Review – Kidney Cancer

Retroperitoneal Robot-assisted Partial Nephrectomy: A Systematic Review and Pooled Analysis of Comparative Outcomes

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Article info

Abstract

Context: Robot-assisted partial nephrectomy (RAPN) has gained increasing popularity as primary minimally invasive surgical treatment for localized renal tumors, and it has preferably been performed with a transperitoneal approach. However, the retroperitoneal approach represents an alternative approach given potential advantages.

Objective: To provide an updated analysis of the comparative outcomes of retroperitoneal RAPN (R-RAPN) versus transperitoneal RAPN (T-RAPN).

Evidence acquisition: A systematic review of the literature was performed up to September 2021 using MEDLINE, EMBASE, and Web of Science databases, according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses

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(PRISMA) recommendations. A sensitivity analysis was performed considering only matched-pair studies.

Evidence synthesis: Seventeen studies, which were published between 2013 and 2021, were retrieved. None of them was a randomized clinical trial. Among the 6,266 patients included in the meta-analysis, 2261 (36.1%) and 4,005 (63.9%) underwent R-RAPN and T-RAPN, respectively. No significant difference was found in terms of baseline features. The T-RAPN group presented a higher rate of male patients (odds ratio [OR]: 0.86, $p = 0.03$) and larger tumor size (weighted mean difference [WMD]: 0.2 cm; $p = 0.003$). The R-RAPN group reported more frequent posterior renal masses (OR: 0.23; $p < 0.0001$). The retroperitoneal approach presented lower estimated blood loss (WMD: 30.41 ml; $p = 0.001$), shorter operative time (OT; WMD: 20.36 min; $p = 0.0001$), and shorter length of stay (LOS; WMD: 0.35 d; $p = 0.002$). Overall complication rates were 13.7% and 16.05% in the R-RAPN and T-RAPN groups, respectively (OR: 1.32; $p = 0.008$). There were no statistically significant differences between the two groups regarding major (Clavien-Dindo classification ≥ 3 grade) complication rate, "pentafecta" achievement, as well as positive margin rates. When considering only matched-pair studies, no difference between groups was found in terms of baseline characteristics. Posterior renal masses were more frequent in the R-RAPN group (OR: 0.6; $p = 0.03$). Similar to the analysis of the entire cohort, R-RAPN reported lower EBL (WMD: 35.56 ml; $p < 0.0001$) and a shorter OT (WMD: 18.31 min; $p = 0.03$). Overall and major complication rates were similar between the two groups. The LOS was significantly lower for R-RAPN (WMD: 0.46 d; $p = 0.02$). No statistically significant difference was found between groups in terms of overall PSM rates.

Conclusions: R-RAPN offers similar surgical outcomes to T-RAPN, and it carries potential advantages in terms of shorter OT and LOS. Available evidence remains limited by the lack of randomized clinical trials.

Patient summary: In this review of the literature, we looked at comparative outcomes of two surgical approaches to robot-assisted partial nephrectomy. We found that the retroperitoneal technique offers similar surgical outcomes to the transperitoneal one, with potential advantages in terms of shorter operative time and length of hospital stay.

1. Introduction

Robot-assisted partial nephrectomy (RAPN) has gained increasing popularity as primary minimally invasive surgical treatment for localized renal tumors [1,2]. RAPN has preferably been performed with a transperitoneal approach, given familiarity with the anatomy and availability of adequate working space [3]. On the contrary, the retroperitoneal approach represents a valid alternative especially for posterior-laterally located renal masses, as it allows direct access to the renal artery without the need for colon mobilization [3].

While the core operative principles for both approaches are similar, important differences exist in terms of patient positioning, working space creation/port placement, and key anatomical landmarks [4]. The selection of the optimal approach plays a critical role in renal surgery, and the debate for defining the role of retroperitoneal and transperitoneal techniques is still ongoing, as shown by the increasing comparative studies over the past few years [5–21].

The aim of the current systematic review is to provide an updated analysis of the comparative outcomes of retroperitoneal RAPN (R-RAPN) versus transperitoneal RAPN (T-RAPN) based on the available literature.

2. Evidence acquisition

2.1. Search strategy and data extraction

An independent systematic review of the literature was performed up to September 2021 by two different authors (F.C. and A.V.), using MEDLINE, EMBASE, and Web of Science databases. The results were assessed by a third author (U.C.). The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) recommendations were followed to design search strategies, selection criteria, and evidence reports [22]. After a first screening based on the title and abstract, full texts of potentially eligible studies were evaluated, and those meeting the inclusion criteria were selected. Patient-related and intervention search terms were combined to build the following search string: "(renal OR kidney) AND (mass OR cancer OR malignancy) AND (robot OR "robot-assisted" OR robotic) AND (transperitoneal OR retroperitoneal)."

Study eligibility was defined using the patient, intervention, comparator, outcome, study type (PICOS) approach. The inclusion criteria were as follows: (P) studies focused on adults (>18 yr old) with a diagnosis of kidney tumor, (I) undergoing R-RAPN (C) in which T-RAPN was performed as a comparator, and (O) evaluating one or more of the surgical and pathological outcomes (S) in retrospective or prospective comparative studies. The study was prospectively registered and approved by the PROSPERO website (www.crd.york.ac. uk/PROSPERO; registration number CRD42017064102).

Noncomparative studies, conference abstracts, editorials, reviews, case reports, letters to the editor, notes, book chapters, and non–English-language articles were excluded. Possible missing articles were retrieved by the assessment of the references of the article included and previous review.

For studies published by the same authors or institutions, only the most recent or largest study was reported to reduce the risk of repeated data. Whenever two studies examined the same national database for overlapping periods, only the larger ones were included. However, the smaller ones could be used to analyze outcomes not reported by the former.

The authors independently carried out data extraction collecting the following information:

1. *Demographics and clinical characteristics:* number, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, baseline estimated glomerular filtration rate (eGFR), tumor-node-metastasis staging, tumor size, and location.
2. *Surgical outcomes:* operative time (OT), estimated blood loss (EBL), warm ischemia time (WIT), length of hospital stay (LOS), overall postoperative complications (defined as Clavien-Dindo grade ≥ 1), major complications (Clavien-Dindo classification ≥ 3 grade), and "pentafecta" achievement (defined as no positive surgical margin [PSM], no 30-d complications, WIT <25 min, preservation of eGFR >90% from baseline at 9–12 mo, and no upstaging of chronic kidney disease) [23].
3. *Pathological outcomes*: PSM and histological features.

2.2. Quality assessment

The level of evidence was established according to the Oxford Level of Evidence Working Group 2011 (https:// www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence). The quality of the included studies was determined using the Newcastle-Ottawa scale for nonrandomized controlled trials (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). A total score of ≤ 5 was considered low quality, 6–7 was considered intermediate quality, and 8–9 was considered high quality.

