



Partial nephrectomy versus ablative therapies for cT1a renal masses: A Systematic Review and meta-analysis



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ABSTRACT

Objectives: ablative techniques have been increasing as an alternative to surgical approaches, especially in patients who are unfit for surgery. This study was performed to compare oncologic and functional outcomes after partial nephrectomy (PN) and ablation for treating clinical T1a renal masses.

Methods: An electronic search was completed on the basis of PubMed, Embase and Cochrane Central Register of Controlled Trials. Studies comparing partial nephrectomy versus ablative therapies in patients with small renal masses were enrolled.

Results: Twenty articles incorporating 5,011 patients were eligible for the present meta-analysis. Perioperative complications were fewer in the ablation group than in the PN group (OR = 0.76; 95%CI, 0.60–0.97; P = 0.025), but ablation group was associated with increased risk of local recurrence (OR = 1.88; 95%CI, 1.29–2.72; P = 0.001) and lower OS (HR = 1.53; 95% CI, 1.16–2.00; P = 0.002). CSS and DFS were comparable in two groups. Decline of renal function at 6-month follow up was lower in ablation than PN (WMD = 3.32; 95% CI, 0.04–6.60; P = 0.047). Beside, ablation had a trend towards lower reduction of renal function of long-term follow up (WMD = 3.06; 95% CI, –2.13–8.25; P = 0.247).

Conclusion: Compared to PN, ablation may have a significantly lower OS and higher local recurrence rates in selected patients, while CSS and DFS were comparable between the two treatments. On the other hand, ablation had a significantly decreased risk of perioperative complication and the potential advantage of long-term renal function preservation. More large randomized controlled trials are needed further to enhance the evidence of ablation in patients with small renal tumors. We believe that ablation is an attractive addition to the urologist's treatment options for small renal masses.

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Introduction

Renal cancer represents 2%–3% of all cancers, with an estimated 403,262 new cases and 175,098 deaths worldwide in 2018 [1]. Currently, it is commonly detected incidentally on non-invasive imaging as a result of unrelated reasons [2]. Most of these incidentally detected renal masses are typically small, localized within the renal capsule (low stage) [3]. Small renal masses (SRMs) measured less than 4 cm (stage T1a) compose 48%–66% of all renal

cancers [4]. Nephron-sparing treatments are generally recommended, aimed at renal function preservation and prevention of associated comorbidities [5].

Current guidelines by the American Urological Association, European Association for Urology for the SRMs recommend partial nephrectomy (PN) as the standard-of-care, compared to radical nephrectomy (RN) [5,6]. Nevertheless, in the last decades, ablative techniques have been increasing as an alternative to surgical approaches, especially in patients who are unfit for surgery or with the low probability of aggressive malignancy [5–7]. The most widely used ablative therapies consist of radiofrequency ablation (RFA), cryoablation (CRA) and microwave ablation (MVA) [8].

Compared to PN, ablation has some potential benefits, such as no need to incise the renal parenchyma and to clamp vessels [9]. Ablative strategies have shown encouraging oncologic outcome,

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minimal invasiveness and fewer complications rate [10,11]. Recently, some studies have compared the clinical outcomes of ablation versus PN. Reportedly, ablation was associated with fewer perioperative complications, but the survival outcome is controversial [7,12,13]. As far as we know, there is no review compare PN versus ablation strategies for T1a renal masses.

Thus, the aim of this study was to summarize relevant articles to compare oncologic and functional outcomes after PN and ablation for treating clinical T1a renal masses.

Method

Search strategy

We performed the study according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [14]. In November 2018, the Pubmed, Embase, and Cochrane Central Register of Controlled Trials online database were searched by using items about renal cancer (carcinoma, tumor, mass or neoplasm), surgical treatment (nephron-sparing surgery, partial nephrectomy or PN) and ablative techniques (ablative, ablation, radiofrequency ablation, RFA, microwave ablation or thermal ablation therapy) as keywords and Mesh terms. Additionally, the lists of pertinent articles were also screened individually for potentially relevant citations. Two investigators performed the articles search independently (any disagreement was resolved by the third one).

