Complications and blood loss after invasive treatments for small renal masses: A systematic review

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KEY MESSAGES

- The systematic review presents the most comprehensive estimates of major complications and EBL associated with OPN, LPN, RAPN, and percutaneous TA in patients with SRMs.
- We found that the pooled proportion of major complications was highest for OPN (5.4%) and lowest for TA (2.5%), with LPN and RAPN at 4.7% and 2.9%, respectively. The certainty of evidence ranged from low to moderate.
- EBL was found to be highest during OPN (262 ml) and lowest during RAPN (163 ml), with LPN showing intermediate values (224 ml). Certainty of evidence for EBL also varied from low to moderate.
- These findings provide critical insights for patient and physician decision-making, suggesting that minimally invasive approaches like RAPN and TA may offer better safety profiles compared to OPN and LPN.

ABSTRACT

Introduction: This systematic review and meta-analysis provides estimates of major complications and blood loss for open partial nephrectomy, conventional laparoscopic partial nephrectomy, and

robot-assisted partial nephrectomy. Additionally, it outlines the incidence of major complications associated with percutaneous thermal ablation in patients with small renal masses.
Methods: We searched MEDLINE, EMBASE, and CINAHL from inception to the end of July 2023. We supplemented the electronic search with a hand search of references in the included studies and suggestions from two content experts. We used random effect meta-analysis to obtain pooled estimates of major complications and blood loss. We used the QUIPS tool for risk of bias assessment and applied a prognosis approach to rate the quality of evidence using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) framework.
Results: We included 65 eligible studies that provided pooled estimates of major complications after open partial nephrectomy of 5.4% (95% confidence interval [CI] 2.9–9.9); after conventional laparoscopic partial nephrectomy of 4.7% (95% CI 2.6–8.3); after robot-assisted partial nephrectomy of 2.9% (95% CI 2.2–3.7); and after thermal ablation of 2.9% (95% CI 2.3–3.8). Pooled estimates demonstrating mean estimated blood loss of 262 ml (95% CI 200–324) for open partial nephrectomy; 224 ml (95% CI 193–254) for conventional laparoscopic partial nephrectomy; and 163 ml (95% CI 136–190) for robot-assisted partial nephrectomy.
Conclusions: This review provides the best available estimates of major complications and mean blood loss after partial nephrectomy in patients with small renal masses.

INTRODUCTION

Small renal masses (SRMs), defined as masses measuring ≤4cm, account for a significant proportion of all renal masses. Between 1988 and 2003, SRMs represented 48-66% of diagnosed renal masses, and this proportion has since increased due to the rise in incidental diagnoses among asymptomatic patients[1,2]. When malignant, the vast majority of these SRMs are pT1a kidney tumors[3]. Compared to historical data, incidentally discovered SRMs tend to be in an earlier disease stage, specifically T1a. This shift in the stage and size of diagnosed renal tumors has led to a change in treatment recommendations for patients with SRMs, prompting the emergence of partial nephrectomy (PN) as the preferred and recommended treatment option, particularly for patients who require preservation of their renal function[4-7].

Minimally invasive PN techniques have gained prominence in the surgical management of SRMs. Among these techniques, conventional laparoscopic partial nephrectomy (LPN) and robot-assisted partial nephrectomy (RAPN) have become increasingly preferred over the traditional open partial nephrectomy (OPN)[6-8]. The main drivers behind this shifting preference are the documented lower morbidity rates and reduced blood loss associated with these approaches. Advances in performing LPN and RAPN have contributed to wider adoption of these surgical alternatives to OPN. Consequently, patients are thought to benefit from reduced postoperative complications and improved long-term outcomes [9-11]. Similarly, emphasis on less invasive therapies also led to development of ablative approaches to treating small renal masses.

Thermal ablation (TA) that utilizes heating or freezing techniques to effectively target and treat tumors is thought to have an advantage over PN with fewer complications and a quicker recovery time[12]. Within the realm of TA, percutaneous ablation has demonstrated similar oncologic outcomes and a potential decrease in procedural burdens compared to laparoscopic ablation and is generally favored [6-8].

Our focus is on investigating the major complications and estimated blood loss (EBL) associated with the available treatment modalities for SRMs, including OPN, LPN, RAPN, and percutaneous TA. By examining these treatment modalities individually, we aim to provide insights into patient outcomes in SRM management.

METHODS

We registered the protocol of this review in the PROSPERO (International Prospective Register of Systematic Review), registration ID is CRD42022308375. We used guidance from PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) in reporting our review.

Data sources and searches

To conduct a comprehensive search, we explored the following databases: MEDLINE (Medical Literature Analysis and Retrieval System Online), EMBASE (Excerpta Medica database), and CINAHL (Cumulative Index of Nursing and Allied Health Literature). Our search encompassed the period from the inception of the databases until the end of July 2023. Additionally, our research team engaged in manual searches of reference lists from the included articles and benefited from the expertise of two urologist members, PR and PV, who provided valuable suggestions.

Eligibility criteria

Inclusion criteria encompassed RCTs, cohort studies, and case series with at least 10 patients undergoing PN or PTA for SRMs. Eligible studies reported major complications (Clavien-Dindo grade ≥III) within 30 days post-procedure[13] and EBL during PN.
We included studies reporting the number of complications, extracting only those with Clavien-Dindo grade ≥3. For studies not reporting all complications separately, we included those considering a complication as major with a Clavien-Dindo grade ≥3.

Exclusion criteria were studies not providing major complication frequencies or necessary EBL statistics (e.g., mean and standard deviation). We did not restrict based on publication status, country, or period but limited to English articles. We excluded studies focused on highly selected patient populations, those not specifying treatments, and those not outlining eligibility criteria for SRM patients.
The types of each procedure are as follows:

Nephrectomy: Included transperitoneal and retroperitoneal nephrectomy; restricted to OPN, LPN, and RAPN.

Thermal ablation: Included percutaneous TA; restricted to cryoablation and radiofrequency ablation (RFA). If 80% or more of TA procedures were percutaneous, cryoablation, or radiofrequency ablation, we included the study.

Potentially eligible studies used different SRM definitions (≤4 cm, ≤5 cm, ≤7 cm). We included studies if ≥80% of masses were ≤4 cm.

Study selection and data extraction
Reviewers received detailed instructions for title and abstract screening, full-text reading, risk of bias (ROB) assessment, and data abstraction. Pairs of reviewers independently screened titles and abstracts reviewed the full text of potentially eligible studies, abstracted data (JD, RL, HS, DT, JS, WT), and assessed ROB (AS and MK). Reviewers resolved discrepancies through discussion or consultation with a third reviewer (MK). We recorded study country, participants' age, gender, tumor size, sample size, type of intervention, major complications for PN and PTA procedures, and EBL for PN.

Risk of bias
We focused on prognosis related to SRM treatment outcomes, specifically EBL during procedures and major complications within 30 days[13]. We used the Quality In Prognosis Studies (QUIPS)[14] instrument, considering study design and outcomes. We assessed four QUIPS domains: "study participation," "outcome measurement," "study attrition," and "statistical analysis and reporting," excluding "prognostic factor measurement" and "study confounding." Studies with high risk in any assessed domain were classified as high risk of bias.

