

Original Article

Robot-assisted versus laparoscopic partial nephrectomy for localized renal tumors: a meta-analysis

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Abstract: Background: Robot-assisted partial nephrectomy (RAPN) is being performed more frequently for the minimally invasive management of localized renal tumors. However, it's unclear whether RAPN is more efficacious than the standard laparoscopic partial nephrectomy (LPN). The objective of this meta-analysis is to compare RAPN and LPN in terms of perioperative and oncologic outcomes for the treatment of localized renal tumors. Methods: A systematic search of electronic databases including MEDLINE, EMBASE and OVID was conducted. Comparative studies comparing RAPN and LPN for the treatment of localized renal tumors were regarded eligible. The mean difference (MD), odds ratio (OR) and their corresponding 95% confidence intervals (CI) were calculated for each outcome. The methodologic quality of the included studies was evaluated using the strict criteria of the Newcastle-Ottawa scale. Results: 14 comparative studies (n = 1539 participants) were included in the present meta-analysis. Operative time was similar for RAPN and LPN (MD = 6.33, 95% CI [-23.93, 36.59]), however, warm ischemia time favored RAPN (MD = -3.29, 95% CI [-6.47, -0.10]). There was no significant difference in estimated blood loss (EBL) (MD = -42.24, 95% CI [-87.10, 2.61]) and length of stay (LOS) (MD = -0.29, 95% CI [-0.89, 0.32]). The incidence of intraoperative complications was similar for RAPN and LPN (OR = 0.68, 95% CI [0.29, 1.58]), as well as incidence of postoperative minor complications (OR = 1.10, 95% CI [0.80, 1.51]) and postoperative major complications distributions by Clavien classification (OR = 0.99, 95% CI [0.61, 1.61]). In addition, no significant difference was found in terms of positive surgical margin rate (OR = 1.12, 95% CI [0.56, 2.25]). Conclusions: RAPN had similar operative time, LOS, EBL, and perioperative complications compared with LPN, as well as positive margin rates. RAPN appears to offer the advantage of decreased WIT compared with LPN. Studies with long-term follow up are needed to compare RAPN and LPN in terms of long-term complications and oncologic outcomes.

Keywords: Laparoscopic partial nephrectomy, meta-analysis, nephron-sparing surgery, robot-assisted partial nephrectomy

Introduction

The laparoscopic approach to nephron sparing surgery (NSS) was introduced to decrease the morbidity associated with traditional open surgery [1-3]. With the advances of laparoscopic surgery, LPN has become a technically feasible procedure. However, technical difficulty including intra-corporeal suturing and dissection is the largest obstacle to the widespread use of LPN [4]. Robotic minimally invasive surgery has several advantages, including three-dimensional imaging, tremor filtration, and augmented dexterity, allowing more precision in a smaller operative field and easier resection and repair [5-10]. In the last decade, some observational

studies comparing RAPN and LPN for treating localized renal tumors were published. However, their results were inconsistent. As a result, it's unclear whether RAPN is more efficacious than LPN. The objective of this meta-analysis is to compare RAPN and LPN in terms of perioperative and oncologic outcomes for the treatment of localized renal tumors.