Eligibility criteria

In this meta-analysis, we enrolled the articles if meeting the following criteria: (1) randomized controlled trials (RCTs) or observational studies, (2) involved renal masses patients treated with PN or ablation, (3) comparison of PN versus ablation, (4) reported the outcome such as cancer-specific survival (CSS), overall survival (OS), disease-free survival (DFS), local recurrence, complications or change in renal function. We excluded the following articles: (1) fewer than 20 patients, (2) non-English language, (3) animal-based studies, (4) renal masses larger than 4 cm, (5) did not report the clinical outcomes, (6) conference literature and studies based on national database because of no detailed information. If reported data duplicated, we only enrolled data from the latest report.

Data extraction

Two authors extracted the data independently, with disagreements resolved by discussion or consulting with the third one. The following data was extracted from the enrolled studies: the first author, published year, study type, study location, enrollment data, intervention, sample size, age, tumor size and duration of follow up, study endpoints such as OS, CSS, DFS, complications, local recurrence, and change in renal function.

Quality assessment

For RCTs, we used the Cochrane Collaboration Risk of Bias Tool based on six bias domains [15]. For nonrandomized studies, we used the Newcastle-Ottawa Quality Assessment Scale to assess quality [16]. Studies were assessed according to three aspects: selection, comparability, and exposure/outcome. Studies with a score of no less than 7 were considered high quality. Any disagreement was resolved by discussing or consulting the third one.

Outcomes

The primary endpoint for this study was OS, defined as the time between the initial diagnosis and the death from all causes because it can reflect the overall physical condition of the patients. The secondary endpoints were CSS, DFS and local recurrence which reflects the oncologic outcome. CSS was defined as the time between the initial diagnosis and the death from renal cancer. DFS is the length of time after primary treatment for renal cancer ends that the patient survives without any signs or symptoms of renal cancer. Local recurrence following ablation was defined as new focal enhancement in the ablation bed or enlargement of the ablation defect on follow-up imaging. Local recurrence following PN was defined as a mass in the ipsilateral kidney. Besides perioperative and functional outcome such as complications and change in renal function were also analyzed. Perioperative complications were defined as the sum of intraoperative and postoperative complications. Change in renal function was analyzed as the change from the baseline to different periods such as the estimated glomerular filtration rate (eGFR) in ml/min/1.73 m².

Statistical analysis

For time-to-event data such as OS, CSS, and DFS, HR is the most appropriate statistic. HRs and 95%CI were generally obtained directly from each eligible study. If not, based on the method by Tierney, we could estimate HRs indirectly according to Kaplan-Meier curve [17]. Local recurrence was evaluated using odds ratios (OR). Perioperative complications were evaluated by OR. Change in renal function was evaluated by the weighted mean difference (WMD). WMD is used for the continuous variable which has the same unit. All data were calculated using STATA version 12 (StataCorp, College Station, TX, USA). A two-sided P value < 0.05 was considered a statistically significant difference. Statistical heterogeneity was evaluated by calculating the Q and I² statistics. If

