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SYSTEMATIC REVIEW **Open Access**

Comparative efficacy of cryoablation versus robot-assisted partial nephrectomy in the treatment of cT1 renal tumors: a systematic review and meta-analysis

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Abstract

Purpose This study utilizes a meta-analytic approach to investigate the effects of cryoablation and robot-assisted partial nephrectomy on perioperative outcomes, postoperative renal function, and oncological results in patients.

Methods This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Four electronic databases (PubMed, Embase, Web of Science, and the Cochrane Library database) were systematically searched to identify relevant studies published in English up to November 2023. The primary outcomes were perioperative results, complications, postoperative renal function and oncologic outcomes. Review Manager 5.4 was used for this analysis.

Results This study included a total of 10 studies comprising 2,011 patients. Compared to RAPN (Robot-Assisted Partial Nephrectomy), the CA (Cryoablation) group had a shorter hospital stay [MD -1.76 days; 95% CI -3.12 to -0.41; $p = 0.01$], less blood loss [MD -104.60 ml; 95% CI -152.58 to -56.62; $p < 0.0001$], and fewer overall complications [OR 0.62; 95% CI 0.45 to 0.86; $p = 0.004$], but a higher recurrence rate [OR 7.83; 95% CI 4.32 to 14.19; $p < 0.00001$]. There were no significant differences between the two groups in terms of operative time, minor complications (Clavien-Dindo Grade 1–2), major complications (Clavien-Dindo Grade 3–5), changes in renal function at 12 months post-operation, RFS (Recurrence-Free Survival), and OS (Overall Survival).

Conclusion The evidence provided by this meta-analysis indicates that the therapeutic effects of Cryoablation (CA) are similar to those of Robot-Assisted Partial Nephrectomy (RAPN) in terms of perioperative outcomes and renal function. However, the recurrence rate of tumors treated with CA is significantly higher.

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Systematic review registration The study has been registered on the International Prospective Register of Systematic Reviews (PROSPERO: CRD42023465846).

Keywords Renal tumors, Ablation, Cryoablation, Robot-assisted partial nephrectomy, Meta-analysis

Introduction

Kidney cancer accounts for over 3% of all new cancer cases globally, affecting more than 430,000 people annually. Moreover, the incidence of kidney cancer is on the rise [1]. Recent advancements in imaging technology have enabled earlier diagnosis of kidney cancer for many patients [2]. As a result, a large portion of newly diagnosed renal tumors are asymptomatic and incidentally discovered, with tumor diameters smaller than 7 cm. Partial nephrectomy is generally considered the gold standard for the treatment of renal tumors [3], and now we can achieve better treatment outcomes with the aid of robotic assistance [4]. Recently, ablation therapy has garnered attention as a viable treatment option for patients with multiple comorbidities or deemed unsuitable for surgery [3, 5, 6]. Among ablation techniques, radiofrequency ablation and cryoablation are often preferred as first-line treatments [7]. In fact, compared to radiofrequency ablation, cryoablation can achieve a broader tumor coverage, thereby preventing tumor recurrence [8]. Moreover, cryoablation (CA) is favored due to the visualization of the ablation area, allowing for continuous monitoring of the ablated zone [9, 10]. Therefore, comparative studies between CA and robot-assisted partial nephrectomy (RAPN) are highly meaningful. The purpose of this article is to conduct a systematic review and meta-analysis to evaluate the perioperative, complication, renal function, and oncological outcomes of CA and RAPN.

Methods

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement 2020 [11] (Supplemental Digital Content 1). Quality assessment was performed according to Assessing the Methodological Quality of Systematic Reviews (AMSTAR) 2 (Supplemental Digital Content 2) and was registered in PROSPERO [12].

Eligibility criteria

Eligibility criteria were formulated using the specific population, intervention, comparison, outcomes, and study design (PICOS) framework. This review included studies that met the following criteria: (P): Patients with Clinical stage T1 renal tumors; (I): Treatment with cryoablation technology; (C): Use of robot-assisted surgery as a comparative treatment; (O): Perioperative, renal function, and oncological outcomes; (S): Retrospective and prospective cohort studies. Case series, surveys, letters, editorial comments, reviews, and animal studies were not included. In addition, studies without original data and articles in languages other than English were excluded.

Information sources, search strategy, and selection process

A systematic search was conducted in PubMed, Embase, Web of Science, and the Cochrane Library databases. The search terms used were: (Renal) AND (Neoplasms) AND (Cryoablation) AND (Partial Nephrectomy OR Robot-assisted).