Materials and methods

Data sources and searches

The meta-analysis was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIS-

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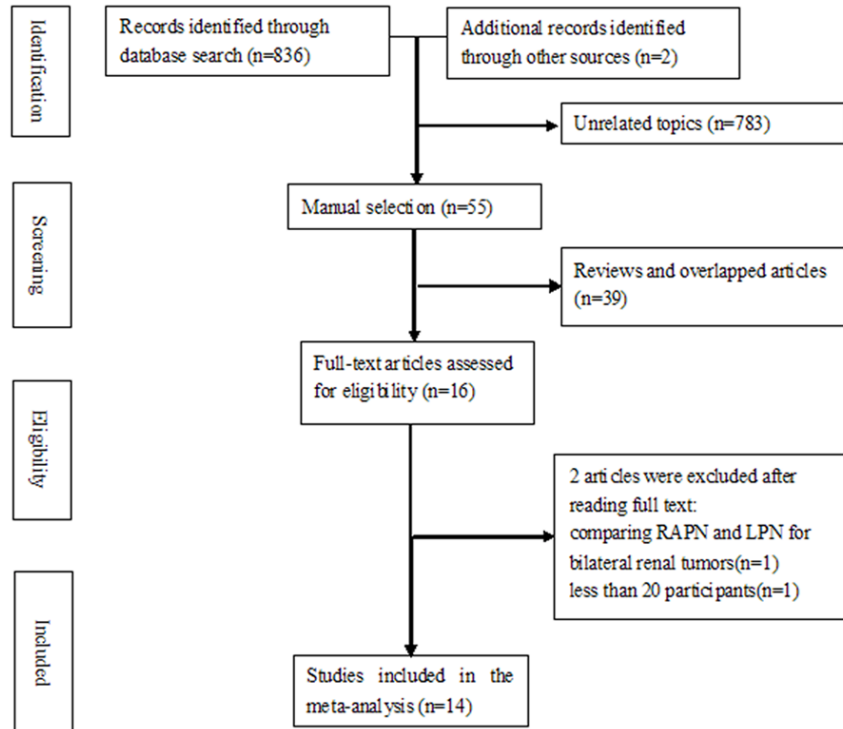


Figure 1. Flow diagram of screened, excluded, and analyzed publications.

MA) [11]. A literature search was carried out using MEDLINE, EMBASE and OVID to identify all articles published between January 1966 and January 2014 which compared RAPN and LPN in terms of perioperative outcomes and complications for the treatment of localized renal tumors. There were no restriction of origin and languages. We utilized the search terms “robotic”, “laparoscopic”, “partial nephrectomy”, “nephron-sparing surgery”, and “renal”, and we used both free text and MeSH searches for keywords. The reference list of each comparative study and previous reviews were manually examined to find additional relevant studies.

Study selection

Two reviewers independently selected eligible trials. Disagreement between the two reviewers was settled by discussing with the third reviewer. Inclusion criteria: comparative studies comparing RAPN and LPN for the treatment of localized renal tumors; studies with greater than 20 patients; patient age older than 16 years. Exclusion criteria: RAPN and LPN for the treatment of bilateral synchronous renal tumors; letters; single case reports; reviews;

and studies containing previously published data.

Data extraction and quality assessment

The following data was collected by two reviewers independently using a purpose-designed form: name of first author, publishing time, journal, study design, number of patients, baseline data, warm ischemia time (WIT), operative time, length of stay (LOS), estimated blood loss (EBL), incidence of intraoperative complications, incidence of postoperative minor complications (Clavien 1 and 2), incidence of postoperative major complications

(Clavien ≥ 3). We used Newcastle-Ottawa scale to assess the methodologic quality of each study. Two reviewers who were blinded regarding the source institution, the journal, and the authors for each included publication independently assess the methodologic quality. Disagreement between the two reviewers was settled by discussing with the third reviewer.

Data synthesis and analysis

All the data analysis was carried out using professional meta-analysis software Review Manager (V5.1.0). Outcomes are baseline parameters including age, sex, body mass index (BMI), American Society of Anesthesiologist (ASA), tumor size, laterality; WIT; operative time; LOS; EBL; incidence of intraoperative complications, incidence of postoperative minor complications (Clavien 1 and 2); incidence of postoperative major complications (Clavien ≥ 3); positive surgical margin rate. The mean difference (MD), pooled odds ratio (OR) and their 95% confidence intervals (CI) were calculated for each outcome. I^2 test was used to analyze heterogeneity of trials. Heterogeneity was interpreted as absent (I^2 : 0%-25%), low (I^2 : 25.1%-50%), moderate (I^2 : 50.1%-75%), or high

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Table 1. Characteristics of participants in included studies. Data are presented as mean (SD)/(range)

