analysis revealed that the results of meta-analysis of EBL would not change after removing any recruited studies. Meta-regression analysis revealed that the Hedges' g on EBL was positively associated with percentage of patients with RENAL score  $\geq$  9 (k = 10, slope = 0.010, P = 0.003), which means difference of EBL between RaPN and OPN attenuated while tumor complexity increasing.

Significant heterogeneity (Q value = 30.326, df = 19,  $I^2$  = 37.348%, P = 0.048) but not publication bias (t value = 0.373, df = 18, P = 0.713) was noted for blood transfusion rate. The sensitive analysis revealed that the results of meta-analysis of blood transfusion rate would not change after removing any recruited studies. Meta-regression analysis

	Study	Study	Study			No. of Patients		Mean Age, Year		Mean BMI		Mean Tumo cm	r Size,	Mean REN Score	AL
Study	Design	Origin	Period	SQ	Щ	RaPN	NdO	RaPN	NGO	RaPN	NAO	RaPN	NGO	RaPN	NGO
Lee, S	Retro	Korean	2003-2010	7	с	69	234	53.48	54.35	25.5	24.49	2.37	2.58	:	:
Stroup, SP	Retro	NS	2003-2011	9	ო	31	153	61	56	27.7	28.9	2.0*	4.2*	8	6.7
Yu, H	Retro	US	2008	9	ო	445	3049	:	:	:	:	:	:	:	:
Ficarra, V	Retro, MP	Multiple	2008-2011	8	с	200	200	62.4	62.4	:	:	2.8*	3.5*	:	:
Alemozaffar, M	Retro	US	2008-2010	80	ო	25	25	55.9	61.9	27.5	30.1	2.5	3.3	6.08	7
Masson-Lecomte, A	Pro	France	2008-2010	8	2	42	58	61.7	60.8	26.9	26.5	2.8	3.1	:	:
Zagar, H <sup>†</sup>	Retro	US	2007-2013	œ	ы	40	85	61.3	61.5	30	31.7	2.5* 4.15*	3.5* 4.3*	6* 9.5*	7* 10*
Vittori, G	Retro	Italy	2010-2011	7	ო	105	198	62.3	63.8	25.7*	26.2*	2.8	3.5	:	:
Webb, CM	Retro	Egypt	2005-2011	7	ო	14	21	60.5	53.6	:	:	2.99	4.22	:	:
Porpiglia, F	Retro	Italy	2009-2012	œ	ო	95	133	57.3	62.3	25.8*	26*	5*	5*	:	:
Takagi, T	Retro	Japan	2012-2014	7	с	100	179	58	57	24	24	2.8	4.2	:	:
Kara, O	Retro	NS	2011-2016	00	с	87	56	58.3	61.1	29*	29.5*	2.8*	3.1*	6*	*6
Mearini, L	Retro	Italy	2006-2015	8	с	31	80	67.6	63	27.8	26.7	3.05	3.54	:	:
Patton, MW	Retro	US	1999-2013	00	ო	60	37	63	65	29*	29*	:	:	:	:
Malkoc E	Retro	US	2011-2015	8	ო	177	90	54.9	55.9	33.4*	34.1*	2.5*	2.8*	7*	7*
Lucas, SM	Retro	NS	2004-2010	7	с	27	54	62.1	57.6	31.4*	29.6*	2.4*	2.3*	*9	*9
Simhan, J	Retro	US	2007-2010	7	ო	91	190	:	:	:	:	:	:	:	:
Laydner, H	Retro	NS	20092010	7	ო	145	133	59	61	30	28	2.6	4	7	Ø
Ghani, KR	Retro	NS	2008-2010	9	ო	9095	25461	57.82	58.33	:	:	:	:	:	:
Luciani, LG	Pro	US	2005-2016	œ	2	110	73	61	63	:	:	3.6	3.6	:	:
Wu, Z	Retro, PS	China	2009-2013	7	ო	51	94	53	52	24.8*	$25.1^{*}$	:	:	:	:
Mano, R	Retro	NS	2011	7	с	63	190	57	59	29.1*	29*	2.6*	°*	:	:
Peyroneet, B	Retro	France	2006-2014	7	ო	937	863	69.6	57.5	26.6	26.5	3.29	3.99	6.8	6.7
Wang, Y	retro, MP	China	2007-2014	00	ო	190	190	61.8	59.8	25.4	24.6	3.8	3.6	8.4	8.2
Pak, J	Retro	NS	2009-2012	9	с	1531	2959	59	60	:	:	:	:	:	:
Malkoc E	Retro	NS	2009-2015	00	с	54	56	61.7	61.5	30.4*	27.9*	7.3*	7.9*	10*	6*
oh, JJ	Retro, PS	Korea	2003-2015	7	ო	317	385	52.13	54.88	24.73	24.55	2.168	2.305	:	:
Lee, C	Retro, PS	Korea	2007-2013	7	с	114	289	52.9	53.3	25.4	25	2.5	2.7	:	:
Klaasen, Z	Retro	US	2006-2012	7	с	35	23	56	62	32.8	28.9	3.6	3.8	7.4	9.0
Tabayoyong, W	Retro	NS	2010-2011	9	ო	4812	5094	:	:	:	:	:	:	:	:
														(Co	intinues)