Certainty of evidence
To rate the certainty of the evidence, we utilized the GRADE approach specifically tailored for prognostic questions[15] in which observational studies are initially considered high certainty evidence. We considered five factors that might lower certainty of evidence: risk of bias, inconsistency, imprecision, indirectness, and publication bias.

To address publication bias, we used Begg's test which is based on assessing whether a significant correlation is seen between the ranks of estimations and their variances. We also used funnel plots to visualize if a publication bias is suspected.

Data analysis
To determine the pooled estimates of EBL, we extracted mean and standard deviations when available. If not reported, we collected the median and interquartile range or range, converting them to mean and standard deviations using equations by Wan et al[16]. Pooled means were calculated using the DerSimonian-Laird random effects inverse variance method.

We conducted a Chi-square test to assess differences in complications among studies with various sample sizes, ROB, and geographic regions. Welch t-tests evaluated potential variations in EBL across studies with different sample sizes and ROB. To assess potential variations in EBL across geographic regions, we used the Kruskal-Wallis test. Sample size was dichotomized into large and small groups using a 100-patient threshold. Studies were categorized as high or low risk of bias according to QUIPS criteria, with regions categorized as North America, Europe, Asia, and other areas. All hypothesis tests used a significance level of 0.05. To evaluate the credibility of subgroup analyses based on geographic region, we used the ICEMAN tool[17].

RESULTS

Literature search and study characteristics

We screened 3,456 titles and abstracts and retrieved 438 possibly eligible full texts of which 65 studies including 13,452 patients proved eligible (Chart 1-Figure 1 PRISMA diagram).

The details of study characteristics and summary of finding is presented in table 1.

Risk of bias

Of the 65 included studies, 34 proved high risk of bias. Table 2 presents the details of bias risk assessments.

Assessment of prognostic factor effect

We assessed the prognostic effect of sample sizes, ROB, and geographic regions. Table 3 shows the results of prognostic factor analysis. Among studies on OPN, there was a significant difference in major complications across regions (p-value = 0.003). Among LPN studies, significant differences in major complications were observed across sample sizes (p-value = 0.006), and in EBL across regions (p-value = 0.005). The ICEMAN tool, used to assess credibility, yielded low credibility for all significant effects due to small subgroup sizes. Thus, we report results for pooled estimates of each procedure study group.

Certainty of evidence

To assess the certainty of the evidence, we used the GRADE approach tailored for prognostic questions[15] (see Table 4). Our evaluation focused on addressing prognostic questions for our outcomes, with a key emphasis on inconsistency within study groups. This led to a downward adjustment in the certainty rating, based on differences in point estimates among the included studies. For example, in major complications after OPN (Figure 2), estimates ranged from 2% to 29%, resulting in a very serious rating for inconsistency.

Major complications and estimated blood loss

Major complications

The pooled proportion of major complications after OPN in the 10 included studies was 5.4% (95%CI: 2.9-9.9). The certainty of evidence was low because of the very serious inconsistency (Tables 2, 3 and Figure 1 -2).

The pooled proportion of major complications after LPN from the 11 included studies was 4.7% (95% CI: 2.6-8.3). The certainty of evidence was low because of the very serious inconsistency (Tables 2, 3 and Figure 2 -3).

The pooled proportion of major complications after RPN from the 20 included study was 2.9% (95% CI: 2.3-3.8). The certainty of evidence was moderate because of serious inconsistency (Tables 2, 3 and Figure 3 -4).

The pooled proportion of major complications after TA from the 15 included studies was 2.5 (95%CI: 1.7-3.6). The certainty of evidence was moderate because of serious bias risk (Tables 2, 3 and Figure 4 -5).

Estimated blood loss
The pooled mean of EBL during OPN in the 14 included studies was 262 (95% CI: 200-324) ml. The certainty of evidence was low because of the very serious inconsistency (Tables 2, 3 and Figure 5 -6).

The pooled mean EBL during LPN in the 25 included studies was 224 (95% CI: 193-254) ml. The certainty of evidence was low because of serious bias risk and serious inconsistency (Table 2, 3 and Figure 6 - 7).

The pooled mean EBL during RPN in the 29 included studies was 163 (95% CI: 136-190) ml. The certainty of evidence was moderate because of serious inconsistency (Tables 2, 3 and Figure 7 -8).

DISCUSSION
This systematic review and meta-analysis provides estimates of major complications after different PN approaches and TA. Our findings show that the proportion of major complications was 5.4% (95% CI: 2.9-9.9)for OPN, 4.7% (95% CI: 2.6-8.3) for LPN, 2.9% (95% CI: 2.3-3.8) for RAPN, and 2.5% (95% CI: 1.7-3.6) for TA (Table 4, Figures 1-4).

In terms of EBL, our analysis indicated that EBL was 262 ml (95% CI: 200-324) for OPN, 224 ml (95% CI: 193-254) for LPN, and 163 ml (95% CI: 136-190) for RAPN (Table 4, Figures 5-7).

Our assessment of the quality of evidence revealed a low to moderate certainty of evidence for the outcomes of interest (Table 4). While our analysis provides a comprehensive overview of the available evidence, the quality of the included studies varied, and the certainty of the evidence was limited by factors including risk of bias, inconsistency, and imprecision.

Strengths and limitations
This systematic review and meta-analysis has several strengths. Our comprehensive literature search addressed studies from various regions and publication periods. To ensure consistency in eligibility decisions, we established explicit and rigorous criteria and conducted calibration exercises with the reviewers. We employed established frameworks - QUIPs for risk of bias and the GRADE prognosis approach for assessing certainty of evidence. We adapted the ICEMAN instrument for evaluating the credibility of subgroup analyses in prognostic studies.

Our study does have limitations. We restricted eligibility to articles published in English. The included studies varied in their definition of SRMs, with some including tumors larger than our criteria of 4 cm. To address this, we included only studies in which 80% of the patients' tumor sizes met our criteria. Moreover, we faced limitations in accessing detailed patient characteristics such as age, sex, and tumor size, preventing us from fully exploring the sources of heterogeneity in our results.

Studies adopted different definitions of major complications. While some studies identified Clavien-Dindo Grade ≥2 as major complications, others set a threshold of Clavien-Dindo Grade ≥3. To mitigate the impact of this heterogeneity in defining major complications, we included only those studies that specifically regarded Clavien-Dindo Grade ≥3 as indicative of major complications.

Although microwave ablation is currently favored as a heat-based thermal ablative technique worldwide, our systematic review focused on RFA and cryoablation, which were the predominant techniques in the included studies. Future systematic reviews should consider incorporating data on microwave ablation and other emerging ablative modalities, such as irreversible electroporation and stereotactic body radiation therapy, to further explore their impact on clinical outcomes.

Lastly, for major complications after OPN and LPN, and EBL during LPN, we found only low certainty evidence due to the presence of potential bias and inconsistency in results. Also, TA includes cryoablation and RFA, but these methods have different complications rates and indications.