Author and year	Group	No of participants	Age, yr	No. male (%)	BMI, kg/m ²	ASA	Tumor size, cm	No. Left (%)	No. Right (%)	NOS score
Ellison JS 2012	RAPN	108	59.4 (12.1)	66 (61)	30.9 (6.5)	NR	2.9 (1.6)	56 (52)	52 (48)	9
	LPN	108	55.9 (10.6)	62 (57)	29.3 (6.1)	NR	2.7 (1.4)	51 (47)	57 (53)	
Long JA 2012	RAPN	199	58.5 (11.5)	119 (59.8)	30.7 (7.2)	NR	3.8 (1.8)	110 (55.3)	89 (44.7)	7
	LPN	182	59.5 (13.0)	112 (61.5)	29.2 (5.3)	NR	4.0 (1.7)	96 (52.7)	86 (47.3)	
Williams SB 2011	RAPN	27	55.7 (11.2)	17 (63)	27.2 (3.74)	2.2 (0.42)	2.47 (1.18)	14 (52)	13 (48)	9
	LPN	59	54.6 (11.7)	41 (70)	28.9 (3.92)	2.16 (0.37)	3.08 (2.17)	31 (53)	28 (47)	
Pierorazio PM 2011	RAPN	48	62 (27-77)	27 (56.3)	28.2 (17.8-40.5)	NR	2.0 (0.9-6.0)	26 (54.2)	22 (45.8)	7
	LPN	102	56 (25-81)	63 (61.8)	30.3 (18.7-46.5)	NR	2.2 (0.5-7.7)	47 (46.1)	55 (53.9)	
Seo IY 2011	RAPN	13	54.2 (12.4)	10 (76.9)	23.8 (2.3)	NR	2.7 (1.2)	4 (30.8)	9 (69.2)	5
	LPN	14	53.9 (11.6)	8 (57.1)	24.6 (2.7)	NR	2.0 (1.2)	10 (71.4)	4 (28.6)	
Cho CL 2011	RAPN	10	63 (36-78)	8 (80)	NR	2.0	2.7 (1.7-5.0)	7 (70)	3 (30)	5
	LPN	10	56 (31-79)	5 (50)	NR	1.8	2.8 (1.2-5.0)	5 (50)	5 (50)	
Haber GP 2010	RAPN	75	62.6	44 (58.7)	30.1	2.4	2.8	39 (52)	36 (48)	9
	LPN	75	60.0	40 (53.3)	29.7	2.4	2.5	32 (42.7)	43 (57.3)	
DeLong JM 2010	RAPN	13	59.7	8 (61.5)	28.9	2.3	2.6	6 (46.2)	7 (53.8)	5
	LPN	15	53.6	8 (53.3)	26.6	2.3	2.8	7 (46.7)	8 (52.3)	
Wang AJ 2009	RAPN	40	61.0	NR	29.7	2.3	2.5	23 (57.5)	17 (42.5)	9
	LPN	62	58.0	NR	29.2	2.4	2.4	33 (53.2)	29 (46.8)	
Benway BM 2009	RAPN	129	59.2	NR	29.8	NR	2.9	NR	NR	9
	LPN	118	59.2	NR	28.5	NR	2.6	NR	NR	
Kural AR 2009	RAPN	11	50.8 (13.2)	8 (72.7)	26.7 (3.8)	1.54 (0.52)	3.2 (2.0-4.1)	8 (73)	3 (27)	7
	LPN	20	58.9 (15.4)	14 (70.0)	27.8 (2.9)	1.64 (0.63)	3.2 (1.5-7.0)	12 (60)	8 (40)	
Jeong W 2009	RAPN	31	53.4	15 (48.4)	24.1	NR	3.4	NR	NR	7
	LPN	26	58.7	13 (50)	24.8	NR	2.4	NR	NR	
Aron M 2008	RAPN	12	64.0 (13.8)	8 (66.7)	29 (6.4)	2 (1-3)	2.4 (0.7)	5 (41.7)	7 (58.3)	9
	LPN	12	61.0 (13.8)	8 (66.7)	30 (6.4)	2 (1-3)	2.9 (0.7)	5 (41.7)	7 (58.3)	
Caruso RP 2006	RAPN	10	58.0	NR	28.1	NR	2.0	NR	NR	7
	LPN	10	61.0	NR	28.5	NR	2.2	NR	NR	

ASA = American Society of Anesthesiologist; BMI = body mass index; LPN = laparoscopic partial nephrectomy; NOS = Newcastle-Ottawa scale; NR = not reported; RAPN = robot-assisted partial nephrectomy.