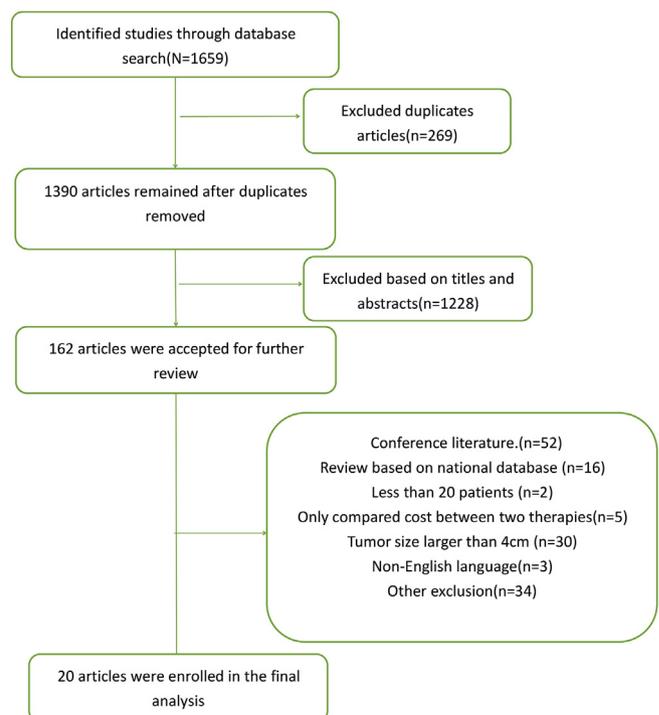


Fig. 1. Flow chart of the search strategy.

Table 1
Baseline characteristics of the included studies.

Study/Published year	Enrollment date/Location	Study type	Intervention(No.of patients)	Mean Age(years)	Tumor size(cm) Mean(SD)	Follow-up (month) Median	NOS
Alam 2018	Since 1 January 2009 Multi-institutional DISSRM Registry	Prospective study	PN(n = 231) Ablation(n = 27)	Median 61.3 71.8	Median 2.4 2.1	3.0 years	7
Park 2018	December 2008 to April 2016 Samsung Medical Center, Sungkyunkwan University School of Medicine	Retrospective study	Robotic PN(n = 63) RFA(n = 63)	57.7 57.1	2.0 (0.6) 2.1 (0.5)	24.6 21	7
Mason 2017	2003 to 2013 Mayo Clinic	Retrospective study	Percutaneous CRA(n = 389) PN(n = 389)	67.7 66.7	3.2 (1.4) 3.1 (1.5)	3 3	7
Liu 2017	February 2005 to April 2014 Nanjing Drum Tower Hospital, Medical School of Nanjing University	Retrospective study	Percutaneous RFA(n = 115) PN(n = 149)	67 58	3.1 3.4	77 80	8
Ji 2016	February 2006 to February 2015 Nanjing Drum Tower Hospital,the Affiliated Hospital of Nanjing University Medical School	Retrospective study	Laparoscopic RFA(n = 105) Laparoscopic PN(n = 74)	64.2 57.3	2.2 2.9	78 82	7
Chang 2015	February 2005 to December 2009 the Affiliated Nanjing Drum Tower Hospital, Medical School of Nanjing University	Retrospective study	RFA(n = 45) PN(n = 45)	52.9 52.8	3.0 (0.6) 3.0 (0.7)	66 72	8
Fossati 2015	2000 to 2013 Vita-Salute San Raffaele University	Retrospective study	Laparoscopic PN(n = 206) Laparoscopic CRA(n = 166)	Median 60 66	Median 2.5 2.0	43 39	8
Thompson 2015	2000 to 2011 Mayo Clinic	Retrospective study	PN(n = 1057) RFA(n = 180) CRA(n = 187)	60.1 70.7 71.6	2.5 2.1 2.9	5.2 years 3.6 years 1.9 years	9
Emara 2014	June 2008 to April 2012 Frimley Park Hospital NHS Foundation Trust	Prospective study	Laparoscopic CRA(n = 56) Robotic PN(n = 47)	69.75 60.5	2.56(0.10) 3.28(0.18)	Mean 31.3 16.5	7
Youn 2013	Since January 2007 Chungnam National University Hospital	Retrospective study	Open PN(n = 14) Laparoscopic RFA(n = 41)	53.92 59.15	2.4 (0.79) 2.3 (1.27)	Mean(SD)50.0 ± 16.9 51.0 ± 15.8	7
Guan 2012	December 2004 to June 2008 Tongji Hospital, Tongji Medical College	Prospective randomized study	PN(n = 54) MVA(n = 48)	46.4 45.5	2.8(1.3) 3.1(0.8)	36 32	-
Guillotreau 2012	January 1998 to December 2010 Cleveland Clinic	Retrospective study	Laparoscopic CRA(n = 226) Robotic PN(n = 210)	67.4 57.8	2.2 (0.9) 2.4 (0.8)	44.5 4.8	8
Olweny 2012	December 1998 to November 2005 University of Texas Southwestern Medical Center	Retrospective study	RFA(n = 37) PN(n = 37)	Median 63.8 54.8	Median 2.1 2.5	6.5 years 6.1 years	8
Klatte 2011	2004 to 2010 Medical University of Vienna	Retrospective study	Laparoscopic CRA(n = 41) PN(n = 82)	Median 74.9 69.8	Median 2.5 2.5	33.6	7
Deklaj 2010	October 2002 to June 2008 University of Chicago Medical Center	Prospective study	Laparoscopic PN(n = 28) Laparoscopic ablative techniques (n = 19)	74.9 76.5	2.4 (0.8) 2.7 (0.9)	Mean 28.9 19.3	7