The search results were limited to human studies, including research published from the inception of the databases up to November 1, 2023. Two authors (GHY and ZL) reviewed the articles based on predetermined inclusion/exclusion criteria. Any conflicts regarding eligibility were resolved by the two authors, and any disagreements were resolved by a third party (WT). Studies that met our PICOS criteria were also included.

Data collection process and data items

We extracted relevant data from studies, including study characteristics (first author, year of publication, country, study design, number of participants), baseline demographic data (age, Body Mass Index (BMI), tumor size, RENAL nephrometry score, Charlson comorbidity index(CCI), follow-up period), perioperative outcomes (operative time, hospital stay, blood loss, overall complications, Minor, Clavien 1–2, Major, Clavien 3–5), renal function, and oncological outcomes (recurrence rate, recurrence-free survival, and overall survival).

Risk of bias assessment

The Newcastle–Ottawa Scale (NOS) [13, 14] was used to assess the quality of non-RCT. The NOS checklist includes three quality parameters: population selection (4 points), comparability of cohorts (2 points), and assessment of outcome for cohort studies (3 points). Each study received a score ranging from 0 to 9. Studies with a score of 7 or higher were considered high-quality articles.

Synthesis methods

The meta-analysis included retrospective and prospective cohort studies and was performed using Review Manager 5.4 (Cochrane Collaboration, Oxford, UK). We pooled clinical effect estimates using the mean difference (MD), odds risk (OR), and their respective 95% CIs. The statistical significance level was set at $p<0.05$. The Mantel–Haenszel effects model and inverse-variance effects model were used to combine the trials. We calculated and depicted forest plots with a 95% CI. The I^2 test and Cochran's Q test were used to assess the heterogeneity. Statistical heterogeneity was indicated by $p<0.05$ in the Cochran's Q test and $I^2 > 50\%$ in the I^2 test. If heterogeneity existed, a random effect model was adopted; otherwise, a fixed effect model was adopted. I^2 values of 25%, 50%, and 75% indicate low, moderate, and high levels of inconsistency, respectively [15]. Further sensitivity analyses were conducted to reduce heterogeneity and confirm the reliability of our findings.

Results

Study selection, characteristics, and risk of bias

We initially identified 3,491 articles, of which 10 were selected for further analysis [16–25]. Figure 1 describes the search process (PRISMA flowchart). Among the included 10 studies, there were 2,011 patients involved, with 1,029 (51.2%) in the Cryoablation (CA) group and 982 (48.8%) in the Robot-Assisted Partial Nephrectomy (RAPN) group. All studies were retrospective, and five were propensity score analysis studies [16, 17, 19, 22, 23]. All studies reported perioperative outcomes and complications, with 8 studies providing results on changes in renal function [16, 18, 20–25]. Table 1 provided baseline characteristics of the patients, including age, BMI, sample