2.3. Statistical analysis

A meta-analysis was performed using Cochrane Collaboration Review Manager software (RevMan v.5.4; Cochrane Collaboration, Oxford, UK). For the computational part of the meta-analysis, various approaches were used to pool effect measures between studies. For continuous results, mean and standard deviation (SD) were used when reported. For primary studies reporting only median and

interquartile range or "minimum/maximum" range, two different validated mathematical models were used to convert results to means and SDs: for data with a likely normal distribution, the sample means estimator described by Luo et al. [24] was used, while for time-based data or other data suspected of being skewed, the Box-Cox and Quantile Estimation methods described by McGrath et al. [25] were used because of better performance non-normal distributed data. As suggested by the Cochrane Collaboration Group, confidence intervals (CIs) were converted in SDs by dividing these by 3.92 and then multiplying by the square root of the sample size [26].

For continuous data measured on the same scale, pooled weighted mean difference (WMD) and 95% CIs were estimated using the inverse variance method. The pooled odds ratio (OR) and 95% CI were calculated using the Mantel-Haenszel method for binary data. Taking account of predictable substantial between-trial heterogeneity, a random-effect model was used through all the analyses, relying on sensitivity analysis to assess the influence of small-study effects on the results.

A comparative analysis of baseline patient and tumor characteristics was performed to identify statistically significant differences between treatment arms. A sensitivity analysis was performed by considering only studies with a "matched-pair" design.

Statistical heterogeneity between studies was assessed using the I^2 statistic. The results were displayed as forest plots and summary tables showing average effect sizes, I^2, and 95% CI. Data not suitable for meta-analytical evaluation were presented narratively. For all analyses, statistical significance was set to $p < 0.05$. Any disagreement between reviewers was resolved by consensus.

3. Evidence synthesis

3.1. Results

3.1.1. Description of included studies and quality assessment
The PRISMA flow chart is shown in Fig. 1. Our initial research identified 1957 studies. After initial screening and full-text review, 17 studies, which were published between 2013 and 2021, were identified (Table 1) [5–21]. A single study was a prospective nonrandomized study [10]. Seven were observational retrospective case-control studies [5,6,11,13–16], nine were retrospectively matched pair cohort studies [7–9,12,17–21]. No randomized controlled trial was included in the present review.

3.1.2. Demographics and clinical characteristics
Among the 6266 patients included in the meta-analysis, 2261 (36.1%) and 4005 (63.9%) underwent R-RAPN and T-RAPN, respectively [5–21]. There was no statistically significant difference between groups in terms of age ($p = 0.1$) [5,7–21], BMI ($p = 0.8$) [5–13,16,17,19,21], ASA score ($p = 0.9$) [5,9,12,13,16,17,20], RENAL score ($p = 0.07$) [5–8,10,11,13,14,16,17,20,21], baseline eGFR ($p = 0.8$) [6–13,16,19,21], and hilar mass position ($p = 0.85$) [8,13,16–18,21]. The R-RAPN group presented a lower rate
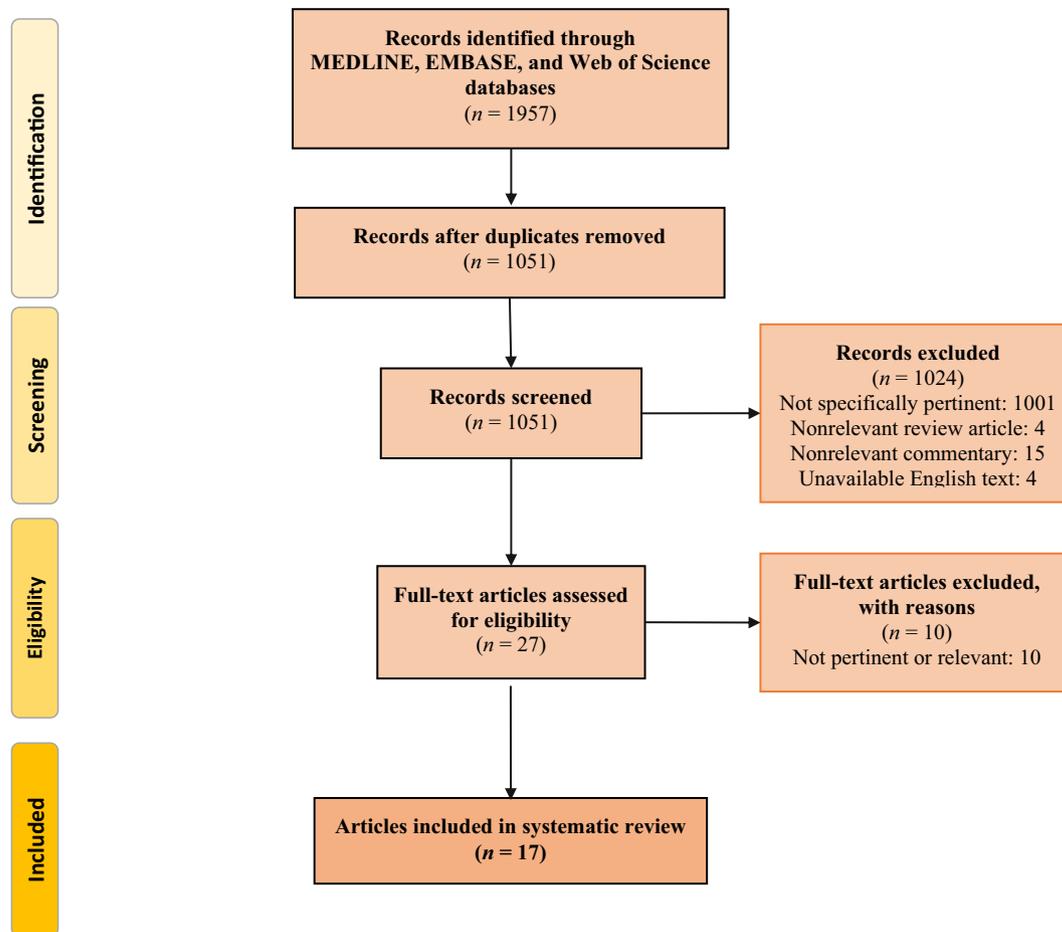
Fig. 1 – PRISMA flowchart. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Table 1 – Overview of collected studies