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Table 2. Meta-analysis of baseline parameters

Outcomes	Odds Ratio [95% CI] or Mean Difference [95% CI]	Heterogeneity
Age	1.88 [1.74, 2.02]	$I^2 = 99\%$
Sex	1.04 [0.82, 1.32]	$I^2 = 0\%$
BMI	0.10 [-0.75, 0.95]	$I^2 = 96\%$
ASA	-0.01 [-0.10, 0.08]	$I^2 = 0\%$
Tumor size	0.06 [-0.14, 0.25]	$I^2 = 85\%$
Laterality	1.16 [0.93, 1.46]	$I^2 = 0\%$

ASA = American Society of Anesthesiologist; BMI = body mass index; CI = confidence intervals.

(I^2 : 75.1%-100%) [12]. In the absence of a statistically significant heterogeneity (I^2 : 0%-25%), Mantel-Haenszel fixed model was used; otherwise, Mantel-Haenszel random model was performed. Sensitivity analysis were carried out by study design and tumor characteristics.

Results

Characteristics of studies included in the meta-analysis

Figure 1 shows the flow diagram for study inclusion. A total of 838 citations were identified during the initial search. On the basis of the title and abstract, we identified 16 papers. After reading the full manuscripts, two studies were excluded for reasons described in **Figure 1**. At last, 14 studies [13-26] published between 2006 and 2012 were included in the meta-analysis, involving 1539 participants, 704 participants in the robotic group and 835 participants in the laparoscopic group. All of the included studies were observational studies. Baseline data and NOS scores are shown in **Table 1**.

Results of the meta-analysis

Baseline parameters

There was no significant difference between the two groups for any of baseline parameters except for age (MD = 1.88, 95% CI [1.74, 2.02]) (shown in **Table 2**).

Operative time

There were nine studies investigating operative time. This result was influenced by heterogeneity ($I^2 = 97\%$), and so the meta-analysis was performed using a random model. Meta analysis results (**Figure 2**) showed that there was no sig-

nificant difference in operative time (MD = 6.33, 95% CI [-23.93, 36.59]).

Warm ischemia time

There were nine studies investigating warm ischemia time. This result was influenced by heterogeneity ($I^2 = 82\%$), and so the meta-analysis was performed using a random model. Meta analysis results (**Figure 3**) showed that warm ischemia time were significantly shorter for RPN than for LPN (MD = -3.29, 95% CI [-6.47, -0.10]).

Estimated blood loss

There were nine studies investigating estimated blood loss. This result was influenced by heterogeneity ($I^2 = 41\%$), and so the meta-analysis was performed using a random model. Meta analysis results (**Figure 4**) showed that there was no significant difference in estimated blood loss (MD = -42.24, 95% CI [-87.10, 2.61]).

Length of stay

There were eight studies investigating length of stay. This result was influenced by heterogeneity ($I^2 = 86\%$), and so the meta-analysis was performed using a random model. Meta analysis results (**Figure 5**) showed that there was no significant difference in length of stay (MD = -0.29, 95% CI [-0.89, 0.32]).

Incidence of complications

There were six studies investigating incidence of intraoperative complications. A fixed-effect model was used due to the fact that there was no heterogeneity ($I^2 = 0\%$). Meta analysis results showed that there was no significant difference in incidence of intraoperative complications (OR = 0.68, 95% CI [0.29, 1.58]).

There were five studies investigating incidence of postoperative minor complications. A fixed-effect model was used due to the fact that there was no heterogeneity ($I^2 = 0\%$). Meta analysis results showed that there was no significant difference in incidence of postoperative minor complications (OR = 1.10, 95% CI [0.80, 1.51]).