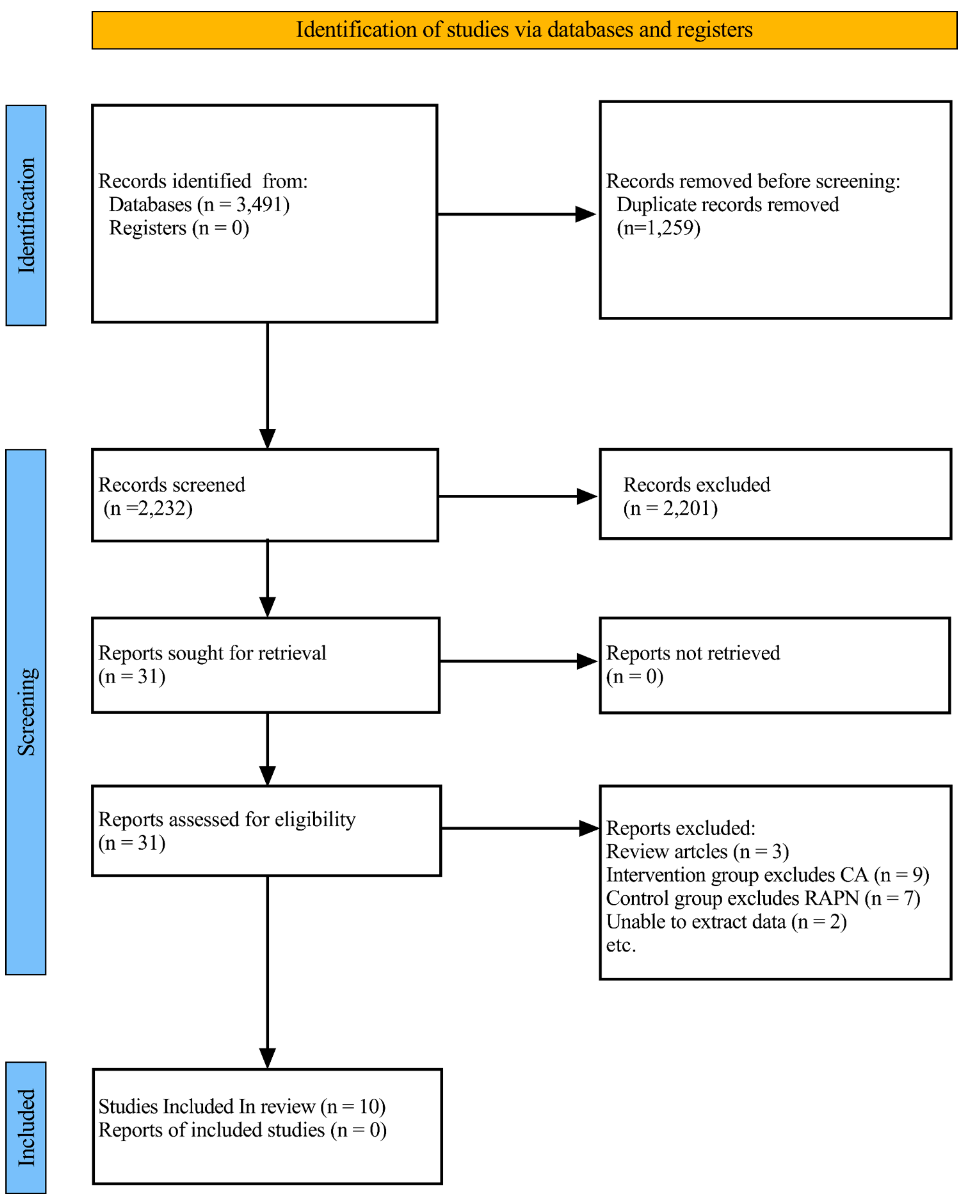

Fig. 1 PRISMA flowchart

Table 1 Baseline characteristics

		Patients(n)		Age(year)		BMI(kg/m^2)		Tumor size(cm)		RENAL ≥ 10(n)		CCI(n)		Surgical approach	Follow-up duration(month)	
Reference	**Country**	**CA**	**RAPN**	**CA**	**RAPN**	**CA**	**RAPN**	**CA**	**RAPN**	**CA**	**RAPN**	**CA**	**RAPN**		**CA**	**RAPN**
Kawaguchi, S [21]	Japan	49	50	78.44(4.7)	75.35(3.12)	23.7(3.8)	23.1(2.4)	2.4(0.8)	2.7(1.2)	0	1	NA.	NA.	PCA/RAPN	20.1(14.5)	24.3(14.5)
Uemura, T [25]	Japan	48	78	76.58(9.17)	60.65(12.84)	23.35(3.82)	23(3.02)	2.67(1.07)	1.9(0.6)	5	3	NA.	NA.	PCA/RAPN	16.96(19.87)	20.26(13.6)
Liu, HY [22]	Taiwan	55	55	59.44(14.77)	57.27(13.28)	25.04(4.23)	25.29(4.58)	3.86(2.13)	4.06(2.01)	14	11	NA.	NA.	LCA/RAPN	54.96(34.59)	33.2(19.55)
Rembeyo, G [23]	France	55	36	71.67(4.39)	60.09(2.65)	26.92(1.10)	29(1.51)	4.62(0.29)	4.55(0.34)	19	4	NA.	NA.	CA/RAPN	20.14(2.57)	23.73(3.95)
Fraisse, G [19]	France	177	177	69.94(9.38)	59.89(10.75)	NA.	NA.	2.59(0.86)	2.77(0.92)	10	10	3.21(1.72)	2.87(2.06)	PCA/RAPN	NA.	NA.
Bertolo, R [16]	America	65	65	79.3(4.1)	79.3(3.3)	27.9(5.9)	27.4(4.9)	3(1)	2.9(1)	NA.	NA.	2.3(1.6)	2(1.5)	PCA/RAPN	45.65(11.37)	36.65(11.37)
Caputo, P. A [17]	America	31	31	68.47(2.92)	68.47(2.92)	29.77(7.46)	31.49(8.63)	NA.	NA.	NA.	NA.	6(1.48)	4(1.48)	PCA/RAPN	11.71(12.44)	36.16(39.48)
Emara, A. M [18]	Britain	56	47	69.75(12)	60.5(10.5)	NA.(NA.)	NA.(NA.)	2.56(0.72)	3.28(1.22)	NA.	NA.	NA.	NA.	LCA/RAPN	31.3(13.48)	16.5(6.49)
Tanagho, Y [24]	America	267	233	69.3(11)	57.4(11.9)	30.4(7.8)	30.1(6)	2.5(1)	2.9(1.5)	NA.	NA.	6.5(2.2)	2.1(1.8)	LCA&PCA/RAPN	39.8(34.3)	21.9(18.8)
Guillotreau, J [20]	America	226	210	67.4(11.3)	57.8(11.8)	30.1(6.4)	29.3(6.2)	2.2(0.9)	2.4(0.8)	NA.	NA.	NA.	NA.	LCA/RAPN	39.76(43.35)	4.55(5.15)