Reference	Study design	Study origin	Study setting	Study quality[a]	No. of cases (R-RAPN/T-RAPN)	Tumor location	Robotic system
Abaza (2020) [5]	Retrospective	USA	Single center	Low	30/107	Any	Xi
Carbonara (2021) [13]		USA	Multicenter	Low	231/216	Posterior & lateral	–
Choi (2020) [6]		Korea	Single center	Low	213/310	Any	–
Hughes-Hallett (2013) [14]		UK	Multicenter	Low	44/59	Any	–
Kim (2015) [15]		USA	Single center	Low	116/97	Posterior	–
Sharma (2016) [16]		USA	Single center	Very low	25/40	Any	–
Stroup (2017) [11]		USA	Two centers	Low	141/263	Any	–
Arora (2018) [12]	Retrospective, matched pair	USA	Multicenter	Low	99/394	Any	–
Choo (2014) [17]		Korea	Single center	Low	50/57	Any	–
Dell'Oglio (2021) [18]		Italy	Multicenter	Moderate	384/384	Any	–
Harke (2021) [19]		Germany	Multicenter	Moderate	203/551	Any	S, Si, & Xi
Laviana (2018) [20]		USA	Two centers	Low	78/78	Any	–
Maurice (2017) [21]		USA	Multicenter	Low	87/523	Posterior	–
Mittakanti (2020) [7]		USA	Single center	Moderate	281/263	Any	Si & Xi
Paulucci (2019) [8]		USA	Multicenter	Low	162/357	Posterior	–
Takagi (2021) [9]		Japan	Single center	Moderate	48/290	Lateral	–
Tanaka (2013) [10]	Prospective, nonrandomized	Japan	Single center	Moderate	10/16	Any	S

RAPN = robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; T-RAPN = transperitoneal RAPN.
[a] The quality of the included studies was determined using Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group quality assessment (www.gradeworkinggroup.org).

of male patients (OR: 0.86; 95% CI: 0.75–0.99; p = 0.03) [5,6,8–13,15–21] as well as higher tumor size (WMD: 0.2 cm; 95% CI: 0.07–0.33; p = 0.003) [5–17,19,21]. In the R-RAPN group, renal masses were more frequent posteriorly (OR: 0.23; 95% CI: 0.11–0.48; p < 0.0001; Table 2) [6,10,11,14,16–19].

Table 2 – Patient and tumor preoperative characteristics (R-RAPN vs T-RAPN)

Variable	No. of studies with available data	WMD/OR/RR	95% CI	p value
Age (yr)	16	−0.58	−1.35 to 0.19	0.1
Male (n)	15	0.86	0.75–0.99	**0.03**
BMI (kg/m²)	13	−0.07	−0.58 to 0.43	0.8
ASA score	7	1.03	0.65–1.64	0.9
Baseline eGFR (ml/min)	11	0.19	−1.22 to 1.61	0.8
Tumor size (cm)	15	0.2	0.07–0.33	**0.003**
RENAL score (n)	12	0.12	−0.01 to 0.26	0.07
Anterior position (n)	8	3.47	1.59–7.57	**0.002**
Posterior position (n)	8	0.23	0.11–0.48	**<0.0001**
Hilar position (n)	5	1.06	0.56–2.03	0.85

ASA score = American Society of Anesthesiologists score; BMI = body mass index; CI = confidence interval; eGFR = estimated glomerular filtration rate; OR = odds ratio; RAPN= robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; RR = relative risk; T-RAPN = transperitoneal RAPN; WMD = weighted mean difference.
Statistically significant values were reported in bold.
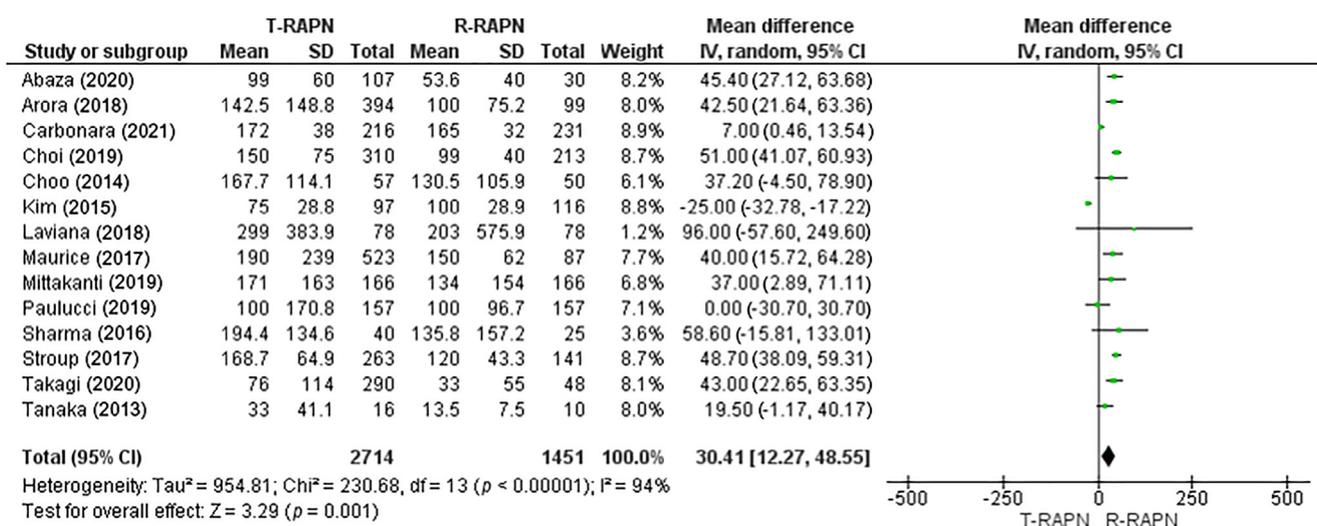
Fig. 2 – The forest plot for estimated blood loss of R-RAPN and T-RAPN groups. CI = confidence interval; df = degrees of freedom; IV = inverse variance; RAPN = robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; SD = standard deviation; T-RAPN = transperitoneal RAPN.

3.1.3. Surgical outcomes

Forest plots for the intraoperative outcomes are illustrated in Figs. 2 and 3, and Supplementary Fig. 1. R-RAPN reported lower EBL (WMD: 30.41 ml; 95% CI: 12.27–48.55; $p = 0.001$) [5–13,15–17,20,21], shorter OT (WMD: 20.36 min; 95% CI: 10.04–30.68; $p = 0.0001$) [5–17,19–21], and shorter console time (WMD: 31.72 min; 95% CI: 7.22–56.21; $p = 0.01$) [7,9].

Overall complication rates were 13.7% and 16.05% in the R-RAPN and T-RAPN groups, respectively (OR: 1.32; 95% CI: 1.08–1.63; $p = 0.008$) [5,7–11,13–17,19–21]. There were no statistically significant differences between the two groups regarding the major (Clavien-Dindo classification ≥3 grade) complication rate (OR: 0.98; 95% CI: 0.62–1.56; $p = 0.93$; Fig. 4) [5–17,19–21].