Relation to prior work

Several systematic reviews and meta-analyses have investigated pooled estimations for major complications and EBL. However, none of these reviews specifically focused on OPN, LPN, RPN, and TA separately, and the research questions differed from our study. They centered around comparative analyses of treatment strategies rather than individual description of each treatment modality, which distinguishes our current investigation.

A systematic review published in 2014[18] compared major complications following RFA and PN for patients with SRMs in two groups of studies on tumors at pathological stage of T1a and the other group of studies on tumors at pathological stage of T1.They reported a major complication proportion of 10.2% for OPN, 7.2% for combined RPN and LPN , and 4.3% for RFA in the T1a group of included studies. In our study, the proportions of major complications for OPN, LPN, RPN, and TA were 5.4%, 4.7%, 2.9%, and 2.5%, respectively. These proportions were lower than those reported in the previous systematic review. One possible explanation is that the prior review included 31 studies that we did not; we included 31 studies published later than 2014 that the prior review did not. Older studies may have encapsulated less contemporary procedures, potentially yielding outcomes that differ in certain aspects and may have been less favorable. It is plausible that older studies encompassed earlier stages of learning curves and were conducted before the refinement of patient selection criteria. Totally, our included studies are more recent, and the estimates are indicative of contemporary practice.

Another systematic review published in 2013[19] reported the EBL and complications for both LPN and RAPN. Our findings align closely with slightly lower EBL for RAPN (163 ml vs.

257 ml), potentially indicative of more contemporary outcomes. Notably, our study spans various regions and a more extended timeframe, including European studies, while the previous review focused on North American and Asian studies until June 2012. Furthermore, the earlier review reported higher pooled rates of postoperative complications for both LPN and RAPN compared to our study (LPN: 13.3% vs 4.7%; RPN: 13.1% vs 2.7%). The discrepancy could be attributed to their inclusion of all complications, not just major ones and we maintained rigor by excluding studies lacking clear definitions based on the Clavien grading system. In total, all studies from the previous review were included in our analysis, and we added 35 studies published after 2012, previously unaccounted for in the earlier review.

Another systematic review published in 2017[20] which specifically addressed major complications following OPN and RAPN, corroborated our findings. The major complication rates reported in the earlier review (OPN: 6.0%, RAPN: 2.9%) closely mirror our results (OPN: 5.4%, RAPN: 2.7%). Importantly, the 2017 review focused solely on major complications related to OPN and RAPN, unlike our comprehensive analysis that covers a broader range of procedures and complications. In essence, our comprehensive analysis was both valuable and justified.

Implications of findings

Our systematic review and meta-analysis offer crucial insights for clinical practice, providing contemporary data on major complications with various SRMs treatment options and EBL for PN methods. This information empowers both patients and physicians, fostering informed decision-making and healthcare policy development.

Our systematic review estimates not only support patients and physicians in making informed treatment decisions but also contribute to the enhancement of existing decision aids. The widely used tools[21] ensure that decision-making tools remain reflective of the latest evidence, benefiting both patients and healthcare professionals.

Our findings serve as a foundational reference for researchers engaged in values and preference studies. By enriching investigations, our work contributes to a broader understanding of patient preferences in the context of SRM treatment decisions.

Finally, our findings are valuable for informing guideline panels and policy decision-makers. We envision our work as a resource for initiatives such as urological guidelines, providing insights into the relative harms of different treatment approaches for SRMs.

CONCLUSIONS

This systematic review and meta-analysis presents the most comprehensive estimates of major complications following PN and PTA as well as mean EBL for PN in patients with SRM. By synthesizing a large body of evidence, this review enhances our understanding of the harms of each intervention and helps guide clinical practice.

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FIGURES AND TABLES

Figure 1. PRISMA flow diagram.

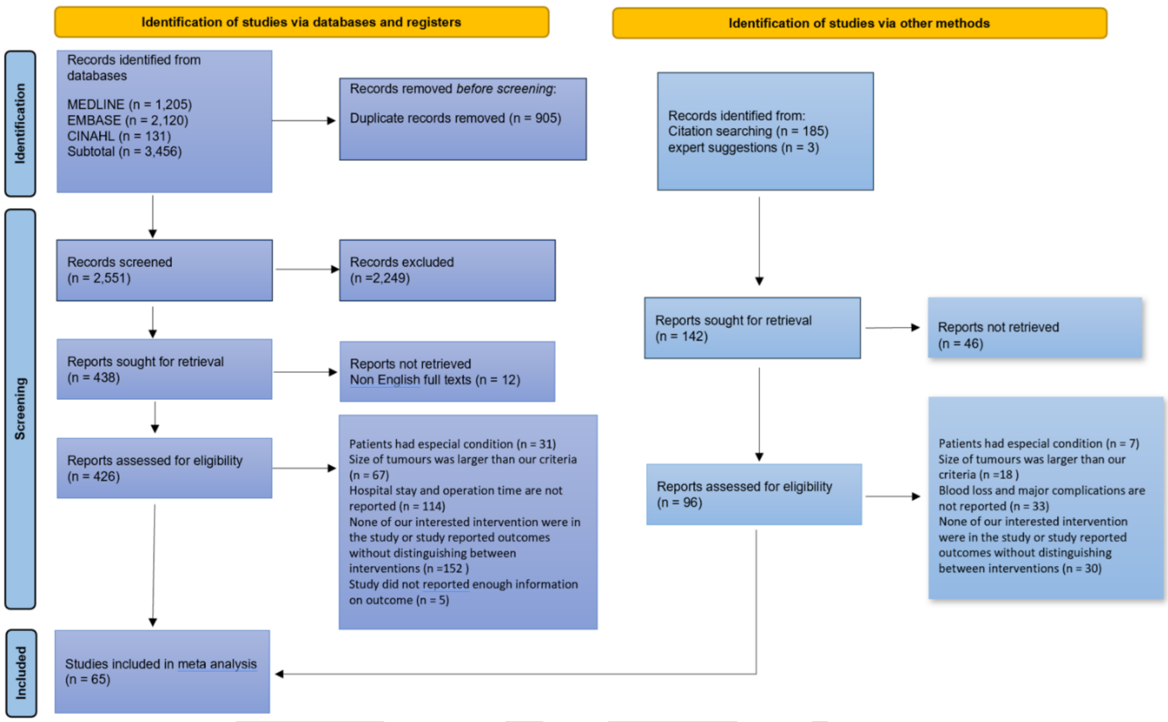

Figure 2. Forest plot of proportion of major complications in patients with SRM, after open partial nephrectomy. CI: confidence interval.