CA, Cryoablation

PCA, Percutaneous Cryoablation

LCA, Laparoscopic Cryoablation

RAPN, Robot-Assisted Partial Nephrectomy

BMI, Body Mass Index

R.E.N.A.L. score, Renal Nephrometry Score

CCI, Charlson comorbidity index

size, tumor diameter, surgical method, renal nephrometry score, and follow-up period. There was no statistical significance in BMI ($P=0.84$), tumor size ($P=0.34$), renal nephrometry score ($P=0.05$) and CCI ($P=0.13$) between the two groups, but the CA group was older than the RAPN group ($P<0.001$). The data for perioperative outcomes and renal function changes are provided in Tables 2 and 3, respectively. All included studies were of high quality (Supplemental Digital Content 3).

Assessment of quality

Six studies received a NOS score of 8 [16–19, 22, 23], three studies scored 7 [20, 21, 25], and one study was rated at 6 [24].

Perioperative outcomes and complications

The perioperative meta-analysis results indicate that no statistically significant difference was found between the two groups in terms of operative time ($p=0.05$) (Fig. 2A). Notably, the amount of blood loss in the CA group was significantly less than that in the RAPN group [MD -104.60 ml; 95% CI -152.58 to -56.62; p=<0.0001] (Fig. 2C), and the length of hospital stay for the CA group was also significantly shorter than that for the RAPN group [MD -1.76 days; 95% CI -3.12 to -0.41; $p=0.01$] (Fig. 2B).

Cumulative analysis of complications showed that the overall incidence of complications was lower in the CA group compared to the RAPN group [OR 0.62; 95% CI 0.45 to 0.86; $p=0.004$] (Fig. 2D), but there was no difference between the groups in terms of the occurrence of minor, Clavien 1–2, and major, Clavien 3–5 complications ($p=0.31$, $p=0.58$) (Fig. 2E, F).

Renal function

The results for changes in renal function 12 months post-surgery are derived from three studies (Table 3). The analysis reveals that there is no significant statistical difference in the changes in kidney function at 12 months post-surgery between the CA group and the RAPN group [MD 1.10; 95% CI -4.33 to 6.54; $p=0.69$]. (Fig. 3).

Oncological outcomes

The oncological outcomes between the CA and RAPN groups show no statistical significance in terms of RFS (Recurrence-Free Survival) and OS (Overall Survival) (RFS: $p=0.88$; OS: $p=0.92$) (Fig. 4B, C). However, in terms of tumor recurrence rates, nine studies reported recurrences[16–24], with the CA group showing a significantly higher recurrence rate compared to the RAPN group [OR 7.83; 95% CI 4.32 to 14.19; $p<0.00001$] (Fig. 4A).

Heterogeneity

The majority of perioperative outcomes and changes in renal function demonstrated moderate to high heterogeneity across studies (operative time, I^2=97%; length of hospital stay, I^2=99%; blood loss, I^2=98%; changes in kidney function, I^2=79%), while the heterogeneity in oncological outcomes was lower.

Sensitivity analysis

Due to the significant heterogeneity observed in operative time, length of hospital stay, blood loss, and renal function 12 months post-surgery, sensitivity analyses were conducted to quantify the sources of heterogeneity and assess the robustness of the results. Ultimately, no substantial changes in heterogeneity were found among these outcomes, indicating that the sources of heterogeneity for these four outcomes are stable.

Assessment of publication bias

We were unable to assess publication bias because the testing ability was insufficient when there were 10 or fewer studies [26, 27].