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	Study	Study	Study			No. of Patients		Mean Age Year		Mean BM	_	Mean Tur cm	nor Size,	Mean REI Score	NAL
Study	Design	Origin	Period	SQ	E	RaPN	NdO	RaPN	NGO	RaPN	NGO	RaPN	NGO	RaPN	NGO
Miyake, H	Retro	Japan	2012-2014	ø	ო	16	15	63.3	64.2	24.9	24.4	ę	3.2	:	÷
Hamilton, ZA	Retro	US	2002-2015	00	e	302	426	67.4	66.8	29.8	30.1	3.4	4.5	7.6	8.7
Tan, J	Retro	Australia	2010-2016	00	ю	145	55	57.68	64.64	27.9*	27.43*	*°	*°	:	÷
Borghesi, M.	Retro	Italy	2011-2015	7	ო	52	52	61*	61*	26*	26*	°*	°*	*9	۶*
Data presented as mea	an if not specific	marked. Abbrev	iations: BMI, bod)	/ mass in	dex; LE, 1	level of evide	snce MP, ma	itch paired; N	Aultiple, mul	tiple countrie	es; PS, proper	isity score ma	atching; Pro, pr	ospective stu	dy; Retro,

(Continued)

TABLE 1

et al divided the participants into simple (RENAL score 4-8) and complex (RENAL score 9-12) groups for comparison. \*data presented as median. †Zagar

retrospective study; SQ, score of quality US, United States

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revealed that the OR on blood transfusion rate is inversely associated with mean female proportion (k = 18, slope = -0.044, P = 0.038), which means the advantage of RaPN increased in female patients.

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Significant heterogeneity (*Q* value = 196.327, *df* = 27,  $l^2 = 86.247\%$ , *P* < 0.001) but not publication bias (*t* value = 1.661, *df* = 26, *P* = 0.109) was noted for operative time. No confounding factors associated with operative time differences were found with meta-regression. The sensitive analysis revealed that the results of meta-analysis of operative time would not change after removing any recruited studies.

Significant heterogeneity (Q value = 30.702, df = 15,  $l^2 = 51.143\%$ , P = 0.010) without publication bias (t value = 0.544, df = 14, P = 0.595) was noted for intraoperative complication rate. However, intraoperative complication rate favored RaPN rather than OPN after removing Lee et al<sup>23</sup> (OR = 0.678, 95% Cl, 0.603-0.762, P < 0.001). Meta-regression analysis revealed that the OR of intraoperative complication rate is inversely associated with renal hilar control rate in RaPN groups (k = 11, slope = -0.025, P = 0.003), which means the advantage of RaPN increased with renal hilar control rate in RaPN group.

### 3.3 | Postoperative outcomes

### 3.3.1 | Main result

Figure 3A to C tabulated the postoperative outcomes of included studies. In comparison with OPN, RaPN was associated with decreased overall postoperative complication rate (OR = 0.578, 95% CI, 0.514-0.649, P < 0.001), decreased readmission rate (OR = 0.660, 95% CI, 0.524-0.832, P < 0.001), and shorter hospital stay (Hedges' g = -0.492, 95% CI, -0.588 to -0.396, P < 0.001, difference in means -1.781 d, 95% CI, -2.221 to -1.341).