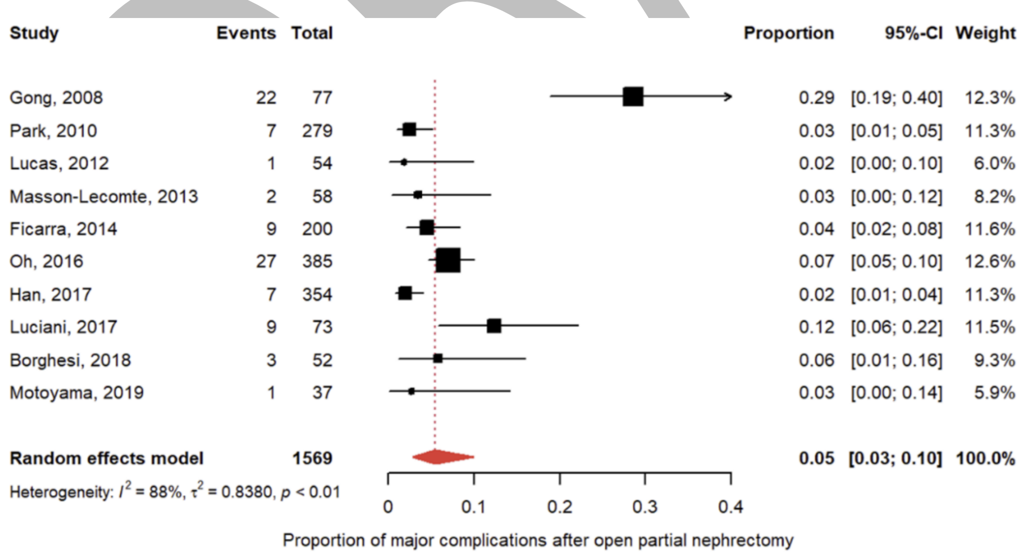

Figure 3. Forest plot of proportion of major complications in patients with small renal mass, after conventional laparoscopic partial nephrectomy. CI: confidence interval.

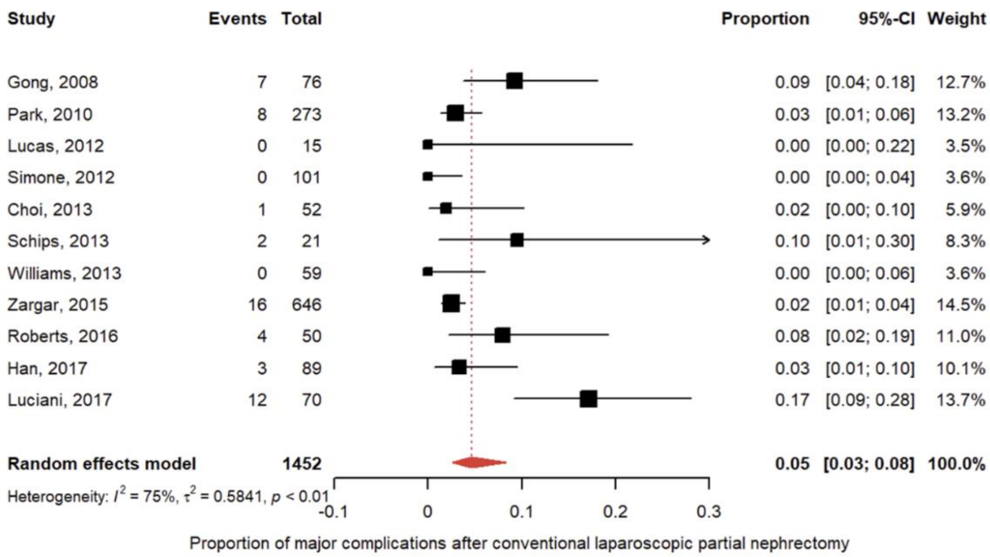

Figure 4. Forest plot of proportion of major complications in patients with small renal mass, after robot-assisted partial nephrectomy. CI: confidence interval.

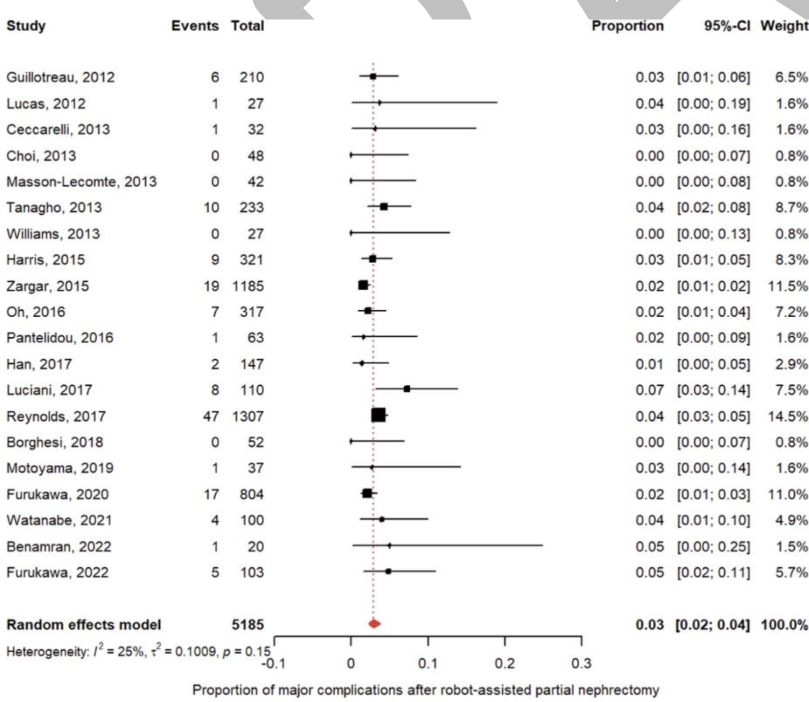

Figure 5. Forest plot of proportion of major complications in patients with small renal mass, after thermal ablation. CI: confidence interval.

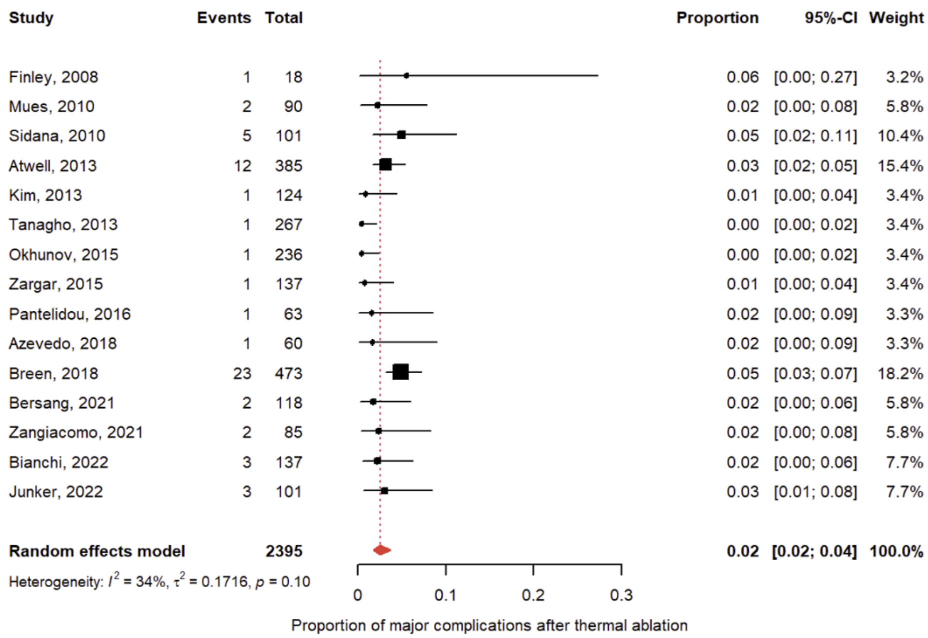

Figure 6. Forest plot of estimated blood loss in patients with small renal mass, after open partial nephrectomy. CI: confidence interval; SD: standard deviation.