Discussion

This study offers a meta-analysis concerning perioperative outcomes, changes in renal function, and oncological outcomes, meriting further discussion. For localized cT1 renal tumors, robot-assisted partial nephrectomy (RAPN) might be the optimal treatment choice, as RAPN demonstrates favorable oncological outcomes while preserving renal function [3]. Because RAPN, compared to open surgery, demonstrates favorable oncological outcomes while preserving renal function, it is particularly beneficial in reducing the likelihood of high-grade postoperative complications (HGC) in elderly patients and those with comorbidities [28]. Although RAPN can reduce related complications and shorten hospital stay duration for treating cT1 renal tumors [29], it may not be feasible for patients with comorbidities who cannot tolerate RAPN. Cryoablation (CA) as a minimally invasive surgery is a viable treatment option for patients with multiple comorbidities or deemed unsuitable for surgery.

Our analysis indicates that the CA group had better outcomes in terms of hospital stay, blood loss, and overall complications compared to the RAPN group, possibly due to the complex tissue dissection required by RAPN, leading to longer hospital stay, postoperative blood loss, and complications. However, studies suggest no difference in overall complication rates between the CA and RAPN groups [30, 31], and discrepancies could arise from the insufficiency of results included in the meta-analysis. When categorized into Minor, Clavien 1–2, and Major, Clavien 3–5, CA slightly outperforms RAPN, but

Table 2 Perioperative outcomes and complications of the included studies

Reference	Operative time(min)		Hospital stay(day)		Blood loss(ml)		Overall complications(n)		Minor, Clavien 1–2(n)		Major, Clavien 3–5(n)	
	CA	RAPN	CA	RAPN	CA	RAPN	CA	RAPN	CA	RAPN	CA	RAPN
Kawaguchi, S [21]	NA	NA	NA	NA	NA	NA	0	1	0	0	0	1
Uemura, T [25]	NA	NA	NA	NA	NA	NA	NA	NA	NA.	NA.	1	2
Liu, HY [22]	138.56(45.28)	267.45(104.53)	4.15(2.71)	6.11(5.1)	30.73(50.31)	300.56(360.73)	5	2	3	0	2	2
Rembeyo, G [23]	NA	NA	NA	NA	NA	NA	13	7	13	7	0	0
Fraisse, G [19]	NA	NA	1.22(1.94)	4.15(3.48)	NA	NA	NA	NA	NA.	NA.	NA.	NA.
Bertolo, R [16]	140(60)	200(50)	1(1)	4(2)	100(140)	195(139)	6	20	5	16	1	4
Caputo, P. A [17]	NA	NA	NA	NA	NA	NA	13	7	9	6	4	1
Emara, A. M [18]	147.88(36.08)	166.02(50.69)	1.68(0.18)	1.38(0.12)	47.14(16.24)	94.26(40.1)	5	4	4	2	1	2
Tanagho, Y [24]	164.8(60.2)	140.6(41.6)	NA	NA	74.2(100.1)	136.3(112.2)	8	21	4	15	4	6
Guillotreau, J [20]	175.53(44.77)	180(44.79)	2(1.49)	3.35(0.75)	75(8.87)	200(36.35)	27	42	19	36	8	6

CA, Cryoablation

RAPN, Robot-Assisted Partial Nephrectomy

Table 3 Renal function

	12 months post-operation(eGFR ml/min/1.73 m^2)	
Reference	**CA**	**RAPN**
Kawaguchi, S [21]	-14.1(33.88)	-6.2(17.64)
Uemura, T [25]	NA	NA
Liu, HY [22]	NA	NA
Rembeyo, G [23]	-6.4(3.89)	-6.7(3.89)
Fraisse, G [19]	NA	NA
Bertolo, R [16]	NA	NA
Caputo, P. A [17]	NA	NA
Emara, A. M [18]	NA	NA
Tanagho, Y [24]	-5(24.67)	-11.1(21.71)
Guillotreau, J [20]	NA	NA

CA, Cryoablation

RAPN, Robot-Assisted Partial Nephrectomy

eGFR, estimated glomerular filtration rate

without significant statistical significance, aligning with related research [25, 32].