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Table 1 (continued)

Study/Published year	Enrollment date/Location	Study type	Intervention(No. of patients)	Mean Age(years)	Tumor size(cm) Mean(SD)	Follow-up (month) Median	NOS
Takaki 2010	May 2002 to December 2008 Mie University School of Medicine	Retrospective study	RFA(n = 51) PN(n = 10)	69.4 64.0	2.4 (0.7) 1.9 (0.7)	Mean(SD)34.0 (3.2) 26.0 (16.9)	7
Ko 2008	April 2004 to June 2007 Korea University School of Medicine	Prospective study	Open PN(n = 20) Laparoscopic CRA(n = 20)	57.6 56.3	2.16 (1.08) 2.38 (1.67)	Mean (range)28.7(12-41) 27.3 (12-45)	8
Lucas 2008	July 1995 to March 2005 University of Texas Southwestern Medical Center	Retrospective study	RFA(n = 86) PN(n = 85)	Median 61.5 56.2	2.34 2.63	40 44	8
Stern 2007	July 1996 to January 2004 University of Texas Southwestern Medical Center	Retrospective study	PN(n = 37) RFA(n = 40)	56.4 60.5	2.43 (0.80) 2.41 (0.70)	Mean (range) 46.7(24-93) 29.8 (13-42)	7
Desai 2005	September 1997 to June 2003 Cleveland Clinic Foundation	Prospective study	Laparoscopic PN(n = 153) Laparoscopic CRA(n = 78)	60.59 65.55	2.25 (0.67) 2.05 (0.56)	Mean (range) 5.8(1-36) 24.6 (1-60)	7
Cochrane Collaboration Risk of Bias Tool		Allocation concealment (selection bias)	Blinding of participants and researchers (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Guan 2012		Low risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk

PN: Partial Nephrectomy; RFA: Radiofrequency ablation; CRA: Cryoablation; MVA: Microwave ablation; NOS: Newcastle-Ottawa Quality Assessment Scale.

I² statistics showed P < 0.10 and I² > 50%, a random-effect model was applied [18]. To further evaluate the robustness of the final results, we performed the sensitivity analyses. Egger's test and Begg's test were performed to assess publication bias. If publication bias existed, we used trim and fill method to estimate missing studies and recalculated the results [19].

Results

Search results

Our search strategy yield 1,659 articles, 269 of which were duplicated articles. Based on titles and abstracts, 1,228 articles were excluded, a total of 162 full-text articles were left. Finally, a total of 20 articles incorporating 5,011 patients were enrolled in the present study after removing irrelevant articles [9,20–38](see Fig. 1).