The LOS was significantly lower for R-RAPN than for T-RAPN (WMD: 0.35 d; 95% CI: 0.13–0.58; $p = 0.002$; Fig. 5) [5–14,17,19–21]. No difference was found in "pentafecta" achievement between the groups (Supplementary Fig. 2) [6,11].

No statistically significant difference was found between groups in terms of overall PSM rates (OR: 1.11; 95% CI: 0.72–1.72; $p = 0.64$; Fig. 6) [5–12,14,16–21], conversion to radical nephrectomy, as well as histological features (Supplementary Figs. 3 and 4) [6,7,10,14,16,17,19,20].

3.1.4. Sensitivity analysis

When considering only matched-pair studies, no difference between groups was found in terms of age ($p = 0.5$) [7–9,12,17,19–21], male gender rate ($p = 0.07$) [7–9,12,17,20,21], BMI ($p = 0.9$) [7–9,12,17,19,21], ASA score ($p = 0.29$) [9,12,17,20], tumor size ($p = 0.44$) [8,12,17,18,20,21], RENAL score ($p = 0.24$) [7,8,17,20,21], baseline eGFR ($p = 0.7$) [7–9,12,21,27], and hilar mass location ($p = 0.7$) [17,18,21]. Posterior renal masses were more frequent in the R-RAPN group (OR: 0.6; 95% CI: 0.38–0.94; $p = 0.03$; Supplementary Table 1) [17–19]. Forest plots of paired-design studies are illustrated in Supplementary Figs. 5–10. Similar to the analysis of the entire cohort, R-RAPN reported lower EBL (WMD: 35.56 ml; $p < 0.0001$) and a shorter OT (WMD: 18.31 min; $p = 0.03$) [7–9,12,17,19–21]. Overall and major complication rates were similar between the two groups [7–9,12,17–21]. The LOS was significantly lower for R-RAPN (WMD: 0.46 d; $p = 0.02$) [7–9,12,17,19–21]. No statistically significant difference was found between groups in terms of overall
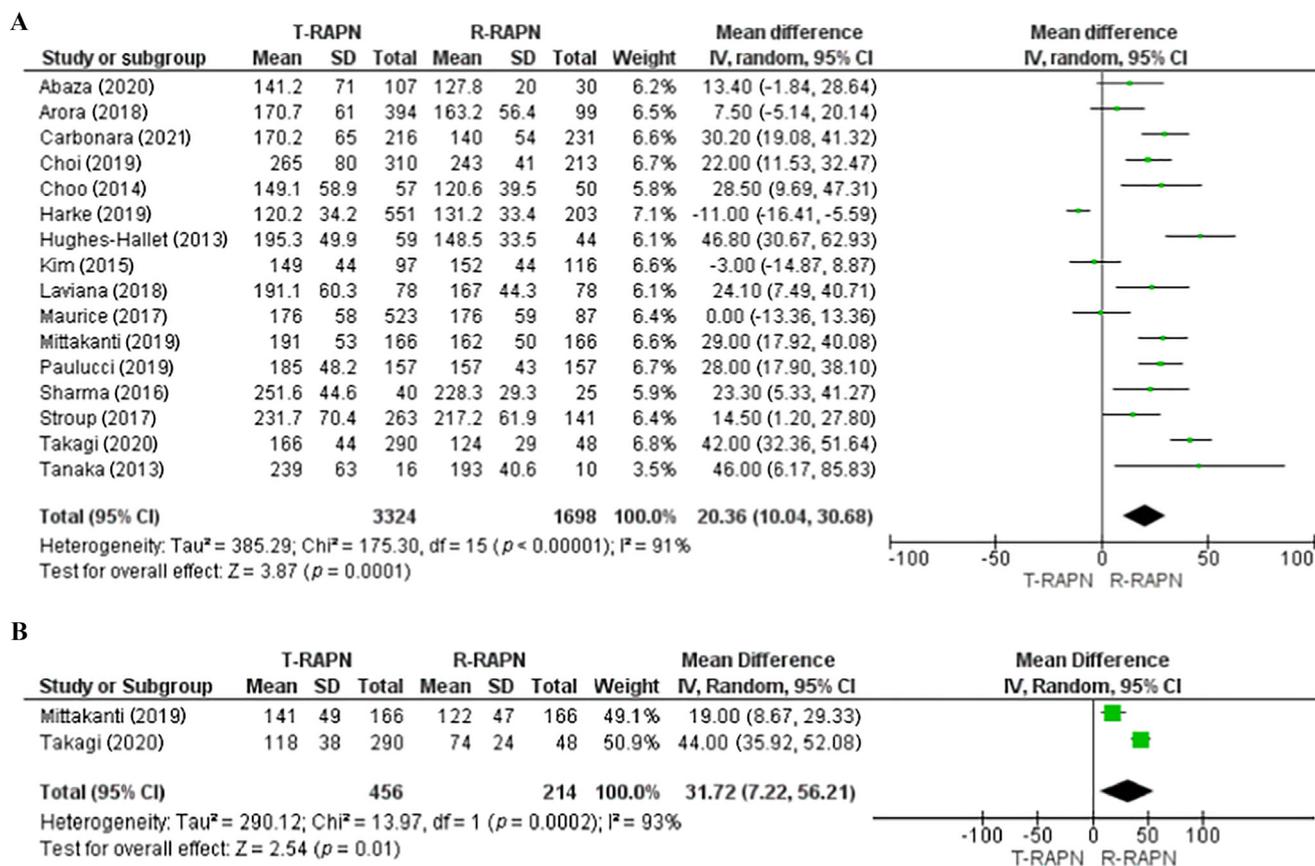
Fig. 3 – (A) Forest plots for (A) operative time of the R-RAPN and T-RAPN groups, and (B) console time of the R-RAPN and T-RAPN groups. CI = confidence interval; df = degrees of freedom; IV = inverse variance; RAPN = robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; SD = standard deviation; T-RAPN = transperitoneal RAPN.

PSM rates (OR: 1.1; p = 0.71) [7–9,12,17–21]. No matched-pair studies assessed the "pentafecta" achievement.

3.1.5. Heterogeneity

Moderate to high heterogeneity among studies was found for most of the outcomes. High heterogeneity ($I^2 > 60\%$) was found for EBL, OT, console time, and mean LOS. However, one should assume that the I^2 statistic might carry a substantial bias when the number of studies is very small [28].

3.1.6. Risk of bias within studies

The quality of the studies' assessment according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group (www.gradeworkinggroup.org) is shown in Table 1. Five studies reported moderate scores according to GRADE [7,9,10,18,19]. Eleven studies reported low quality [5,6,8,11–15,17,20] and a single paper reported very low grade [16]. These findings can be explained by the retrospective study design of the intermediate-quality study. Moreover, no randomized controlled trial is present in the current analysis. Moreover, no differences were observed in the subgroup analysis when compared according to the specified categories.