### 3.3.2 | Heterogeneity, publication bias, sensitivity test, meta-regression, and subgroup meta-analysis

Nonsignificant heterogeneity (Q value = 29.253, df = 25,  $l^2 = 14.538\%$ , P = 0.253) but significant publication bias (t value = 2.257, df = 24, P = 0.033) was noted for the postoperative complication rate. The trim and fill test still favored RaPN after adjustment by publication bias (OR = 0.617, 95% CI, 0.540-0.705). The sensitivity test revealed that the difference between RaPN and OPN would not change after removal of any single study. No confounding factors associated with PSM rate differences were found with meta-regression. RaPN associated with both decreased major (Clavien classification  $\geq 3$ ; OR = 0.599, 95% CI, 0.435-0.825, P = 0.002) and minor (Clavien classification 1-2; OR = 0.600, 95% CI, 0.498-0.725, P < 0.001) complication rates in subgroup meta-analysis.

Nonsignificant heterogeneity (Q value = 5.061, df = 5,  $l^2$  = 1.210%, P = 0.408) but significant publication bias (*t* value = 3.640, df = 4, P = 0.022) was noted for the readmission rate. The trim and fill test revealed that difference in readmission between groups became into nonsignificant after adjustment to publication bias (OR = 0.661, 95% CI, 0.433-1.007). The sensitivity test revealed same result after

Hedges' g and 95% Cl

Statistics for each study Study name Hedges Lower Upper limit Relative weight p-Value q Borghesi, M. (2018) Ficarra, V. (2014) 3.02 4.97 -0.660 -1.052 -0.268 0.001 -0.528 -0.331 -0.134 0.001 Hamilton, Z.A. (2018) Lucas, S.M. (2012) -0.248 -0.798 -0.396 0.001 5.49 2.43 -0.100 -0.324 -0.099 -0.496 -0.394 -0.791 0.196 3.91 3.91 Luciani, L.G. (2017) 0 509 Malkoc, E. (2017) BJUI 0.001 Malkoc, E. (2017) WJU -0.282 -0.483 -0.655 -0.770 0.091 0.139 3.18 3.99 Mano, R. (2015) Mearini, L. (2016) Oh, J.J. (2016) -0.711 -1.133 -0.358 2.78 5.48 -0.288 0.001 -0.060 0.006 Patton, M.W. (2016) Peyronnet, B. (2016) -0.846 -0.248 -0.077 0.019 3.08 5.98 -0.461 -0.155 Porpiglia, F. (2016) Simhan, J. (2012) RENAL7-9 -0.348 -0.467 -0.612 -0.744 -0.083 -0.189 0.010 4.23 4.09 Stroup, S.P. (2012) Tan, J.L. (2017) -0.656 -1.046 -0.942 -0.266 -0.311 0.001 3.03 3.71 Wang, Y. (2017) Wu, Z. (2014) EBL -0.340 -0.581 -0.542 -0.137 -0.236 0.001 4.91 3.42 Zargar, H. (2014) RENAL 4-8 Zargar, H. (2014) RENAL 9-12 -0.954 -1.184 2.30 1.49 -0.459 0.035 0.069 -0.510 0.138 0.164 Alemozaffar, M. (2013) Kara, O. (2016) -0.508 -1.063 0.047 0.073 1.98 3.42 Klaassen, Z. (2014) Lee, S. (2011) 0.005 2.06 4.19 -0.774 -1.312 -0.236 0.072 -0.196 0.340 Masson-Lecomte, A. (2013) Miyake, H. (2015) -0.853 -1.265 -0.442 0.000 2.87 Takagi, T. (2016) -0.681 -0.568 -0.932 -0.809 -0.431 0.000 4.38 4.49 Minervini, A. (2014) -0.328 Overall -0.452 -0.546 -0.358 0.000 100.00