Characteristics of included articles

Of the included 20 articles, 14 articles were retrospective articles [9,20–32], 5 articles were prospective articles [33,34,36–38], 1 article was randomized controlled study [35]. A total of 2,991 patients were treated with open, laparoscopic or robotic PN as PN group, and 2,020 patients were treated with RFA, cryoablation or microwave ablation as ablation group. The mean age of patients in the PN group was 60.48, while the mean age of patients in the ablation group was 65.5. In the PN group, the mean tumor size was 2.62 cm, and in the ablation group, the mean tumor size was 2.55 cm. A majority of studies had a relatively long follow-up except for one study which only reported the change in eGFR at 3-month follow up [21], the median duration of follow-up ranged from 4.8 months to 82 months. 15 studies reported the perioperative complications and local recurrence, 6 studies evaluated OS, 4 studies revealed CSS and DFS, and 8 studies demonstrated the change in renal function. Detailed characteristics of articles were summarized in Table 1. And the quality assessment of included studies was illustrated in Table 1. All studies included in our meta-analysis were considered to be of high quality.

Perioperative complications

Regarding 15 studies involving 2,327 patients demonstrated the incidence of perioperative complications. The incidence of perioperative complications in the ablation group was slightly lower than the PN group, 12.53% (142/1133) versus 17.00% (203/1194). Compared to PN, ablation was associated with decreased risk of perioperative complications, the OR was 0.76 (95%CI, 0.60–0.97; P = 0.025, Fig. 2A). Moderate heterogeneity among studies was revealed (I² = 47.5%, P = 0.021).

Local recurrence

In terms of 15 studies including 3,597 patients reported the occurrence of local recurrence. The occurrence rates of local recurrence in both groups were low, 4.68% (66/1411) vs 2.52% (55/2186). Patients treated with ablation had a significantly increased risk of local recurrence, the OR was 1.88 (95%CI, 1.29–2.72; P = 0.001, Fig. 2B). There was moderate heterogeneity between studies (I² = 35.0%, P = 0.095).

Overall survival

Based on 6 studies involving 2,086 patients revealed the OS. The pooled estimated HR for studies that compared ablation with PN are presented in Fig. 3A. Compared with PN, ablation was

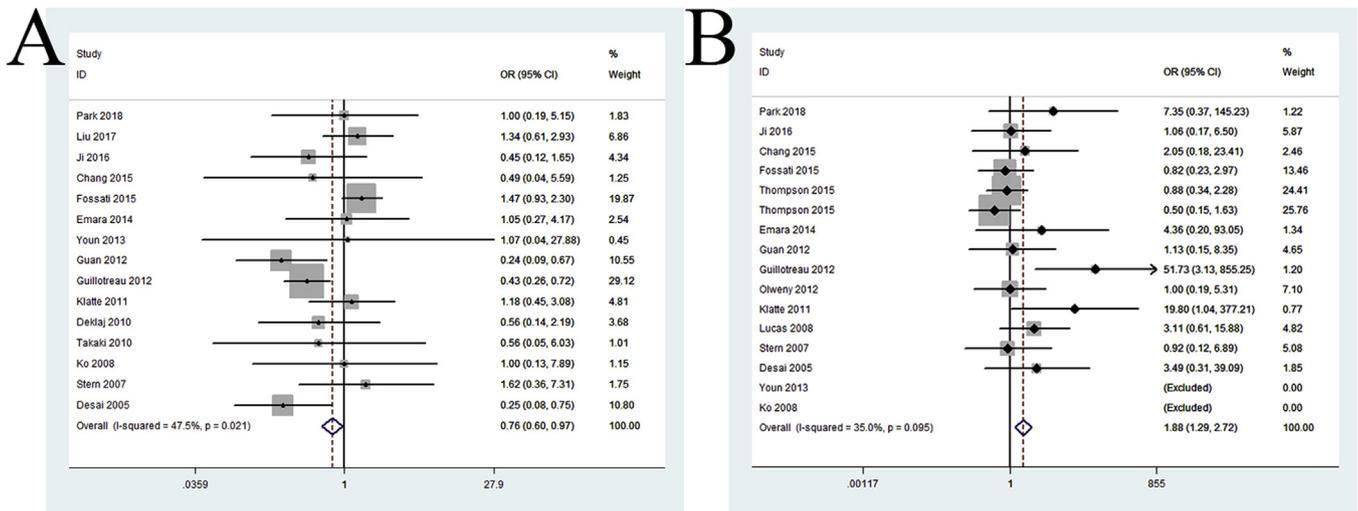


Fig. 2. Ablation versus PN for A: perioperative complications; B: local recurrence.

associated with worse OS, the pooled HR was 1.53 (95% CI, 1.16–2.00; $P = 0.002$). There was no significant heterogeneity between studies ($I^2 = 0.0\%$, $P = 0.879$).