3.2. Discussion

Herein, we present the largest cumulative analysis to date of studies comparing the retroperitoneal and transperitoneal approaches for RAPN. Overall, our findings show that these two approaches provide similar surgical outcomes. In a previous analysis, Pavan et al. [29] included seven studies for a total number of 1379 patients, with R-RAPN reporting shorter OT (WMD: 20.17 min; p = 0.004), lower EBL (WMD: 54.57 ml; p = 0.03), and LOS (WMD: 0.46 d; p = 0.003). Our analysis is based on a much more robust sample, including 16 studies for a total of 5755 patients. Moreover, we also performed a sensitivity analysis with the aim of minimizing selection bias.

In the pooled analysis, the R-RAPN group showed a lower rate of male patients (OR: 0.86; p = 0.03), even though this difference was not statistically significant in the sensitivity analysis. Differences in the subcutaneous and perirenal fat distribution are present between genders, with men exceeding women in perirenal fat [30]. Certainly, renal mass location and characteristics are key factors to assist the surgeon in selecting the most appropriate surgical approach, but other patients' characteristics including perirenal fat might be considered to tailor the surgical strategy [4,31,32]. The retroperitoneal approach is technically challenging in patients with significant peri- and pararenal fat,

Study or subgroup	T-RAPN Events	Total	R-RAPN Events	Total	Weight	Odds ratio M-H, random, 95% CI
3.7.1 Overall complications						
Abaza (2020)	3	107	0	30	0.5%	2.04 (0.10, 40.65)
Carbonara (2021)	54	216	47	231	13.1%	1.30 (0.84, 2.04)
Choo (2014)	5	57	7	50	2.7%	0.59 (0.17, 1.99)
Harke (2019)	38	176	24	176	9.7%	1.74 (1.00, 3.05)
Hughes-Hallet (2013)	6	59	4	44	2.3%	1.13 (0.30, 4.28)
Kim (2015)	10	97	8	116	4.0%	1.55 (0.59, 4.10)
Laviana (2018)	28	78	19	78	7.0%	1.74 (0.87, 3.48)
Maurice (2017)	42	296	9	74	5.9%	1.19 (0.55, 2.58)
Mittakanti (2019)	22	166	26	166	8.5%	0.82 (0.45, 1.52)
Paulucci (2019)	19	157	18	157	7.1%	1.06 (0.54, 2.11)
Sharma (2016)	17	40	4	25	2.6%	3.88 (1.12, 13.40)
Stroup (2017)	36	263	16	141	8.2%	1.24 (0.66, 2.32)
Takagi (2020)	43	290	2	48	1.9%	4.00 (0.94, 17.11)
Tanaka (2013)	1	16	1	10	0.5%	0.60 (0.03, 10.82)
Subtotal (95% CI)		**2018**		**1346**	**74.0%**	**1.32 (1.08, 1.63)**
Total events	324		185			

Heterogeneity: Tau² = 0.00; Chi² = 11.71, df = 13 (p = 0.55); I² = 0%
Test for overall effect: Z = 2.64 (p = 0.008)

Study or subgroup	T-RAPN Events	Total	R-RAPN Events	Total	Weight	Odds ratio M-H, random, 95% CI
3.7.2 Major complications (Clavien-Dindo ≥3)						
Abaza (2020)	0	107	0	30		Not estimable
Arora (2018)	5	394	2	99	1.5%	0.62 (0.12, 3.26)
Carbonara (2021)	2	216	1	231	0.7%	2.15 (0.19, 23.88)
Choi (2019)	2	310	3	213	1.3%	0.45 (0.08, 2.74)
Choo (2014)	0	57	0	50		Not estimable
Harke (2019)	14	176	5	176	3.5%	2.96 (1.04, 8.39)
Hughes-Hallet (2013)	0	0	0	0		Not estimable
Kim (2015)	7	97	5	116	2.8%	1.73 (0.53, 5.62)
Laviana (2018)	5	78	4	78	2.2%	1.27 (0.33, 4.91)
Maurice (2017)	9	523	4	87	2.7%	0.36 (0.11, 1.21)
Mittakanti (2019)	6	166	14	166	3.9%	0.41 (0.15, 1.09)
Paulucci (2019)	5	157	8	157	3.0%	0.61 (0.20, 1.92)
Sharma (2016)	5	40	1	25	0.9%	3.43 (0.38, 31.22)
Stroup (2017)	7	263	4	141	2.6%	0.94 (0.27, 3.26)
Takagi (2020)	13	290	0	48	0.5%	4.72 (0.28, 80.70)
Tanaka (2013)	1	16	0	10	0.4%	2.03 (0.08, 54.83)
Subtotal (95% CI)		**2890**		**1627**	**26.0%**	**0.98 (0.62, 1.56)**
Total events	81		51			

Heterogeneity: Tau² = 0.17; Chi² = 15.81, df = 12 (p = 0.20); I² = 24%
Test for overall effect: Z = 0.09 (p = 0.93)

Total (95% CI)		**4908**		**2973**	**100.0%**	**1.22 (0.99, 1.50)**
Total events	405		236			