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Study name		Statist	ics for each	study
	Odds	Lower	Upper	
	ratio	limit	limit	p-Value
Borghesi, M. (2018)	0.447	0.141	1.413	0.170
Ficarra, V. (2014)	1.056	0.553	2.015	0.869
Ghani, K.R. (2014)	0.518	0.470	0.570	0.000
Hamilton, Z.A. (2018)	0.848	0.455	1.579	0.603
Kara, O. (2016)	0.427	0.128	1.418	0.165
Klaassen, Z. (2014)	0.211	0.008	5.415	0.348
Lee, S. (2011)	0.921	0.250	3.401	0.902
Luciani, L.G. (2017)	0.396	0.172	0.911	0.029
Malkoc, E. (2017) BJUI	0.103	0.020	0.525	0.006
Malkoc, E. (2017) WJU	0.234	0.079	0.691	0.009
Mano, R. (2015)	0.112	0.007	1.927	0.132
Masson-Lecomte, A. (2013)	0.675	0.118	3.869	0.659
Pak, J.S. (2017)	0.419	0.331	0.530	0.000
Patton, M.W. (2016)	0.160	0.060	0.429	0.000
Peyronnet, B. (2016)	0.598	0.440	0.814	0.001
Minervini, A. (2014)	0.334	0.111	1.000	0.050
Wang, Y. (2017)	0.686	0.318	1.479	0.336
Wu, Z. (2014)	1.406	0.302	6.542	0.664
Zargar, H. (2014) RENAL 4-8	1.400	0.379	5.168	0.614
Zargar, H. (2014) RENAL 9-12	0.249	0.013	4.670	0.353
Overall	0.518	0.427	0.628	0.000



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-1.00 0.00

Odds ratio and 95% CI

1.00

Better by OPN

2.00

-2.00

Better by RaPN

### (B) Blood transfusion rate

(C) Operative time

Study name		Stat	istics for eac	h study	
	Hedges' g	Lower limit	Upper limit	p-Value	Relative weight
Alemozaffar, M. (2013)	-0.071	-0.617	0.475	0.799	2.74
Borghesi, M. (2018)	0.660	0.268	1.052	0.001	3.41
Ficarra, V. (2014)	-0.131	-0.327	0.065	0.190	4.22
Kara, O. (2016)	-0.340	-0.676	-0.004	0.047	3.65
Klaassen, Z. (2014)	1.709	1.104	2.314	0.000	2.51
Lee, C. (2016)	0.189	-0.028	0.406	0.088	4.15
Lee, S. (2011)	0.884	0.607	1.161	0.000	3.91
Lucas, S.M. (2012)	0.616	0.149	1.084	0.010	3.07
Luciani, L.G. (2017)	0.598	0.297	0.899	0.000	3.81
Malkoc, E. (2017) BJUI	-0.387	-0.681	-0.093	0.010	3.84
Malkoc, E. (2017) WJU	0.036	-0.335	0.407	0.850	3.50
Mano, R. (2015)	0.359	0.073	0.644	0.014	3.87
Masson-Lecomte, A. (2013)	0.142	-0.253	0.536	0.481	3.39
Mearini, L. (2016)	-0.500	-0.917	-0.083	0.019	3.29
Minervini, A. (2014)	0.937	0.690	1.185	0.000	4.03
Miyake, H. (2015)	0.968	0.241	1.696	0.009	2.09
Oh, J.J. (2016)	-0.022	-0.170	0.127	0.772	4.37
Patton, M.W. (2016)	0.654	0.265	1.043	0.001	3.42
Peyronnet, B. (2016)	0.110	0.017	0.202	0.020	4.50
Porpiglia, F. (2016)	0.419	0.153	0.684	0.002	3.96
Simhan, J. (2012) RENAL7-9	0.363	0.087	0.640	0.010	3.91
Stroup, S.P. (2012)	0.402	0.015	0.788	0.042	3.43
Takagi, T. (2016)	-0.071	-0.315	0.173	0.567	4.04
Tan, J.L. (2017)	0.210	-0.099	0.520	0.183	3.77
Wang, Y. (2017)	-0.165	-0.366	0.036	0.108	4.21
Wu, Z. (2014)	0.581	0.236	0.927	0.001	3.61
Zargar, H. (2014) RENAL 4-8	-0.176	-0.665	0.313	0.480	2.98
Zargar, H. (2014) RENAL 9-12	0.110	-0.559	0.778	0.748	2.28
Overall	0.264	0.121	0.406	0.000	100.00