Cancer-specific survival

On the basis of 4 studies incorporating 601 patients, we got the CSS. The pooled estimated HR for studies that compared ablation with PN is shown in Fig. 3B. No significant differences of CSS were noted, the HR was 1.08 (95% CI, 0.32–3.59; $P = 0.901$). There was no evidence for heterogeneity between studies ($I^2 = 0.0\%$, $P = 0.737$).

Disease-free survival

Regarding 4 studies including 715 patients, we performed the meta-analysis for DFS. There were no significant discrepancies between two groups, the HR was 1.09 (95% CI, 0.61–1.97; $P = 0.764$, Fig. 3C). No significant heterogeneity between studies was found. ($I^2 = 0.0\%$, $P = 0.948$).

Renal function

In terms of 8 studies incorporating 2,285 patients presented the change in renal function of different periods. Compared with PN, ablation had a similar change in renal function at the perioperative period and 3-month follow up. While at 6-month follow up, the decrease of renal function in the ablation group was lower than PN, the WMD was 3.32 (95% CI, 0.04–6.60; $P = 0.047$). And at 1-year follow up, the ablation had a trend towards a lower decline of renal function, the WMD was 2.75 (95% CI, -1.05–6.54; $P = 0.156$). The change in renal function of longer than 3 years was consistent with the previous result, the WMD was 3.06 (95% CI, -2.13–8.25; $P = 0.247$). Detailed information was illustrated in Fig. 4.

Sensitivity analysis

We performed a sensitivity analysis by removing one study each time. After removing the study by Fossati et al. [9], a relatively large change of perioperative complications was observed visually, but did not dramatically change the outcome, the recalculated OR was 0.59 (95% CI, 0.44–0.78). As for local recurrence, the obvious change was revealed after excluding the study by Guillotreau et al. [28], the pooled OR was 1.27 (95% CI, 0.84–1.92). For OS, CSS, DFS, and change in renal function, the pooled result did not tend to alter

after excluding one study each time.

Publication bias

No obvious publication bias were observed in the light of both Begg's funnel plot test (OS: $P = 0.548$, CSS: $P = 0.734$, DFS: $P = 1.000$, perioperative complications: $P = 0.921$, renal function: $P = 0.773$) and Egger's test (OS: $P = 0.886$, CSS: $P = 0.282$, DFS: $P = 1.000$, perioperative complications: $P = 0.559$, renal function: $P = 0.230$). Significant publication bias for local recurrence was found based on the Begg's test ($P = 0.004$) and Egger's test ($P = 0.001$). Therefore, the trim and fill method was applied, assuming that five studies with unpublished results were missing using the fixed effect model (Fig. 5). And this approach resulted in an adjusted pooled OR of 0.96 (95% CI, 0.62–1.48), which change the trend of the previous result.