There were five studies investigating incidence of postoperative major complications. A fixed-effect model was used due to the fact that there was no heterogeneity ($I^2 = 0\%$). Meta

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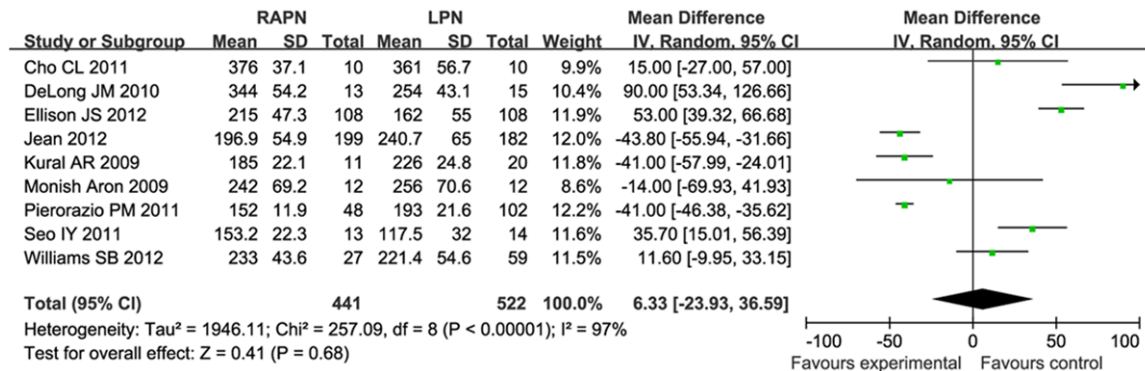


Figure 2. Forest plot of meta-analysis: Operative time. CI: confidence interval.

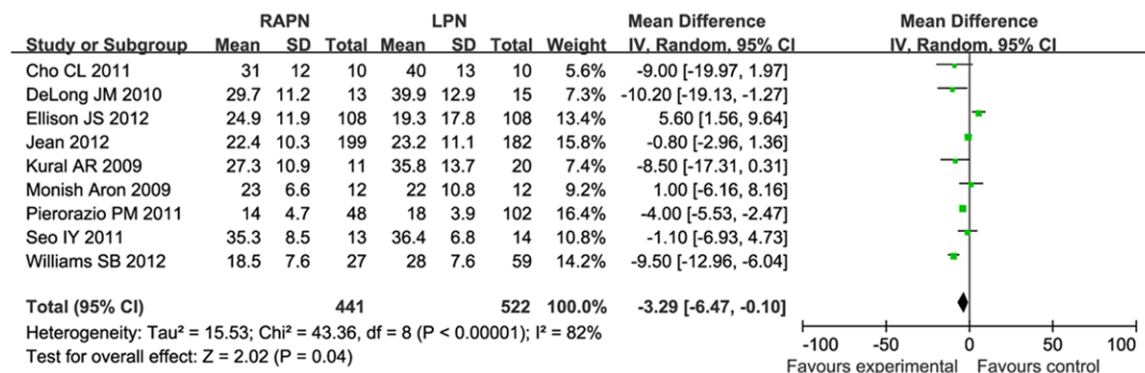


Figure 3. Forest plot of meta-analysis: Warm ischemia time. CI: confidence interval.

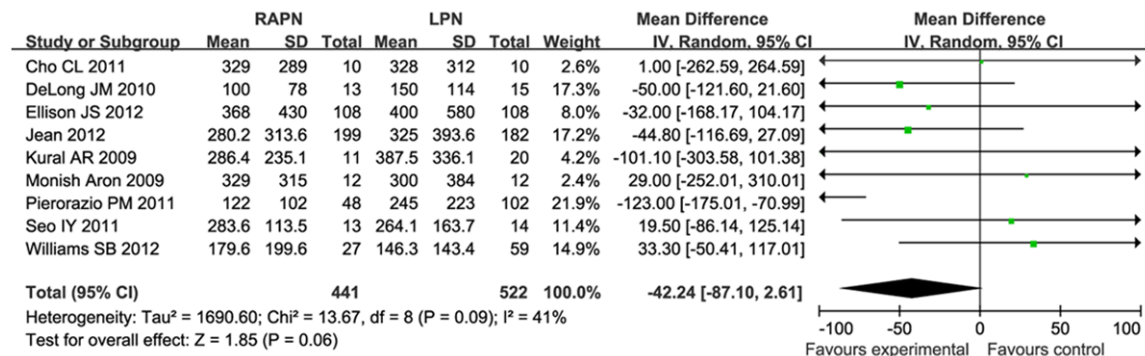


Figure 4. Forest plot of meta-analysis: Estimated blood loss. CI: confidence interval.