--2.00 2.00 -1.00 0.00 1.00 Better by RaPN Better by OPN

Hedges' g and 95% Cl







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Odds ratio and 95% CI

|--|

Study name		Stat	tistics for ea	ch study			Odd	Is ratio and 95
	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight			
Borghesi, M. (2018)	0.311	0.092	1.050	0.060	0.90			
Ficarra, V. (2014)	0.594	0.352	1.003	0.051	4.39			
Ghani, K.R. (2014)	0.644	0.609	0.681	0.000	33.17			
Hamilton, Z.A. (2018)	0.766	0.520	1.127	0.176	7.28			-
Kara, O. (2016)	0.470	0.221	0.998	0.049	2.25		-	
Klaassen, Z. (2014)	0.381	0.104	1.395	0.145	0.79			
Lee, S. (2011)	0.524	0.211	1.301	0.164	1.58			-
Lucas, S.M. (2012)	1.168	0.310	4.397	0.819	0.76			_
Luciani, L.G. (2017)	0.595	0.318	1.114	0.105	3.17			
Malkoc, E. (2017) BJUI	0.406	0.206	0.798	0.009	2.75		-	-
Malkoc, E. (2017) WJU	0.568	0.231	1.396	0.218	1.61			-
Mano, R. (2015)	0.447	0.149	1.340	0.151	1.10			
Masson-Lecomte, A. (2013)	0.658	0.184	2.348	0.519	0.82			-
Minervini, A. (2014)	0.225	0.092	0.549	0.001	1.64			H
Miyake, H. (2015)	0.267	0.025	2.902	0.278	0.24	-	-	
Oh, J.J. (2016)	0.428	0.232	0.791	0.007	3.30		-	-
Patton, M.W. (2016)	0.300	0.110	0.816	0.018	1.31		_	-
Peyronnet, B. (2016)	0.545	0.436	0.681	0.000	15.58			
Porpiglia, F. (2016)	0.440	0.188	1.031	0.059	1.79			
Stroup, S.P. (2012)	0.691	0.223	2.139	0.522	1.04			_
Takagi, T. (2016)	0.792	0.458	1.370	0.405	4.03			
Tan, J.L. (2017)	0.313	0.138	0.710	0.005	1.92			-
Wang, Y. (2017)	0.460	0.279	0.759	0.002	4.73			
Wu, Z. (2014)	1.550	0.682	3.518	0.295	1.92			
Zargar, H. (2014) RENAL 4-8	0.455	0.161	1.285	0.137	1.23		_	-
Zargar, H. (2014) RENAL 9-12	1.067	0.268	4.253	0.927	0.70			-
Overall	0.578	0.514	0.649	0.000	100.00			•
(A) Postonerative co	mnlicat	tion rate	P			0.01 Better b	0.1	1

### (A) Postoperative complication rate

Study name		Statis	tics for each	study	
	Odds	Lower	Upper		Relative
	ratio	limit	limit	p-Value	weight
Alemozaffar, M. (2013)	0.638	0.097	4.188	0.639	1.51
Kara, O. (2016)	0.240	0.045	1.283	0.095	1.90
Malkoc, E. (2017) BJUI	0.426	0.142	1.282	0.129	4.36
Malkoc, E. (2017) WJU	0.071	0.004	1.298	0.074	0.64
Mano, R. (2015)	0.412	0.091	1.866	0.250	2.34
Pak, J.S. (2017)	0.709	0.575	0.875	0.001	89.27
Overall	0.660	0.524	0.832	0.000	100.00