Discussion

Nephron-sparing surgery remains the gold standard management for SRMs, as a result of a much lower level of local recurrence and established long-term outcomes [2,5,6,39]. While ablative therapies are emerging as an alternative with curative intent for SRMs, especially in patients with medical comorbidities or unfit for surgery [2,5,6,39]. And ablation develops fastly in the past years. It can be guided by ultrasound or computed tomography, which means the more alternative choices. Besides, we could perform the ablation under local anesthesia or general anesthesia and could meet the different patients' demand. On this aspect, ablation can be performed in different ways and appropriate for more patients compared with PN. In terms of outcomes, Talenfeld et al. revealed that patients treated with PN had a better overall survival (OS) compared with ablation and cancer-specific survival (CSS) was similar, besides Zhou et al. was consistent with previous results [12,13]. However, Xing et al. Revealed a similar OS and CSS between PN and ablation [7]. The present study compared PN with ablation for SRMs in some aspects. To summarize, we found that perioperative complications were fewer in the ablation group than in the PN group, but ablation group had a slightly higher rate of local recurrence and worse OS. Besides, CSS and DFS were comparable in two groups. The decline of renal function at 6-month follow up was lower in ablation than PN. And ablation had a trend towards lower reduction of renal function of late (1-year, >3-year) follow up. However, no significant difference was observed in the early change

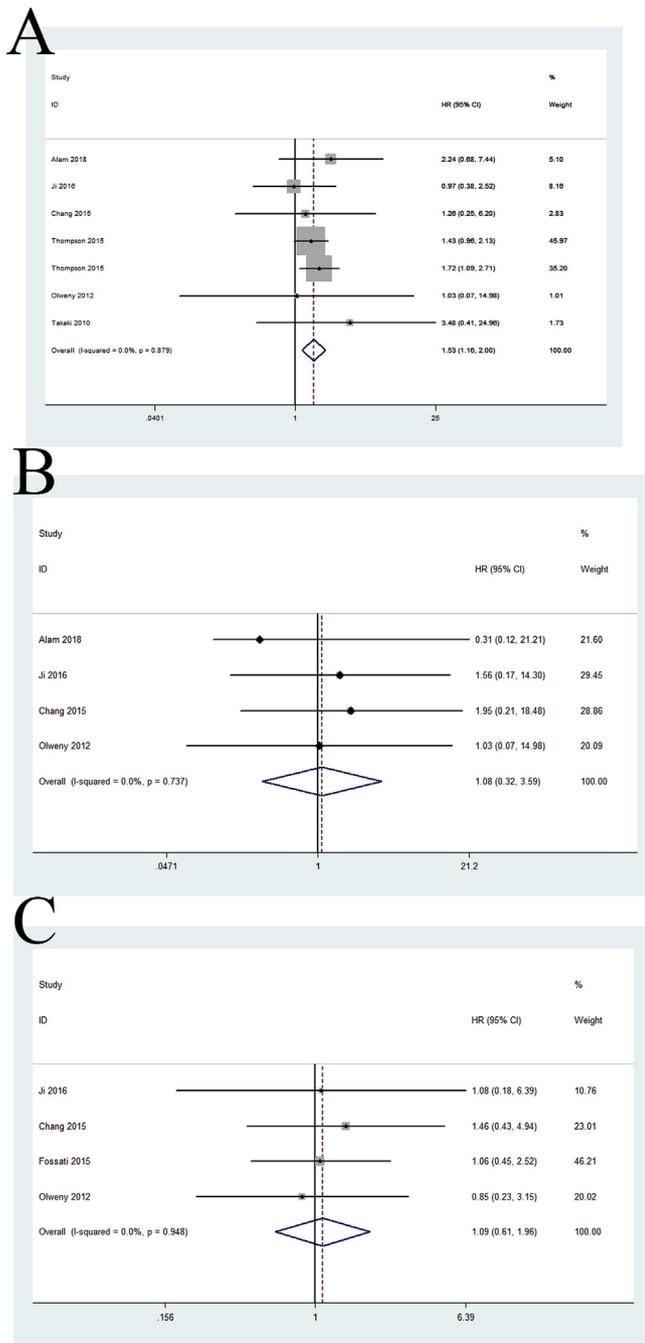


Fig. 3. Ablation versus PN for A: OS; B: CSS; C: DFS

of a renal function (perioperative, 3-month).