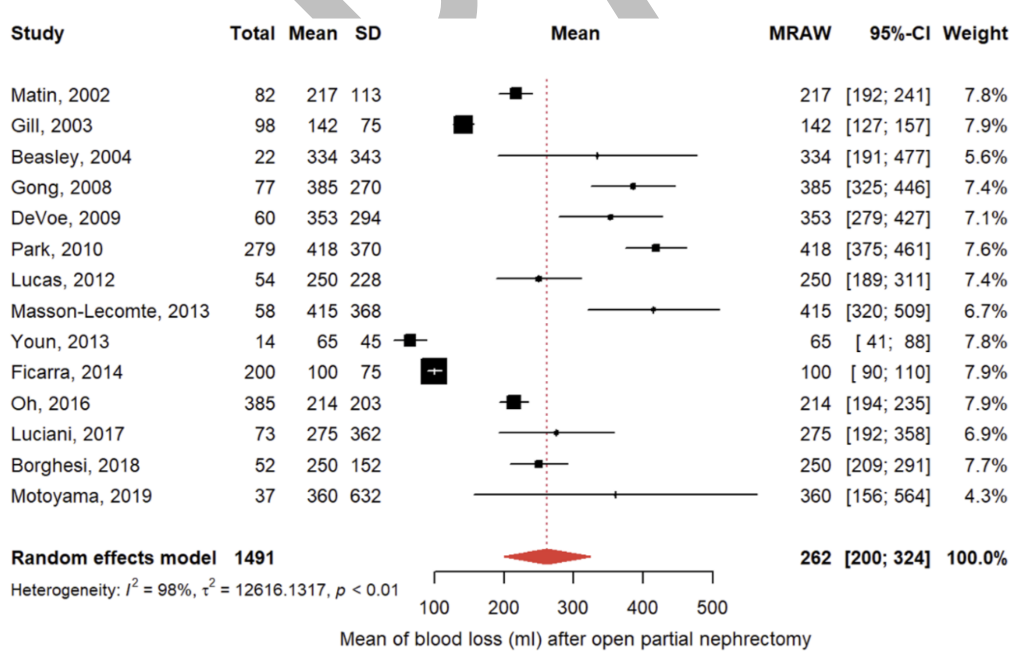

Figure 7. Forest plot of estimated blood loss in patients with small renal masses, after conventional laparoscopic partial nephrectomy. CI: confidence interval; SD: standard deviation.

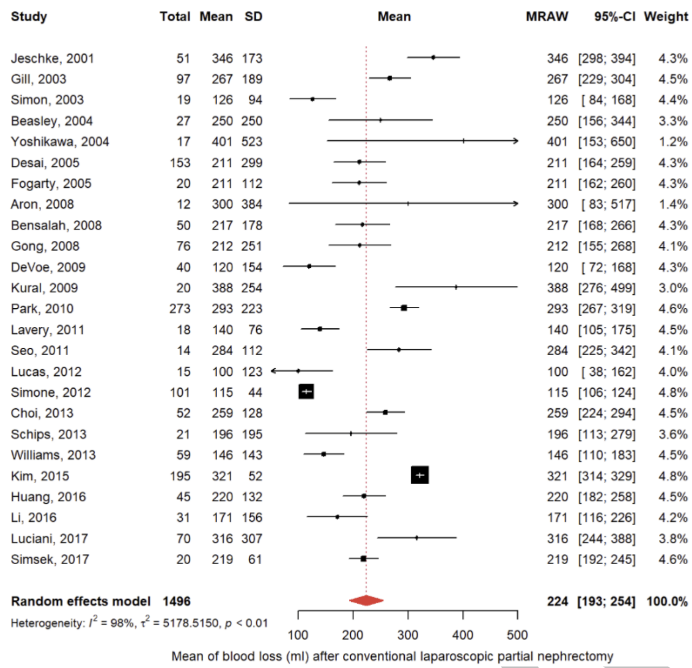

Figure 8. Forest plot of estimated blood loss in patients with small renal mass, after robot-assisted partial nephrectomy. CI: confidence interval; SD: standard deviation.