10 100 Better by OPN

(B) Re-admission rate

Study name		Statist	ics for each	study			Hedges	g and 95%	CI	
	Hedges'	Lower limit	Upper limit	p-Value	Relative weight					
Alemozaffar, M. (2013)	-1.628	-2.260	-0.996	0.000	1.65	<del>(                                      </del>	-	1		1
Klaassen, Z. (2014)	-0.096	-0.615	0.424	0.718	2.16		_			
Lee, C. (2016)	-0.439	-0.658	-0.221	0.000	4.51					
Lee, S. (2011)	-0.930	-1.208	-0.652	0.000	3.94		_			
Masson-Lecomte, A. (2013)	-1.078	-1.499	-0.656	0.000	2.75	-	_			
Miyake, H. (2015)	-0.730	-1.440	-0.021	0.044	1.39					
Takagi, T. (2016)	-0.259	-0.504	-0.014	0.038	4.25		-			
Yu, H.Y. (2012)	-0.265	-0.365	-0.166	0.000	5.54					
Borghesi, M. (2018)	-0.428	-0.814	-0.042	0.030	3.01		_			
Ficarra, V. (2014)	-0.246	-0.443	-0.050	0.014	4.72					
Hamilton, Z.A. (2018)	-0.248	-0.396	-0.100	0.001	5.17			-		
Kara, O. (2016)	-0.573	-0.913	-0.232	0.001	3.38			-		
Laydner, H. (2013)	-0.473	-0.711	-0.235	0.000	4.32		-	H I		
Lucas, S.M. (2012)	-0.616	-1.084	-0.149	0.010	2.45			_		
Luciani, L.G. (2017)	-0.598	-0.899	-0.297	0.000	3.73			-		
Malkoc, E. (2017) BJUI	-0.387	-0.681	-0.093	0.010	3.79		_	-		
Malkoc, E. (2017) WJU	-0.641	-1.021	-0.260	0.001	3.05			_		
Mano, R. (2015)	-0.483	-0.770	-0.195	0.001	3.85		_	H		
Mearini, L. (2016)	-0.350	-0.764	0.065	0.098	2.80		_			
Minervini, A. (2014)	-0.246	-0.483	-0.009	0.042	4.33					
Patton, M.W. (2016)	-0.654	-1.043	-0.265	0.001	2.99			-		
Peyronnet, B. (2016)	-0.155	-0.248	-0.063	0.001	5.58					
Simhan, J. (2012) RENAL 10-12	-1.175	-1.872	-0.478	0.001	1.43					
Simhan, J. (2012) RENAL7-9	-0.467	-0.744	-0.189	0.001	3.94		_			
Tan, J.L. (2017)	-0.627	-0.942	-0.311	0.000	3.60			-		
Wang, Y. (2017)	-0.340	-0.542	-0.137	0.001	4.67			-		
Wu, Z. (2014)	-0.465	-0.809	-0.122	0.008	3.35					
Zargar, H. (2014) RENAL 4-8	-0.861	-1.372	-0.350	0.001	2.20		-	-		
Zargar, H. (2014) RENAL 9-12	-1.180	-1.880	-0.480	0.001	1.42					
Overall	-0.492	-0.588	-0.396	0.000	100.00		•	•		
NUMBER OF STREET						-2.00	-1.00	0.00	1.00	2.00

#### (C) Length of hospital stay

Study name		Statis	tics for each	study	
	Hedges' g	Lower limit	Upper limit	p-Value	Relative weight
Ficarra, V. (2014)	-0.010	-0.205	0.186	0.923	17.56
Hamilton, Z.A. (2018)	-0.069	-0.216	0.079	0.362	30.96
Lee, S. (2011)	0.026	-0.242	0.294	0.850	9.37
Mearini, L. (2016)	-0.310	-0.724	0.104	0.142	3.92
Miyake, H. (2015)	0.057	-0.629	0.743	0.870	1.43
Patton, M.W. (2016)	-0.374	-0.758	0.009	0.055	4.58
Porpiglia, F. (2016)	-0.209	-0.472	0.054	0.120	9.71
Wang, Y. (2017)	-0.169	-0.370	0.032	0.100	16.63
Wu, Z. (2014)	-0.057	-0.396	0.283	0.744	5.84
Overall	-0.101	-0.183	-0.019	0.016	100.00

Hedges' g and 95% CI

Better by OPN



FIGURE 3 Forest plots of significantly different postoperative and functional outcomes for robotic-assisted partial nephrectomy versus open partial nephrectomy

### (D) eGFR change

Better by RaPN

Better by RaPN

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Significant heterogeneity (Q value = 101.336, *df* = 28,  $I^2 = 72.369\%$ , P < 0.001) and publication bias (*t* value = 6.543, *df* = 27, P < 0.001) were noted for the hospital stay. The trim and fill test revealed unchanged result after adjustment for publication bias (Hedges' *g* = -0.343, 95% CI, -0.443 to -0.244). The difference between RaPN and OPN would not change after removal of any single study. No confounding factors associated with length of hospital stay differences were found with meta-regression.

### 3.4 | Oncological outcomes

### 3.4.1 | Main result

There was no significant difference between RaPN and OPN in PSM (OR = 0.926, 95% Cl, 0.657-1.304, P = 0.660) and tumor recurrence rates (OR = 0.328, 95% Cl, 0.078-1.381, P = 0.129).

### 3.4.2 | Heterogeneity, publication bias, sensitivity test, meta-regression, and subgroup meta-analysis

Significant heterogeneity (Q value = 45.977, df = 24,  $l^2 = 47.800\%$ , P = 0.004) and publication bias (t value = 2.921, df = 23, P = 0.008) were noted for PSM. The trim and fill test revealed similar result after adjustment for publication bias (OR = 0.943, 95% CI, 0.673-1.322). The sensitivity test revealed same result after removal of any single studies. Subgroup analysis revealed that the PSM favored RaPN group when patient BMI was less than 28 (OR = 0.663, 95% CI, 0.488-0.900, P = 0.008).