Heterogeneity: Tau² = 0.03; Chi² = 29.55, df = 26 (p = 0.29); I² = 12%
Test for overall effect: Z = 1.90 (P = 0.06)
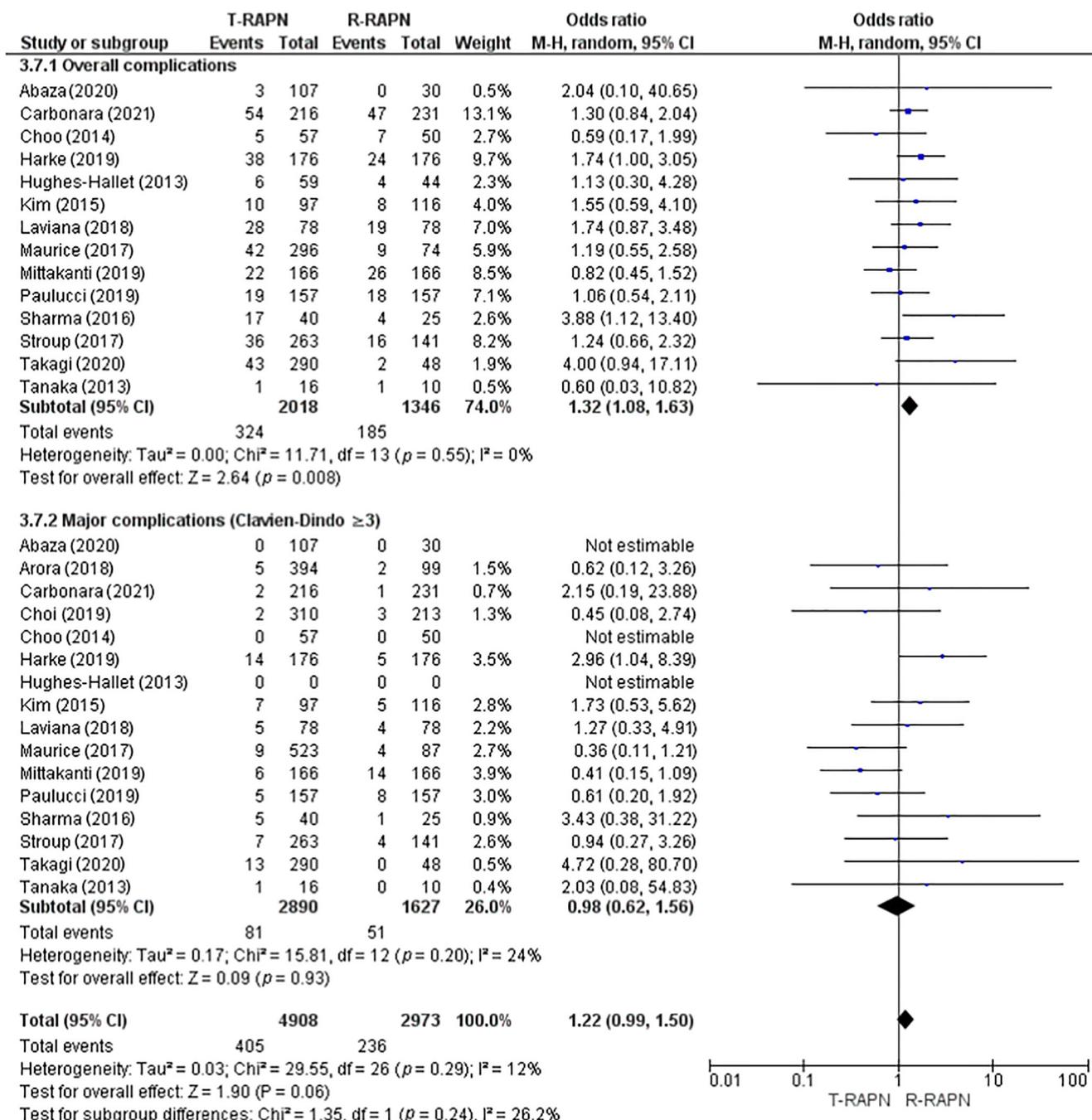Test for subgroup differences: Chi² = 1.35, df = 1 (p = 0.24), I² = 26.2%

Fig. 4 – Forest plot for overall and major (Clavien-Dindo classification ≥3 grade) complications of the R-RAPN and T-RAPN groups. CI = confidence interval; df = degrees of freedom; M-H = Mantel-Haenszel; RAPN = robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; T-RAPN = transperitoneal RAPN.

and the transperitoneal approach may be preferable if one is at the beginning of the experience with the retroperitoneal approach [33].

Not surprisingly, the retroperitoneal approach was mostly used for posteriorly located tumors (OR: 0.23; p < 0.0001) and the transperitoneal approach for anterior ones (OR: 3.47; p = 0.002). Overall, four studies compared the outcomes of the two approaches in posterior renal masses only [8,13,15,21]. In a matched-pair analysis, Paulucci et al. [8] showed a lower OT (157 vs 185 min)

and shorter LOS (1 vs 2 d) in the R-RAPN group. Conversely, the other two studies both reported a similar OT with a shorter LOS for patients undergoing R-RAPN [15,21]. The difference in the study period, as well as the early phase of the R-RAPN learning curve, could have influenced these intraoperative outcomes. From a technical point of view, potential advantages of R-RAPN in posterior renal tumors might have been offset by potential technical challenges such as compromised instrument triangulation, limited and unfamiliar working space, and heightened robotic arm

Study or subgroup	T-RAPN Mean	SD	Total	R-RAPN Mean	SD	Total	Weight	Mean difference IV, random, 95% CI	Mean difference IV, random, 95% CI
Abaza (2020)	0.9	1	107	0.7	1	30	8.3%	0.20 (−0.20, 0.60)	
Arora (2018)	3	1.4	394	1.7	1.5	99	9.1%	1.30 (0.97, 1.63)	
Carbonara (2021)	2	1	216	2	1	231	10.4%	0.00 (−0.19, 0.19)	
Choi (2019)	9	1.2	310	9	1.2	213	10.2%	0.00 (−0.21, 0.21)	
Choo (2014)	0	0	0	0	0	0		Not estimable	
Harke (2019)	8.14	3.27	551	10.3	8.4	203	2.8%	−2.16 (−3.35, −0.97)	
Hughes-Hallet (2013)	4.6	5.6	59	2.5	11.2	44	0.4%	2.10 (−1.50, 5.70)	
Laviana (2018)	2.7	1.7	78	1.8	0.9	78	8.0%	0.90 (0.47, 1.33)	
Maurice (2017)	2.6	1.2	523	2.2	0.9	87	10.1%	0.40 (0.18, 0.62)	
Mittakanti (2019)	1.9	1.3	166	1.7	0.9	166	9.9%	0.20 (−0.04, 0.44)	
Paulucci (2019)	1.6	0.75	157	1.4	0.75	157	10.5%	0.20 (0.03, 0.37)	
Stroup (2017)	2.5	0.7	263	2.2	0.6	141	10.8%	0.30 (0.17, 0.43)	
Takagi (2020)	4.2	1.8	290	3.3	0.7	48	9.5%	0.90 (0.61, 1.19)	
Tanaka (2013)	0	0	0	0	0	0		Not estimable	
Total (95% CI)			3114			1497	100.0%	0.35 (0.13, 0.58)	