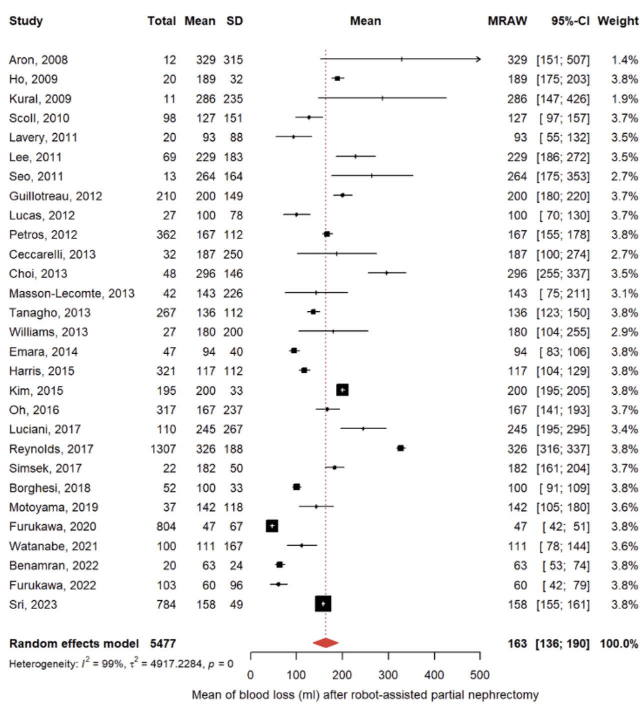

Table 1. Characteristics of original studies included in meta-analysis

References	Country	Treatment type	Sample size	Population characteristics		Mean tumor size, cm (SD)	Estimated blood loss (ML) mean (SD)	Number of major complications (%)
				% male	Mean age (SD)			
Jeschke, 2001[22]	Austria	LPN	51	27.5	59.8 (11.1)	2.0 (0.9)	346 (173)	NR
Matin, 2002[23]	U.S.	OPN	82	61.0	56.2 (11.5)	2.6 (NR)	217 (113)	NR
Gill, 2003[24]	U.S.	OPN	76	67.0	58.8 (11.6)	3.4 (0.8)	267 (189)	NR
		LPN	100	58.2	65.1 (11.4)	2.9 (1.5)	142 (75)	NR
Simon, 2003[25]	U.S.	LPN	19	78.9	65.5 (11.7)	2.2 (1.3)	126 (94)	0 (0.0)
Beasley, 2004[26]	Canada	OPN	22	63.6	51.1 (16.4)	2.9 (1.1)	334 (343)	NR
		LPN	27	59.3	53.5 (17.7)	2.4 (1.2)	250 (250)	NR
Yoshikawa, 2004[27]	Japan	LPN	17	76.5	55.2 (16.7)	2.5 (1.1)	401 (523)	NR
Desai, 2005[28]	U.S.	LPN	153	58.2	60.6 (13.2)	2.3 (0.7)	211 (299)	NR
Fogarty, 2005[29]	U.S.	LPN	20	75.0	65.8 (11.3)	2.6 (0.9)	211 (113)	NR
Aron, 2008[30]	U.S.	LPN	12	66.7	61.0 (13.8)	2.9 (0.7)	300 (384)	NR
		RAPN	12	66.7	64.0 (13.8)	2.4 (0.7)	329 (315)	NR
Bensalah, 2008[31]	U.S.	LPN	50	62.0	56.5 (11.7)	2.6 (0.9)	217 (178)	NR
Finley, 2008[32]	U.S.	PTA	18	NR	NR	2.7 (0.8)	NR	1 (5.5)
Gong, 2008[33]	U.S.	OPN	77	54.5	59.7 (13.6)	2.4 (0.9)	385 (270)	22 (28.6)
		LPN	76	46.1	60.1 (12.5)	2.9 (0.8)	212 (251)	7 (9.2)
DeVoe, 2009[34]	U.S.	OPN	60	56.5	60.0 (9.8)	2.6 (1.1)	353 (294)	NR
Ho, 2009[35]		LPN	40	67.3	59.2 (12.4)	2.6 (1.2)	120 (154)	NR

Kural, 2009[36]	Austria	RAPN	20	65.0	58.2 (7.9)	3.5 (0.5)	189 (32)	NR
DeVoe, 2009[34]	Turkey	LPN	20	70.0	58.9 (15.4)	3.1 (1.5)	388 (254)	NR
		RAPN	11	72.7	50.8 (13.2)	3.2 (0.7)	286 (235)	NR
Mues, 2010[37]		PTA	90	NR	67.0 (-)	2.1 (0.7)	NR	2 (2.2)
Park, 2010[38]	Korea	OPN	279	74.2	53.1 (13.2)	2.3 (0.9)	418 (370)	7 (2.5)
		LPN	273	70.0	54.6 (13.2)	2.1 (0.8)	293 (223)	8 (2.9)
Scoll, 2010[39]	U.S.	RAPN	100	68.0	55.0 (12.0)	3.5 (1.4)	127 (151)	NR
Sidana, 2010[40]	U.S.	PTA	101	64.4	68.8 (11.6)	2.4 (1.1)	NR	5 (5.0)
Lavery, 2011[41]	U.S.	LPN	18	77.8	53.6 (11.1)	2.3 (1.2)	140 (76)	NR
		RAPN	20	55.0	55.4 (11.1)	2.5 (0.9)	93 (88)	NR
Lee, 2011[42]	Korea	RAPN	69	72.5	53.5 (11.8)	2.4 (1.3)	229 (183)	NR
Seo, 2011[43]	Korea	LPN	14	57.1	53.9 (11.6)	2.0 (1.2)	284 (112)	NR
		RAPN	13	76.9	54.2 (12.4)	2.7 (1.2)	264 (164)	NR
Guillotreau, 2012[44]	U.S.	RAPN	210	58.6	57.8 (11.8)	2.4 (0.8)	200 (149)	NR
Lucas, 2012[45]	U.S.	OPN	54	70.4	58.0 (13.4)	2.3 (0.8)	250 (229)	1 (1.9)
		LPN	15	41.2	49.4 (20.3)	2.2 (1.6)	100 (123)	0 (0.0)
		RAPN	27	70.4	62.1 (12.0)	2.4 (0.5)	100 (78)	1 (3.7)
Petros, 2012[46]	U.S.	RAPN	362	67.7	60.0 (11.0)	2.3 (0.6)	167 (112)	NR
Simone, 2012[47]	Italy	LPN	101	62.4	59.0 (5.6)	2.6 (0.5)	115 (44)	0 (0.0)
Atwell, 2013[48]	U.S.	PTA	408	64.4	68.5 (11.5)	2.1 (0.5)	NR	12 (2.9)
Ceccarelli, 2013[49]	Italy	RAPN	32	68.7	60.8 (14.3)	3.6 (1.2)	187 (250)	1 (3.1)

Choi, 2013[50]	Korea	LPN	52	63.5	51.1 (11.3)	2.2 (1.1)	259 (128)	1 (1.9)
		RAPN	48	70.8	50.9 (11.4)	2.5 (1.0)	296 (146)	0 (0.0)
Kim, 2013[51]	U.S.	PTA	124	NR	72.6 (10.2)	2.7 (1.1)	NR	1 (0.8)
Masson-Lecomte, 2013[52]	France	OPN	58	69.0	60.8 (11.2)	3.1 (1.2)	415 (368)	2 (3.4)
		RAPN	42	52.4	61.7 (10.9)	2.8 (1.4)	143 (226)	0 (0.0)
Schips, 2013[53]	Italy	LPN	21	66.7	58.4 (9.0)	2.0 (0.3)	196 (195)	2 (9.5)
Tanagho, 2013[54]	U.S.	RAPN	267	54.5	57.4 (11.9)	2.9 (1.5)	136 (112)	10 (3.7)
		PTA	267	61.0	69.3 (11.0)	2.5 (1.0)	NR	1 (0.4)
Williams, 2013[55]	U.S.	LPN	59	69.5	54.6 (11.7)	3.1 (2.2)	146 (143)	0 (0.0)
		RAPN	27	63.0	55.7 (11.2)	2.5 (1.2)	180 (200)	0 (0.0)
Youn, 2013[56]	Korea	OPN	14	57.1	53.9 (16.1)	2.4 (0.8)	65 (45)	NR
Emara, 2014[57]	U.K.	RAPN	47	46.3	60.5 (9.5)	2.6 (1.0)	94 (40)	NR
Ficarra, 2014[58]	Italy	OPN	200	65.5	62.4 (11.8)	2.8 (1.1)	100 (75)	9 (4.5)
Harris, 2015[59]	U.S.	RAPN	321	NR	59.3 (11.7)	2.7 (1.3)	117 (112)	9 (2.8)
Kim, 2015[60]	Korea	LPN	195	66.7	54.7 (12.7)	2.3 (1.1)	321 (52)	NR
		RAPN	195	63.6	54.4 (13.0)	2.4 ± 1.2	200 (33)	NR
Okhunov, 2015[61]	U.S.	PTA	236	67.4	68.2 (10.6)	2.4 (1.0)	NR	1 (0.4)
Zargar, 2015- Study 1[62]	U.S.	LPN	646	61.4	57.4 (12.4)	2.0 (1.0)	NR	16 (2.5)
		RAPN	1185	59.8	59.3 (11.2)	2.3 (1.0)	NR	19 (1.6)
Zargar, 2015- Study 2[63]	U.S.	PTA	137	67.2	67.2 (11.9)	2.3 (0.9)	NR	1 (0.7)