Significant heterogeneity (Q value = 9.070, df = 3,  $l^2 = 66.925\%$ , P = 0.028) but not publication bias (t value = 0.849, df = 2, P = 0.485) was noted for tumor recurrence rates. However, via sensitivity test, the tumor recurrence rates favored RaPN rather than OPN after removing Malkoc et al<sup>47</sup> (OR = 0.213, 95% CI, 0.051-0.884, P = 0.033).

### 3.5 | Functional outcomes

### 3.5.1 | Main result

RaPN group had decreased eGFR change (Hedges' g = -0.101, 95% Cl, -0.183 to -0.019, P = 0.016; difference in means: -0.522, 95% Cl, -1.270 to 0.226) (Figure 3D).

### 3.5.2 | Heterogeneity, publication bias, sensitivity test, meta-regression, and subgroup meta-analysis

Nonsignificant heterogeneity (Q value = 6.174, df = 8,  $l^2 < 0.001\%$ , P = 0.628) and publication bias (t value = 0.878, df = 7, P = 0.409) were noted for eGFR change. The difference in eGFR change turned out to be nonsignificant after removal of the dataset by Wang et al<sup>45</sup> (Hedges' g = -0.087, 95% CI, -0.177 to 0.003, P = 0.057). No confounding factors associated with eGFR change differences were found with meta-regression.

### 4 | DISCUSSION

Utilization of robotic technique for renal masses has rapid increased over time; the role of RaPN versus standard OPN is still debated.<sup>9</sup> The present meta-analysis of a large-pooled sample revealed that RaPN had decreased blood loss, blood transfusion, postoperative complication rate, and length of stay (LOS) when compared with OPN. No difference was noted with ischemic time, conversion rate, PSM, and recurrence rate. RaPN had decreased readmission rate and a favorable postoperative eGFR impact.

Wu et al,<sup>13</sup> Shen et al,<sup>56</sup> and Xia et al<sup>57</sup> previously conducted metaanalyses on this topic. Wu et al<sup>13</sup> pooled 8 studies with 3418 patients, Shen et al<sup>56</sup> pooled 16 studies with 3024 patients, and Xia et al<sup>57</sup> pooled 19 studies with 3551 patients. In our present study, we pooled 34 articles with 60 808 patients and for presumed heterogeneity between studies, random-effect model was applied for our analyses. Meta-regression analyses and sensitivity tests were used to clarify the impact of possible confounding factors for heterogeneity and the outliers of studies to achieve updated and comprehensive analyses.

Decreased EBL was found in RaPN group rather than OPN in the present meta-analysis, consistent with prior literatures.<sup>56,57</sup> With wide application of robotic platform, RaPN even had a decreased EBL for complex renal masses such as endophytic and hilar ones.<sup>34,52</sup> However, our meta-regression analysis revealed that when tumor complexity highly increased (RENAL score  $\geq$  9), the advantage of RaPN in terms of EBL was significant reduced, confirming results for renal mass over 7 cm was reported by Malkoc et al.<sup>47</sup> Accordingly, RaPN associated with lower blood transfusion rate. The superiority of RaPN was strengthened in female patients in meta-regression analysis. Our finding supported that RaPN may reduce overtransfusion in women secondary to liberal transfusion strategy and nonsex specific transfusion threshold.<sup>58</sup>

Decreased postoperative complications was found in RaPN group when compared with OPN in our pooled analysis. Both major (Clavien  $\geq$ 3, *P* = 0.006) and minor (Clavien 1-2, *P* < 0.001) postoperative complications were both reduced in RaPN. Vittori et al reported that RaPN associated with decreased overall postoperative complications<sup>30</sup> (*P* = 0.009). They also demonstrated that OPN was the only independent factor associated with Clavien 3 to 4 surgical complications, compatible with our findings.