Regarding renal function, some studies suggest CA provides better renal function protection than PN [33], as PN often requires clamping of the renal artery during surgery, leading to renal ischemia and a decrease in renal function [34]. CA can be performed with 3D localization and real-time monitoring of the ablation range under CT/MRI imaging, which helps minimize renal parenchymal damage and ischemia, thereby preserving kidney function [35, 36]. Despite the theoretical advantages of RAPN in providing finer dissection and better treatment outcomes, no significant difference in renal function between the two treatments was observed. This could be due to CA being more commonly used in older patients with multiple comorbidities, and the glomerular filtration rate decreases with age [37], while comorbidities can also affect the glomerular filtration rate [38]. Moreover, some studies have indicated that surgical experience can also impact the quality of perioperative outcomes, with more experienced surgeons significantly improving perioperative results, particularly in terms of WIT and operative time [39–41]. Certainly, the impact of precision medicine on surgical outcomes cannot be excluded. Nowadays, 3D virtual models (3DVM) are being utilized in preoperative assessment and to assist in performing RAPN. Compared to cases without the use of 3DVM, the group utilizing 3DVM shows a further reduction in renal ischemia rates, thereby better preserving renal function [42, 43]. Some studies indicate both CA and PN can adequately preserve renal function [44, 45]. For this controversial outcome, further high-quality research is needed for confirmation.

The difference in RFS and OS between the two groups is minimal, with some reports indicating better RFS with RAPN compared to CA [17], and others suggesting RAPN has better RFS but similar OS compared to CA [24]. Given these findings, further research is required