Huang, 2016[64]	China	LPN	45	62.2	50.0 (10.4)	2.9 (0.6)	220 (132)	NR
Li, 2016[65]	Taiwan	LPN	31	61.3	53.0 (7.5)	2.9 (1.1)	171 (156)	NR
Oh, 2016[66]	Germany	OPN	385	69.6	54.9 (13.1)	2.3 (0.8)	214 (203)	27 (7.0)
		RAPN	317	72.6	52.1 (12.2)	2.2 (0.8)	167 (237)	7 (2.2)
Pantelidou, 2016[67]	U.K.	RAPN	63	NR	54.0 (7.0)	2.9 (0.1)	NR	1 (1.6)
		PTA	63	NR	61.0 (21.0)	2.1 (0.2)	NR	1 (1.6)
Robert, 2016[68]	Australia	LPN	50	54.0	56.9 (10.5)	2.5 (1.3)	NR	4 (8.0)
Han, 2017[69]	Korea	OPN	354	76.3	55.3 (12.4)	2.8 (1.4)	NR	7 (2.0)
		LPN	89	69.7	53.6 (9.7)	2.6 (1.1)	NR	3 (3.4)
		RAPN	147	73.5	52.5 (11.9)	2.4 (0.9)	NR	2 (1.4)
Luciani, 2017[70]	Italy	OPN	73	69.9	63.0 (13.0)	3.6 (2.3)	275 (362)	9 (12.3)
		LPN	70	60.0	62.0 (11.0)	3.5 (1.4)	316 (307)	12 (17.1)
		RAPN	110	60.9	61.0 (12.0)	3.6 (1.5)	245 (267)	8 (7.3)
Reynolds, 2017[71]	USA	RAPN	1307	56.2	58.1 (11.8)	2.5 (0.7)	326 (188)	47 (3.6)
Simsek, 2017[72]	Turkey	LPN	20	75.0	50.2 (11.3)	NR	219 (61)	NR
		RAPN	22	54.5	54.8 (9.6)	NR	183 (50)	NR
Azevedo, 2018[73]	Brazil	PTA	60	80.0	63.9 (12.54)	1.6 (0.82)	NR	1 (1.7)
Borghesi, 2018[74]	Italy	OPN	52	57.7	62.7 (16.0)	3.0 (1.5)	250 (153)	3 (5.8)
		RAPN	52	51.1	61.3 (16.0)	3.0 (1.5)	100 (33)	0 (0.0)
Breen, 2018[75]	U.K.	PTA	473	67.7	67.2 (11.8)	3.3 (1.1)	NR	23 (4.9)
Motoyama, 2019[76]	Japan	OPN	37	62.2	59.8 (10.6)	3.3 (1.5)	360 (632)	1 (2.7)

		RAPN	37	59.5	62.0 (12.7)	2.5 (0.8)	143 (118)	1 (2.7)
Park, 2019[77]	Korea	OPN	53	75.5	53.0 (13.2)	2.5 (0.6)	NR	NR
Furukawa, 2020[78]	Japan	RAPN	804	72.6	63.0 (11.1)	2.6 (1.0)	47 (67)	17 (2.1)
Zangiacomo, 2021[79]	Brazil	PTA	85	74.1	62.7 (11.3)	2.3 (0.8)	NR	2 (2.3)
Bersang, 2021[80]	Denmark	PTA	118	73.7	63.8 (10.4)	2.3 (0.5)	NR	2 (1.8)
Watanabe, 2021[81]	Japan	RAPN	100	64.0	62.6 (13.6)	2.5 (1.1)	111 (167)	NR
Benamran, 2022[82]	France	RAPN	20	55.0	61.3 (5.6)	2.5 (0.7)	63 (24)	1 (5.0)
Bianchi, 2022[83]	Italy	PTA	137	65.7	72.0 (10.5)	2.3 (0.8)	NR	3
Furukawa, 2022[84]	Japan	RAPN	103	74.8	61.0 (11.6)	2.7 (1.0)	61 (96)	5 (4.9)
Junker, 2022[85]	Denmark	PTA	101	71.3	69.2 (10.5)	3.1 (0.9)	NR	3
Sri, 2023[86]	U.K.	RAPN	784	68.0	54.8 (10.0)	3.1 (1.5)	158 (49)	NR

*OPN: open partial nephrectomy, LPN: conventional laparoscopic partial nephrectomy, RAPN: robot-assisted partial nephrectomy, PTA: percutaneous thermal ablation

Table 2. Risk of bias assessment in the included studies

Study	Domain				Total ROB assessment	Comment
	Study participation	Outcome measurement	Study Attrition	Statistical Analysis and Reporting		
Jeschke, 2001[22]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Matin, 2002[23]	Yes	No	Yes	Yes	Serious	A clear definition of the outcomes of interest is not provided
Gill, 2003[24]	Yes	Yes	Yes	Yes	Not serious	NA

Simon, 2003[25]	No	No	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria; a clear definition of the outcome (s) of interest is not provided
Beasley, 2004[26]	Yes	Yes	Yes	Yes	Not serious	NA
Yoshikawa, 2004[27]	No	No	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria; a clear definition of the outcome (s) of interest is not provided
Desai, 2005[28]	Yes	Yes	Yes	Yes	Not serious	NA
Fogarty, 2005[29]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame
Aron, 2008[30]	Yes	Yes	Yes	Yes	Not serious	NA
Bensalah, 2008[31]	No	Yes	Yes	Yes	Serious	Inadequate description of inclusion and exclusion criteria
Finley, 2008[32]	Yes	Yes	Yes	Yes	Not serious	NA
Gong, 2008[33]	Yes	Yes	Yes	Yes	Not serious	NA
DeVoe, 2009[34]	No	No	Yes	Yes	Serious	Inadequate description of inclusion and exclusion criteria; a clear definition of the outcomes of interest is not provided
Ho, 2009[35]	Yes	Yes	Yes	Yes	Not serious	NA
Kural, 2009[36]	No	Yes	Yes	Yes	Serious	Inadequate description of inclusion and exclusion criteria

Mues, 2010[37]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Park, 2010[38]	Yes	Yes	Yes	Yes	Not serious	NA
Scoll, 2010[39]	Yes	Yes	Yes	Yes	Not serious	NA
Sidana, 2010[40]	Yes	Yes	Yes	Yes	Not serious	NA
Lavery, 2011[41]	Yes	Yes	Yes	Yes	Not serious	NA
Lee, 2011[42]	Yes	Yes	Yes	Yes	Not serious	NA
Seo, 2011[43]	No	Yes	Yes	Yes	Serious	Inadequate description of inclusion and exclusion criteria
Guillotreau, 2012[44]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Lucas, 2012[45]	Yes	Yes	Yes	Yes	Not serious	NA
Petros, 2012[46]	Yes	Yes	Yes	Yes	Not serious	NA
Simone, 2012[47]	Yes	Yes	Yes	Yes	Not serious	NA
Atwell, 2013[48]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Ceccarelli, 2013[49]	Yes	Yes	Yes	Yes	Not serious	NA
Choi, 2013[50]	Yes	Yes	Yes	Yes	Not serious	NA
Kim, 2013[51]	No	Yes	Yes	Yes	Serious	Inadequate description of exclusion criteria
Masson-Lecomte, 2013[52]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria

Schips, 2013[53]	No	No	Yes	Yes	Serious	Inadequate description of the sampling frame and exclusion criteria; inadequate method of outcome measurement - may not be validated or reliable
Tanagho, 2013[54]	No	Yes	Yes	Yes	Serious	Inadequate description of the inclusion and exclusion criteria
Williams, 2013[55]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Youn, 2013[56]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, Recruitment, inclusion and exclusion criteria, and place of recruitment
Emara, 2014[57]	Yes	Yes	Yes	Yes	Not serious	NA
Ficarra, 2014[58]	No	No	Yes	Yes	Serious	Sampling frames were two different databases resulting in heterogeneity in surgical techniques; outcomes of interest were not measured in a similar way for all participants
Harris, 2015[59]	Yes	Yes	Yes	Yes	Serious	A clear definition of the outcome (s) of interest is not provided
Kim, 2015[60]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria

Okhunov, 2015[61]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Zargar, 2015- Study 1[62]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame and recruitment
Zargar, 2015- Study 2[63]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame and recruitment
Huang, 2016[64]	No	Yes	Yes	Yes	Serious	Inadequate participation in the study by eligible persons
Li, 2016[65]	No	Yes	Yes	Yes	Serious	Inadequate participation in the study by eligible persons
Oh, 2016[66]	Yes	Yes	Yes	Yes	Not serious	NA
Pantelidou, 2016[67]	Yes	Yes	Yes	Yes	Serious	Outcome of interest was not measured in a similar way for all participants, setting of outcome measurement is not the same for all study participants
Robert, 2016[68]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Han, 2017[69]	Yes	Yes	Yes	Yes	Not serious	NA
Luciani, 2017[70]	Yes	Yes	Yes	Yes	Not serious	NA
Reynolds, 2017[71]	Yes	Yes	Yes	Yes	Not serious	NA
Simsek, 2017[72]	No	Yes	Yes	Yes	Serious	Inadequate description of the source population

Azevedo, 2018[73]	Yes	Yes	Yes	Yes	Serious	A clear definition of the outcome (s) of interest is not provided
Borghesi, 2018[74]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Breen, 2018[75]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Motoyama, 2019[76]	Yes	Yes	Yes	Yes	Not serious	NA
Park, 2019[77]	Yes	Yes	Yes	Yes	Not serious	NA
Furukawa, 2020[78]	No	Yes	Yes	Yes	Serious	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Zangiacomo, 2021[79]	Low	Low	Low	Low	Low	NA
Bersang, 2021[80]	Low	Low	Low	Low	Low	NA
Watanabe, 2021[81]	High	Low	Low	Low	High	Inadequate description of the sampling frame, recruitment, inclusion and exclusion criteria
Benamran, 2022[82]	Low	Low	Low	Low	Low	NA
Bianchi, 2022[83]	Low	Low	Low	Low	Low	NA
Furukawa, 2022[84]	Low	Low	Low	Low	Low	NA
Junker, 2022[85]	Low	Low	Low	Low	Low	NA
Sri, 2023[86]	Low	Low	Low	Low	Low	NA

Table 3. Test of prognostic factors, chi square test, Kruskal Wallis test, and Welch t-test					
Prognostic factor	**Outcome**	**Intervention**	**Chi-squared/t**	**df**	**p**
Region of studies	Major complications	OPN	11.51	2	0.003
		LPN	3.51	3	0.32
		RAPN	0.21	2	0.90
		PTA	1.91	3	0.59
	EBL	OPN	0.21	2	0.90
		LPN	10.53	2	0.005
		RAPN	5.42	3	0.14
Sample size of study	Major complications	OPN	1.50	1	0.22
		LPN	7.65	1	0.006
		RAPN	0.03	1	0.87
		PTA	0.00	1	0.95
	EBL	OPN	0.06	1	0.81
		LPN	0.09	1	0.77
		RAPN	0.03	1	0.87
Risk of bias	Major complications	OPN	0.18	1	0.67
		LPN	0.03	1	0.86
		RAPN	2.61	1	0.11
		PTA	1.87	1	0.17
	EBL	OPN	0.86	1	0.35
		LPN	0.13	1	0.72
		RAPN	0.35	1	0.56

EBL: estimated blood loss; LPN: laparoscopic partial nephrectomy; OPN: open partial nephrectomy; PTA: percutaneous thermal ablation; RAPN: robot-assisted partial nephrectomy.

Table 4. GRADE, certainty of evidence assessment

Outcomes	Interventions	No. of studies	No. of patients	Estimates (mean or proportion, 95% CI)	ROB	Inconsistency	Imprecision	Indirectness	Other consider-ations	Certainty
Major complications (percent)	**OPN**	10	1569	5.4 (2.9–9.9)	Not serious	Very serious[a]	Not serious	Not serious	None	⊕⊕◯◯ Low
	LPN	11	1452	4.70 (2.6–8.3)	Not serious	Very serious[b]	Not serious	Not serious	None	⊕⊕◯◯ Low
	RAPN	20	4962	2.9 (2.3–3.8)	Serious	Serious[c]	Not serious	Not serious	None	⊕⊕⊕◯ Moderate
	PTA	15	2395	2.5 (1.7–3.6)	Serious[d]	Not serious	Not serious	Not serious	None	⊕⊕⊕◯ Moderate
Estimated blood loss (ml)	**OPN**	14	1491	262 (200–324)	Not serious	Serious[e]	Not serious	Not serious	None	⊕⊕⊕◯ Moderate
	LPN	25	1496	224 (193–254)	Serious[f]	Serious[g]	Not serious	Not serious	None	⊕⊕◯◯ Low
	RAPN	29	5477	163 (136–190)	Not serious	Serious[h]	Not serious	Not serious	None	⊕⊕⊕◯ Moderate

[a]The point estimates show a range of low (1.8%) to high (28.6%) proportion of major complications after treatment procedures SRMs patients. [b] The point estimates show a range of low (0.0%) to high (17.1%) proportion of major complications after treatment procedures SRMs patients. [c]The point estimates show a range of low (0.0%) to high (7.2%) proportion of major complications after treatment procedures SRMs patients. [d]Seven studies have high risk of bias in the study participation domain and 2 studies have high risk of bias in the outcome measurement domain. [e]The point estimates show a range of low (65.8 ml) to high (418.0 ml) mean of estimated blood loss in SRMs patients. [f]Ten studies have high risk of bias in the study participation domain and 4 studies have high risk of bias in both study population and outcome measurement domains. [g]The point estimates show a range of low (100.0 ml) to high (401.2ml) mean of estimated blood loss in SRMs patients. [h]The point estimates show a range of low (46.67 ml) to high (329.0 ml) mean of estimated blood loss in SRMs patients. LPN: conventional laparoscopic partial; OPN: open partial nephrectomy; nephrectomy; PTA: percutaneous thermal ablation; RAPN: robot-assisted partial nephrectomy.