Although intraoperative complication rate was similar between RaPN and OPN groups in our pooled analysis, RaPN would have a decreased intraoperative complication rate if we removed Lee's study,<sup>23</sup> Lee's study enrolled patients in 2003 to 2010, which involved the period of initial application of robotic technique, and thus underestimated the superiority of contemporary RaPN. Recent epidemiological data had found decreased intraoperative complications of RaPN compared with OPN (OR = 0.69, 95% CI, 0.52-0.93, P = 0.014).<sup>9</sup> Further meta-regression analysis revealed that the advantage of RaPN increased with renal hilar control. Compared with hilar control, off-clamp RaPN associated with higher blood loss, possible leading to compromised visualization of surgical filed and intraoperative complications.<sup>59</sup>

Renal function preservation after PN is confounded by complex perioperative variables, including ischemic time, remaining renal Wile

parenchymal, surgical technique, blood loss, and contralateral renal function. Ischemic time is frequently used as a surrogate of renal function however ischemic time showed no difference between RaPN and OPN in our analysis. Interestingly, we found that RaPN group had minor postoperative eGFR decline compared with OPN. It could be deduced that RaPN is favorable in renal function preservation due to factors other than renal pedicle control. Takagi et al revealed that RaPN tended to preserve more normal parenchyma than OPN<sup>33</sup> (84% versus 79%, P = 0.0504). RaPN also provided narrower peritumoral surgical margin than OPN due to improved vision with 3D capabilities.<sup>48</sup> These evidences suggested that renal parenchyma, a pivotal role on renal function preservation, would be better preserved with robotic technologies. However, it was not possible to perform a pooled analysis of parenchyma preservation as a confounding factor of renal function due to limited study numbers.

PSM, as an indicator of local oncological control, remains a controversial surrogate for long-term recurrence and metastasis.<sup>60,61</sup> Pooled analysis for long-term oncological comparison is not available. Our present study found no significant difference with PSM between RaPN and OPN. In subgroup analysis, we found that in patients with BMI < 28, RaPN associated with a decreased PSM rate. Malkoc et al reported no significant PSM difference in obese patients who underwent RaPN compared with OPN<sup>40</sup> (4% versus 3.4%, P = 0.82). Others revealed no difference in PSM in obese patients undergoing RaPN compared with nonobese ones<sup>62</sup> (3.5% versus 2.8%, P = 0.383). PSM of PN is rare, without collating large series together, the difference is likely diluted. Our analysis supported that abundance of perirenal fat in obese patients may hinder renal tumor dissection with RaPN. Incidence of tumor recurrence was very rare in our analysis, and the result may be interfered easily with few extreme outliers. It could explain the result of tumor recurrence rate turns to favoring RaPN after removal of the study with only three recurrence patients.47

The only advantage of OPN that we found was less operative time. Masson-Lecomte et al, however, revealed that the difference in operative time was insignificant between RaPN and OPN after excluding robotic setup and docking times.<sup>28</sup> Recent studies have found shorter operative times in RaPN patients compared with OPN patients with experienced surgical teams.<sup>35,37</sup> Additionally, studies found that OPN was less expensive, especially when accounting for operating room costs.<sup>39,45</sup> Our meta-analysis with limited study numbers and inconsistent accounting methods was unable to study cost-effectiveness. Further prospective and large scale cost-effective studies should be undertaken to compare these two techniques.

### 4.1 | Limitation

Our analysis has a number of limitations. First, the majority of studies were retrospective, nonrandomized comparisons, except two prospectively derived studies. Second, there was significant variation for EBL, transfusion rate, intraoperative complications, operative time, PSM, recurrence rates, and hospital stay. Although conducting metaregression and subgroup analyses to identify confounding factors and outlier studies for heterogeneities, other factors such size of series, surgeon experience, varied approaches of renal hilar control, and varied methods for measuring clinical variables still contribute to the study heterogeneity. Third, there was publication bias in regard with EBL, postoperative complication rate, hospital stay, PSM, and readmission rates. Trim and fill test only revealed significant change on readmission rate; readmission rate was strongly influenced by publication bias. Finally, most studies reported insufficient and varied follow-up period, and thus our pooled analyses evaluating long-term oncologic and functional outcomes were limited.

### 5 | CONCLUSION

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This meta-analysis showed that compared with OPN, RaPN is associated with decreased blood loss, blood transfusion and complication rates, longer operative time, shorter hospital stay, lower readmission rate, and minor eGFR change. Some advantages of RaPN was strengthen in nonobese patients and/or with renal hilar control but attenuated in patients with highly complex renal tumor. However, these results should be applied with caution in clinical practice due to suboptimal quality of evidence and study heterogeneity. Further prospective randomized clinical studies with adequate follow-up is needed not only to validate our results but also to establish robust safety and efficacy evidence of robotic renal surgery.

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### CONFLICTS OF INTEREST

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