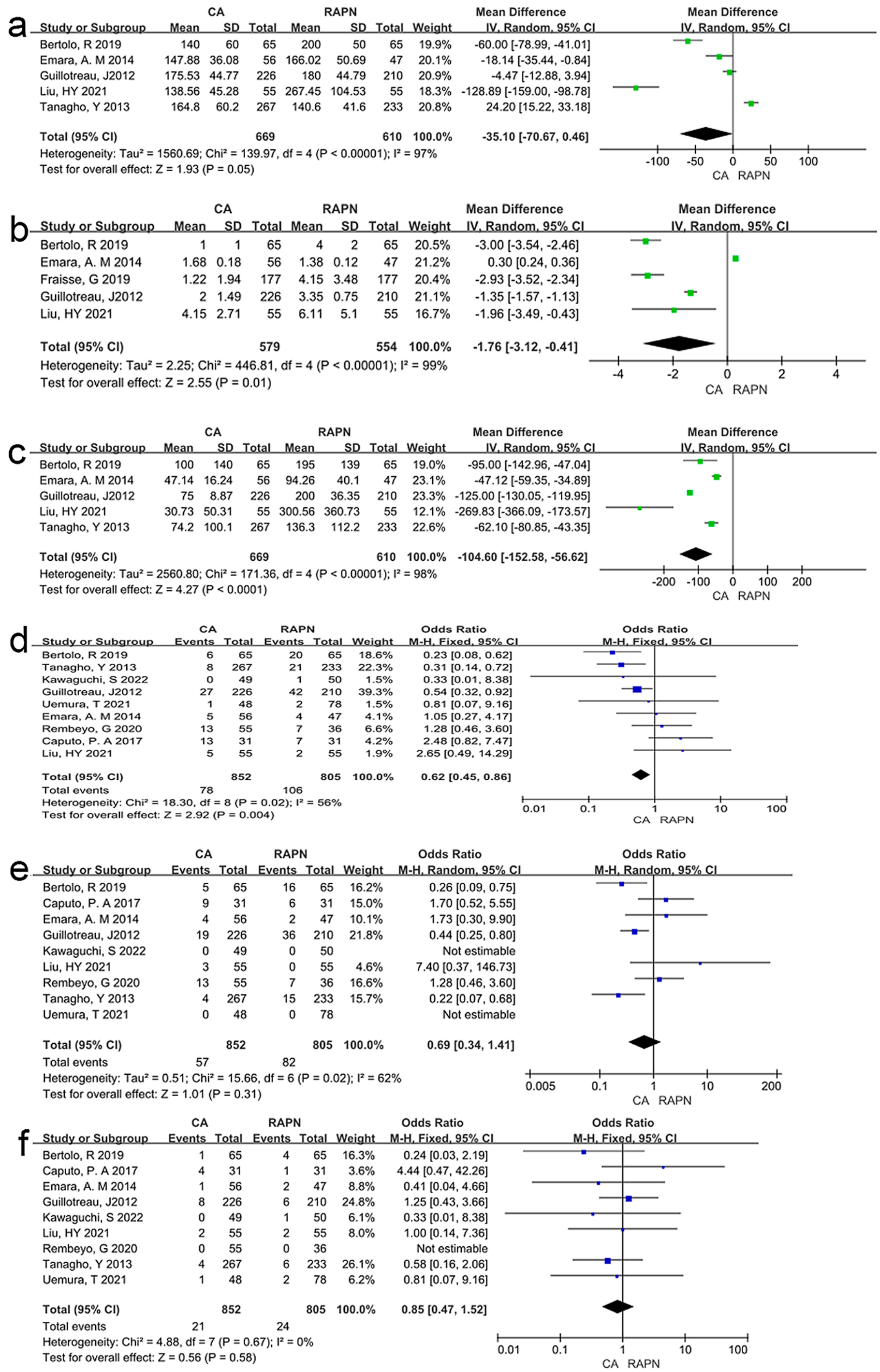

Fig. 2 **A**-Operative Time, **B**-Length of Hospital Stay, **C**-Blood Loss, **D**-Overall Complications, **E**-Minor, Clavien 1–2, **F**-Major, Clavien 3–5

to verify these long-term outcomes. The recurrence rate is significantly higher in the CA group compared to the RAPN group, aligning with findings by T. Klatte [46]. Any form of anatomical removal surgery ensures better local tumor clearance than CA.

This study has several limitations. First, the meta-analysis included retrospective or prospective cohort studies, lacking high-quality randomized controlled trials, thus inherent selection bias may affect these studies. Second, different CA techniques (PCA, LCA) were included in the review without sufficient literature to conduct a subgroup analysis on CA techniques, possibly leading to high heterogeneity. Third, CA is often used in older patients with multiple comorbidities, potentially