analysis results showed that there was no significant difference in incidence of postoperative major complications (OR = 0.99, 95% CI [0.61, 1.61]) (shown in Figure 6).

Positive surgical margin rate

There were 11 studies investigating positive surgical margin rate. A fixed-effect model was used due to the fact that there was no heterogeneity (I² = 0). Meta analysis results (Figure 7)

showed that there was no significant difference in positive surgical margin rate (OR = 1.12, 95% CI [0.56, 2.25]).

Discussion

Result explanation

The incidence of localized renal tumors increases steadily due in large part to the increasing use and sophistication of cross-sectional

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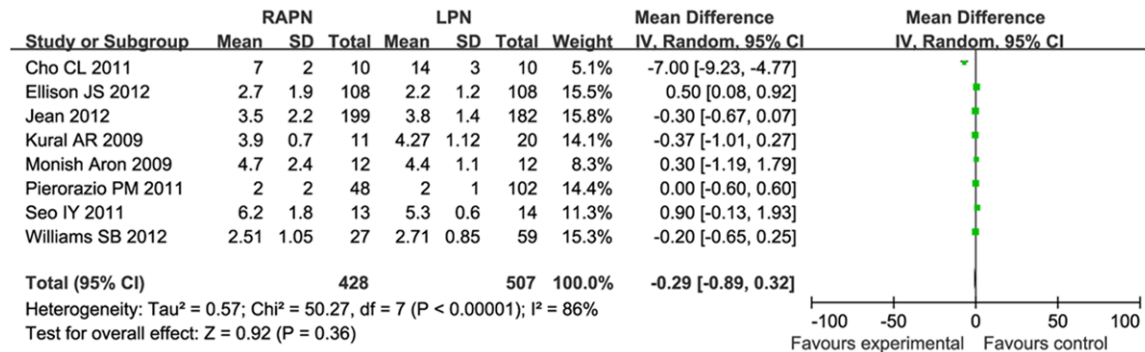
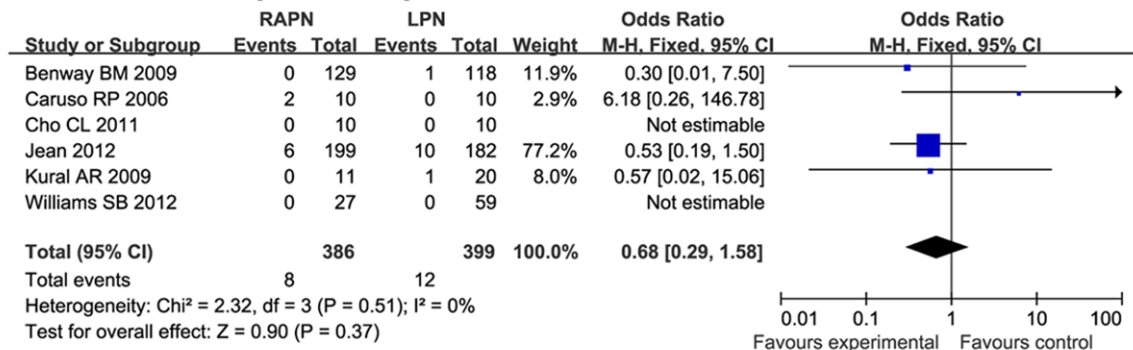
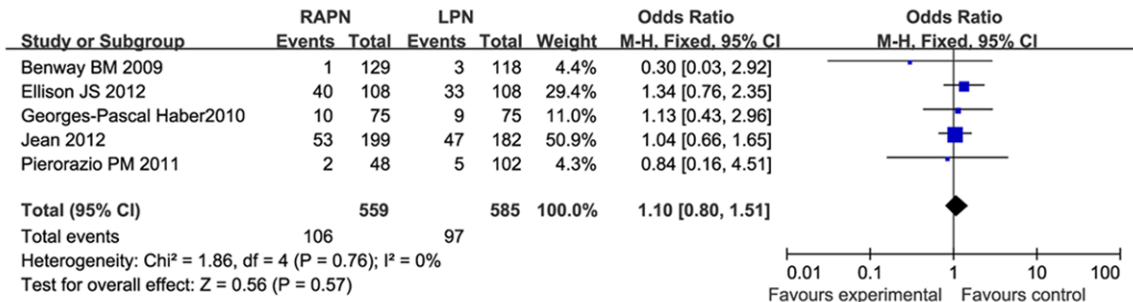