Heterogeneity: Tau² = 0.12; Chi² = 99.02, df = 11 (p < 0.00001); I² = 89%
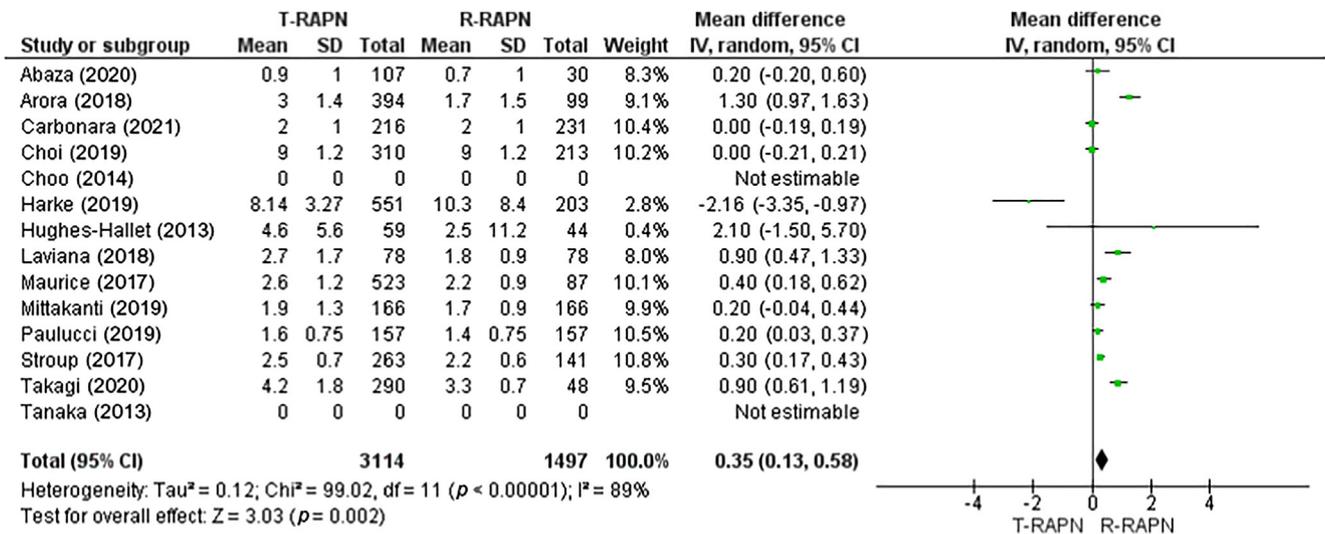Test for overall effect: Z = 3.03 (p = 0.002)

Fig. 5 – Forest plot for length of stay of the R-RAPN and T-RAPN groups. CI = confidence interval; df = degrees of freedom; IV = inverse variance; RAPN = robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; SD = standard deviation; T-RAPN = transperitoneal RAPN.

Study or subgroup	T-RAPN Events	Total	R-RAPN Events	Total	Weight	Odds ratio M-H, random, 95% CI	Odds ratio M-H, random, 95% CI
Abaza (2020)	0	107	0	30		Not estimable	
Arora (2018)	8	394	2	99	6.8%	1.01 (0.21, 4.81)	
Carbonara (2021)	9	216	5	231	13.5%	1.97 (0.65, 5.96)	
Choi (2019)	4	310	0	213	1.9%	6.27 (0.34, 117.05)	
Choo (2014)	1	57	0	50	1.6%	2.68 (0.11, 67.31)	
Dell'Oglio (2018)	14	384	7	384	19.7%	2.04 (0.81, 5.11)	
Harke (2019)	0	176	0	176		Not estimable	
Hughes-Hallet (2013)	3	59	3	44	6.1%	0.73 (0.14, 3.81)	
Laviana (2018)	2	78	3	78	5.0%	0.66 (0.11, 4.05)	
Maurice (2017)	5	296	1	74	3.6%	1.25 (0.14, 10.90)	
Mittakanti (2019)	5	166	8	166	12.8%	0.61 (0.20, 1.92)	
Paulucci (2019)	3	157	5	157	7.9%	0.59 (0.14, 2.52)	
Sharma (2016)	1	40	1	25	2.1%	0.62 (0.04, 10.30)	
Stroup (2017)	11	263	4	141	12.3%	1.50 (0.47, 4.78)	
Takagi (2020)	3	48	2	48	4.9%	1.53 (0.24, 9.61)	
Tanaka (2013)	0	16	1	10	1.5%	0.19 (0.01, 5.20)	
Total (95% CI)		2767		1926	100.0%	1.20 (0.80, 1.81)	
Total events	69		42				

Heterogeneity: Tau² = 0.00; Chi² = 8.18, df = 13 (p = 0.83); I² = 0%
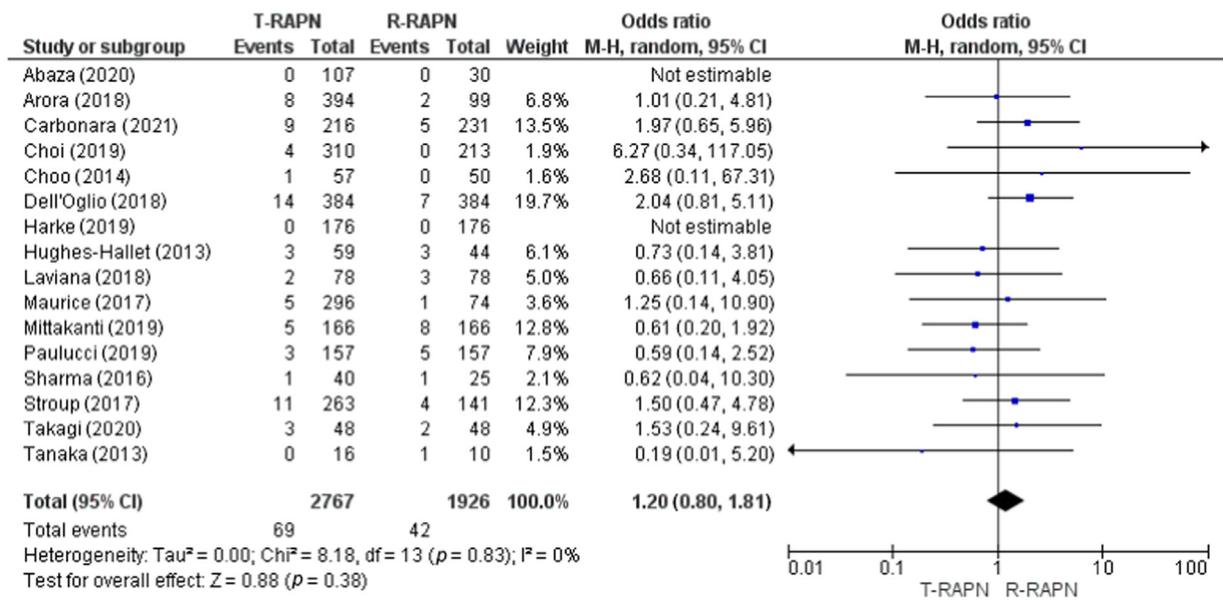Test for overall effect: Z = 0.88 (p = 0.38)

Fig. 6 – Forest plot for positive surgical margins of the R-RAPN and T-RAPN groups. CI = confidence interval; df = degrees of freedom; M-H = Mantel-Haenszel; RAPN = robot-assisted partial nephrectomy; R-RAPN = retroperitoneal RAPN; T-RAPN = transperitoneal RAPN.

clashes that might negatively affect operative outcomes [4]. These issues have partially been overcome with the introduction of the DaVinci Xi system, which features robotic arms mounted on movable overhead boom and thinner robotic arms with additional joints compared with the previous DaVinci Si system. While this might not translate into a difference in the outcomes of T-RAPN, this might not be the case for the retroperitoneal approach where the use of the Xi system is likely to facilitate the procedure, particularly by facilitating the use of the fourth arm [34,35]. Unfortunately, a lack of information regarding the used robotic platform did not allow us to perform a sensitivity analysis on this. An additional technological evolution is represented by the DaVinci SP platform, which is specifically designed to

work in smaller anatomical spaces and could allow for a single approach to comfortably treat either anterior or posterior renal masses [36].