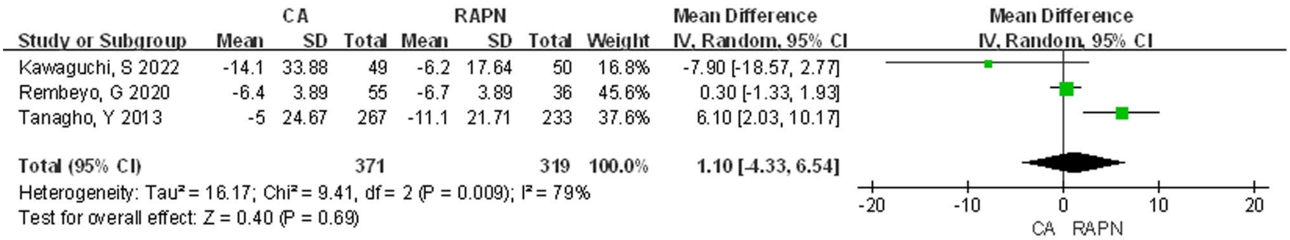

Fig. 3 Renal function 12 months post-surgery

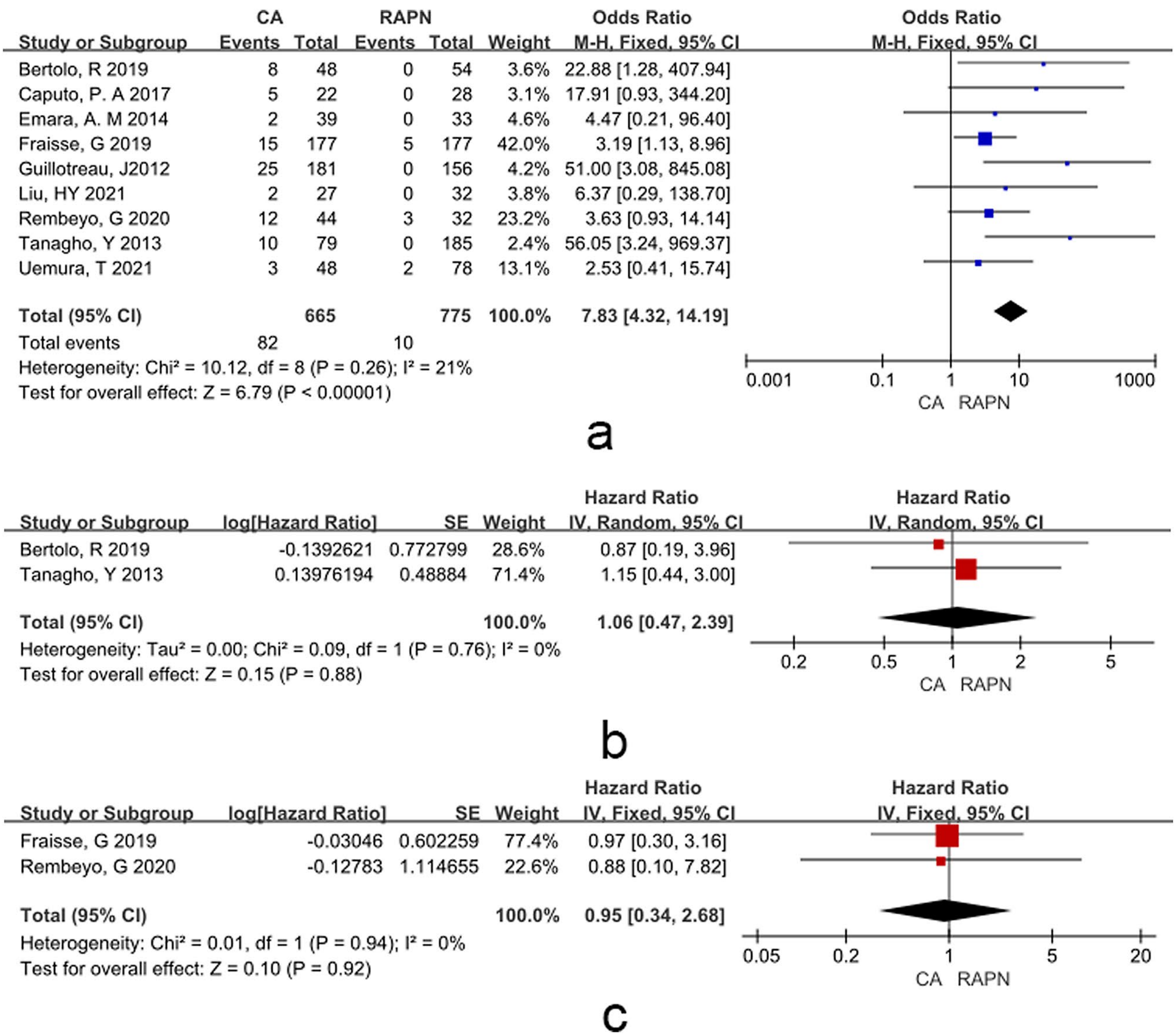

Fig. 4 **A**- Recurrence Rate, **B**-RFS, **C**-OS

increasing data heterogeneity. Fourth, only two to three outcomes were included for oncological outcomes such as RFS and OS, making the results less reliable. Fifth, renal function should be staged and analyzed according to acute and chronic kidney failure. However, we were only able to collect data at 12 months postoperatively from the original data, making the analysis of the impact of the two treatment modalities on renal function less comprehensive. Sixth, the data we have collected do not yet support subgroup analysis of patients with cT1a and cT1b tumors together, and further research is needed in the future. Finally, variations in surgical experience and equipment may lead to differences in outcomes. Regarding heterogeneity, caution is advised for low heterogeneity, as von Hippel PT demonstrated significant bias in I^2 when the number of included studies is small [47]. Some of the included studies exhibit significant heterogeneity, but due to differences in surgical techniques, medical equipment, and countries, the results require further validation.

Conclusion

In summary, CA slightly outperforms RAPN in terms of perioperative outcomes, but there are no significant differences between the two in terms of renal function and oncological outcomes (except for recurrence rate). For patients who cannot tolerate RAPN treatment, CA remains a viable treatment option. However, due to the limited number and quality of studies included, there is great heterogeneity for most of the variables and oncological results are based on very few studies, further research is needed to validate these findings.

Abbreviations

CA	Cryoablation
PCA	Percutaneous Cryoablation
LCA	Laparoscopic Cryoablation
RFA	Radiofrequency Ablation
RAPN	Robot-Assisted Partial Nephrectomy
OPN	Open Partial Nephrectomy
PN	Partial Nephrectomy
MD	Mean Difference
OR	Odds Risk
CI	Confidence Interval
BMI	Body Mass Index
R.E.N.A.L. score	Renal Nephrometry Score
CCI	Charlson comorbidity index
eGFR	Estimated glomerular filtration rate
RFS	Recurrence-free Survival
OS	Overall Survival
CT	Computed Tomography
MRI	Magnetic Resonance Imaging

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-12917-z.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Author contributions

TW and XD had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: TW, HYG and LZ. Acquisition of data: HYG and LZ. Analysis and interpretation of data: HYG, LZ, JBZ, QW, HS and XC. Drafting of the manuscript: HYG, LZ, JBZ, QW and QX. Critical revision of the manuscript for important intellectual content: HYG, LZ, JJZ, WS, XD and TW. Statistical analysis: HYG, LZ, ZYL, YBZ and YT. Supervision: XD, TW. All authors contributed to the article and approved the submitted version. †Equal contributors: This author has contributed equally to this work and share first authorship.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

Not applicable.

Human ethics and consent to participate

Not applicable.

Competing interests

The authors declare no competing interests.

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