Figure 5. Forest plot of meta-analysis: Length of stay. CI: confidence interval.

Incidence of intraoperative complications



Incidence of postoperative minor complications



Incidence of postoperative major complications

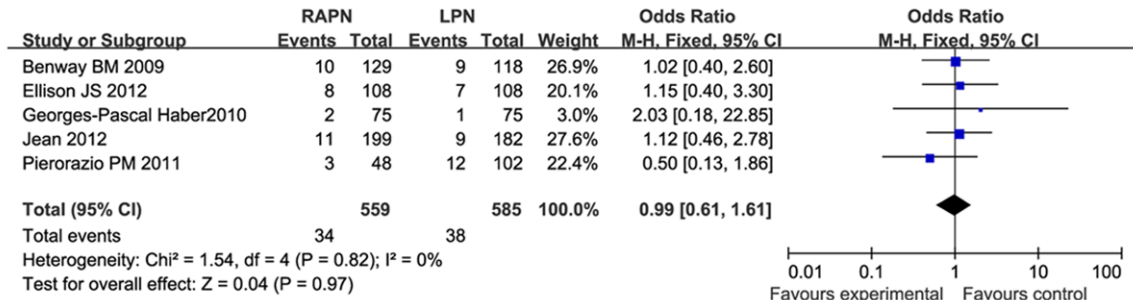


Figure 6. Forest plot of meta-analysis: incidence of complications. CI: confidence interval.

abdominal imaging with technological advancements [27]. Radical nephrectomy (RN) has traditionally been considered the standard of care

for localized renal tumors [28]. However, it has demonstrated worse outcomes for overall mortality than PN for patients with small renal

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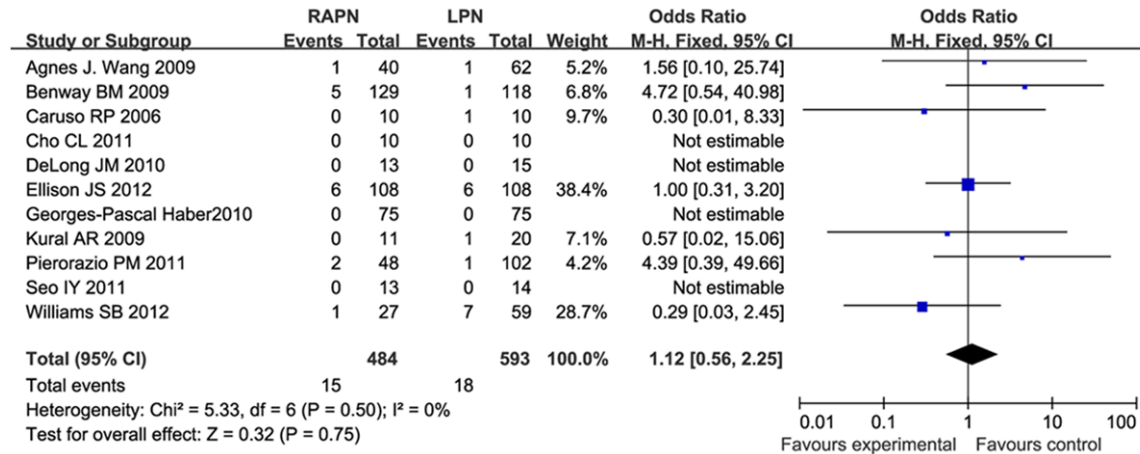