Regarding intraoperative outcomes, a shorter OT was found when considering the entire sample (WMD: 20.36 min; p = 0.0001) [5–17,19–21], and this was also the case when considering matched pair studies only (WMD: 18.3 min; p = 0.03). Intuitively, these findings can be explained considering that the retroperitoneal approach allows immediate access to the kidney, without the need for bowel mobilization and flipping of the kidney, and avoiding intra-abdominal adhesions in patients with previous abdominal surgeries [4,14]. Moreover, most surgeons are more familiar with the transperitoneal approach and would

still use this approach even in posterior tumors, spending more time during the procedure [4,14]. Only two studies had shown the console time to be significantly lower in the R-RAPN group (WMD: 31.72 min; $p = 0.01$) [7,9]. Takagi et al. [9] analyzed the outcomes of 290 and 48 patients with laterally located renal mass who underwent R-RAPN and T-RAPN, respectively. After propensity-score matching, the authors reported a shorter mean OT (124 vs 151 min) with a lower mean console time (74 vs 110 min) in the R-RAPN group. One should consider that both OT and console time are influenced by different variables that would be difficult to account for. This is especially the case in the setting of teaching hospitals where trainees might be involved in the case as console surgeons.

In our analysis, no differences were observed regarding WIT in both approaches. In a recent randomized clinical trial, Antonelli et al. [37] compared the functional outcomes of on- versus off-clamp RAPN performed with the retroperitoneal and transperitoneal approaches. The authors found no differences between clamp techniques in terms of absolute variation of GFR at 6, 12, 18, and 24 mo. Thus, in patients with normal baseline function and normal contralateral kidneys, the impact of WIT on functional outcomes is negligible.

In our cumulative analysis, EBL was lower in patients undergoing R-RAPN (WMD: 33.41 ml; $p = 0.001$). However, such a difference in EBL cannot be considered clinically significant, despite reaching statistical significance. Abaza et al. [5] reported significantly lower mean EBL in the R-RAPN group (53.6 vs 9 ml, $p = 0.001$), explaining this difference with the requirement of a lower amount of tissue dissection.

Concerning postoperative outcomes, our analysis reported a shorter LOS for patients who underwent R-RAPN (WMD: 0.35 d; $p = 0.002$). In a recent study, Porpiglia et al. [38] compared the retroperitoneal and transperitoneal approaches in 1669 patients who were treated with minimally invasive partial nephrectomy at 26 Italian centers. Overall, the R-RAPN group presented a shorter median LOS (2 vs 3 d; $p < 0.0001$). According to the authors, faster return of bowel function and drain removal time were potential reasons for a shorter hospital stay in R-RAPN patients [38]. A significant reduction in the mean LOS was also recorded by Abaza et al. [5], with 0.7 d for the R-RAPN and 0.9 d for the T-RAPN group ($p = 0.01$). In this regard, Kim et al. [15] showed that the transperitoneal approach (OR: 7.39; $p < 0.01$) and tumor size (OR: 1.6; $p = 0.04$) were significant predictors of LOS >1 d on a multivariate analysis when controlling for age, sex, BMI, patient comorbidity, previous abdominal surgery, baseline kidney function, and nephrometry score. In general, postoperative LOS is influenced by factors other than the surgical approach, including surgeon's own experience, and center-specific perioperative care pathways. In general, a single overnight stay is achievable in most patients undergoing RAPN [39]. The omission of a drain in most cases is another factor that might have contributed to this trend of reduced LOS [40].

Regarding postoperative complications, the previous cumulative analysis by Pavan et al. [29] reported a similar rate of overall ($p = 0.67$) and major ($p = 0.82$) postoperative complications. It was interesting to see that our cumulative analysis of all studies showed a lower overall postoperative complications rate for R-RAPN (13.7% vs 16.05%, $p = 0.008$), while no difference was found when considering matched-pair reports only (OR: 1.27; $p = 0.16$). In addition, no difference was found in major complications (OR: 0.98; $p = 0.93$), which, from a clinical standpoint, is likely to be the most meaningful finding.

Concerning pathological outcomes, our analysis showed no difference in terms of PSM as well as malignant/benignant rate. Regarding surrogate of surgical quality, we found no difference in terms of "pentafecta" achievement (defined as no PSM, no 30-d complications, WIT <25 min, preservation of eGFR >90% from baseline at 9–12 mo, and no upstaging of chronic kidney disease), but this was evaluated by only two studies [6,11]. However, further studies are needed to better address the comparison of oncological and functional outcomes between T-RAPN and R-RAPN.

Regarding the cost analysis, a single study reported this finding [20] and no cumulative analysis could be performed. Laviana et al. [20] found that T-RAPN added $2337 in cost considering factors in disposable equipment, OT, LOS, and personnel. Moreover, the R-RAPN group was associated with a 76% lower probability of hospital stay of at least 2 d compared with the T-RAPN group ($p < 0.001$). Of course, these findings might not be generalizable to other hospital centers or healthcare settings, and further studies are needed to better explain these findings [41].

This systematic review of the literature presented some limitations. First and foremost, most of the studies included in the analysis are either retrospective or prospective nonrandomized, and no randomized controlled trials were reported. This might translate into a high likelihood of a selection bias. The second limitation is the lack of a functional outcome analysis as well as short- and long-term oncological outcomes [42]. Last, it was not possible to account for existing differences among centers and single surgeons in terms of surgical technique and expertise, as well as protocols of perioperative management and follow-up.

4. Conclusions

The main findings of our analysis are that R-RAPN offers similar surgical outcomes to T-RAPN, and it carries potential advantages in terms of shorter OT and LOS. These findings should be interpreted by keeping in mind that currently available evidence is based on a good number of high-quality comparative studies, but it remains limited by the lack of randomized clinical trials.

Author contributions: Riccardo Autorino had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Carbonara, Autorino.

Acquisition of data: Carbonara, Crocerossa, Veccia.

Analysis and interpretation of data: Carbonara, Crocerossa, Autorino.

Drafting of the manuscript: Carbonara.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.03.015.

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