Figure 7. Forest plot of meta-analysis: Positive surgical margin rate. CI: confidence interval.

masses [29, 30]. NSS has complemented RN as a standard of care for localized renal tumors now. It preserved healthy renal parenchyma as well as provided similar oncological outcomes compared to radical nephrectomy [30-33]. With the advances of laparoscopic surgery, LPN has become a safe and effective treatment modality [34-36]. However, technical difficulty including intra-corporeal suturing, dissection, and repairing the defect under the time constraints of warm ischemia is the largest obstacle to the widespread use of LPN [35]. Advantages of the robot are three-dimensional imaging with high definition quality, stable motion without tremor, seven degrees of freedom, which allow more precision in a smaller operative field and easier resection and repair [5, 6]. Our meta-analysis results showed that there was no significant difference in most perioperative outcomes between RAPN and LPN, including operative time, estimated blood loss, length of stay, intra-operative complications, postoperative minor complications, and postoperative major complications. Further, no statistical significance was found regarding positive surgical margin rate. However, the warm ischemia time favored RAPN. We think that the shorter warm ischemia time is related to the improved visualization and ease of tumor excision/reconstruction allowed by the articulating robotic instruments, because the technique for LPN and RALPN was otherwise very similar and performed by the same surgical team. It has been demonstrated that there is a significant decrease in eGFR when the warm ischemia time was longer than 30 min [37]. Some authors recommended that the pedicle clamping necessary during partial

nephrectomy should be limited to 20 min of warm ischemia [38, 39]. Minimizing warm ischemia times and preserving renal parenchyma are favorable for avoiding chronic renal disease and the associated morbidity [40]. In the study of Ellison JS et al [24], the operations were performed by experienced laparoscopic surgeon who performed LPN and a heterogeneous group of robotic surgeons who performed RAPN early in their adoption of the robotic technique, which may influence the result. So we made a sensitivity analysis by excluding this study, however, all the results did not changed significantly, which revealed that RAPN was easier to learn. Meta-analysis of baseline parameters showed that the participants in the RAPN group is significantly older than participants in the LPN group, revealing that RAPN can safely accommodate a wider age range than LPN.

Limitations of the included studies and meta-analysis

There are several limitations to the included studies. Firstly, There are no randomized controlled trials (RCTs) comparing RAPN with LPN until now. The nonrandomized nature of the observational study leaves it open to selection bias, confounding bias known or unknown, and reporting bias, all of which have effects on any conclusions drawn from the meta-analysis compiled from these studies. The second limitation is that most of the current studies didn't do sub-analysis of different tumor characteristics such as different TNM classifications and tumor anatomic complexity, so we can not compare long-term oncologic outcomes between

RAPN and LPN for treating localized renal tumors of specific tumor characteristics. The third limitation is that the majority of the comparative studies included in this meta-analysis were from University hospitals from western Europe and north America. The participants included in the studies underwent RAPN or LPN by world leaders in their speciality. As a result, the findings may not be applicable to small centers and the rest of the world.

Implications for future research

As designing and carrying out RCTs may be difficult for surgical practice, future research efforts should focus on improvement in research methodology of observational studies. The recommendation for the reporting of observation studies can be used as a guideline for improvement in research methodology [41]. Researchers should compare RAPN and LPN for treating localized renal tumors of specific tumor characteristics such as different TNM classifications and tumor anatomic complexity. Additionally, studies with long-term follow up are needed to compare RAPN and LPN in terms of long-term complications and oncologic outcomes.

Conclusions

RAPN had similar operative time, LOS, EBL, and perioperative complications compared with LPN, as well as positive margin rates. RAPN appears to offer the advantage of decreased WIT compared with LPN. Studies with long-term follow up are needed to compare RAPN and LPN in terms of long-term complications and oncologic outcomes.

Disclosure of conflict of interest

None.

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