The incidences of perioperative complications in this study for ablation and PN were 12.53% and 17.00%, which are similar to previous reports [40,41]. Talenfeld et al. demonstrated that percutaneous ablation has fewer periprocedural complications compared with PN [12], which is consistent with our finding. Katsanos et al. performed a meta-analysis of thermal ablation versus nephrectomy for small renal tumors on unspecified stage and revealed that complications rate was significantly lower in the ablation group [42]. Interestingly, Guillotreau et al. revealed that estimated blood loss (EBL) was the significant predictor of the incidence of complications (OR = 1.2; 95%CI, 1.1–0.4; P = 0.005) [28]. And PN was associated with significantly increased EBL compared with

ablation. While Fossati et al. hypothesized that postoperative complications greatly depend on patient characteristics as well as tumor complexity [9]. Further evidence from larger controlled randomized trials is need.

In terms of oncologic outcomes, local recurrence rates are significantly higher in the ablation group than the PN group. Some recent studies revealed the similar result [28,43]. Current guidelines by the American Urological Association, European Association for Urology for the SRMs recommend ablation for poor surgical candidates because of higher rates of local tumor recurrence and incomplete ablation [5,6]. The heat sink effect associated with thermal ablation might be an explanation, thermal effects might dissipate resulting from renal sinus vessels and collecting system around an endophytic renal tumors [44]. Therefore, the target temperature might insufficient for ablating tumor margin completely. Besides, positive tumor margin can be checked in PN while it cannot be in ablation. Patients treated with PN are usually younger, which may partially explain the result. The follow-up of patients treated with ablation was closer than patients treated with PN. For example, Chang et al. performed contrast-enhanced CT assessment at 7 days, 3 months, 6 months, and every 6 months sequentially after RFA, and protocol for PN was every 6 months in the initial 3 years and annually thereafter [25]. Besides, Fossati et al. conducted computed tomography scan at 6 mo and yearly thereafter for PN patients, and performed serial magnetic resonance imaging at 3, 6, and 12 mo and yearly thereafter for patients treated with cryoablation [9]. The more closed follow-up of patients treated with ablation may result in a higher rate of local recurrence. Furthermore, Thompson et al. defined the local recurrence of PN and ablation, the local recurrence might be more easily detected in ablation based on the criterion [24]. However, because of potential selection bias and heterogeneity, which may distort our result favoring ablation, further studies are required.

When it comes to time-to-event data such as OS, CSS, and DFS, the results were contradictory. Zhou et al. demonstrated that ablation group had significantly lower OS (HR = 1.442, p = 0.046) but similar CSS (P = 0.402) for cT1A renal cell carcinoma (RCC) after propensity match [13]. Thompson et al. revealed that RFA patients were more likely to die from any cause (HR = 1.43, P = 0.080) and cryoablation was significantly associated with worse OS in the multivariable analysis (HR = 1.72; P = 0.019)[24]. Besides, they found treatment type was not significantly associated with DFS according to Cox regression analysis, (HR = 1.06; 95% CI, 0.45–2.52; P = 0.9). Xing et al. found that OS and CSS were comparable between two groups [7]. However, this study was performed based on Surveillance, Epidemiology, and End Results (SEER) database, which may have inherent selection bias and may not fully represent contemporary patient populations. Such findings were in line with the study by Olweny et al. presenting no difference in OS, CSS, and DFS between two groups [27], while this study enrolled 37 patients each group, and the number of samples is relatively small. They also performed univariable and multivariable analysis, revealing that approach (RFA vs PN) was not significant predictors of DFS. According to our analysis, we found that ablation had a significant decline in OS and similar CSS and DFS compared with PN. OS was lower in ablation patients and likely attributed to older age and more comorbidities. Based on the results from the front analysis, no significant differences in CSS and DFS were observed. It may confirm the conception that discrepancy of OS might be caused by age and physical conditions rather than factors related to therapy and the renal mass itself. However, the included studies were almost non-randomized studies, with the risk of selection bias, and the patients treated with ablation were mostly older and more comorbid patients. And the propensity score analysis in most studies is woefully inadequate. Furthermore, few studies were included

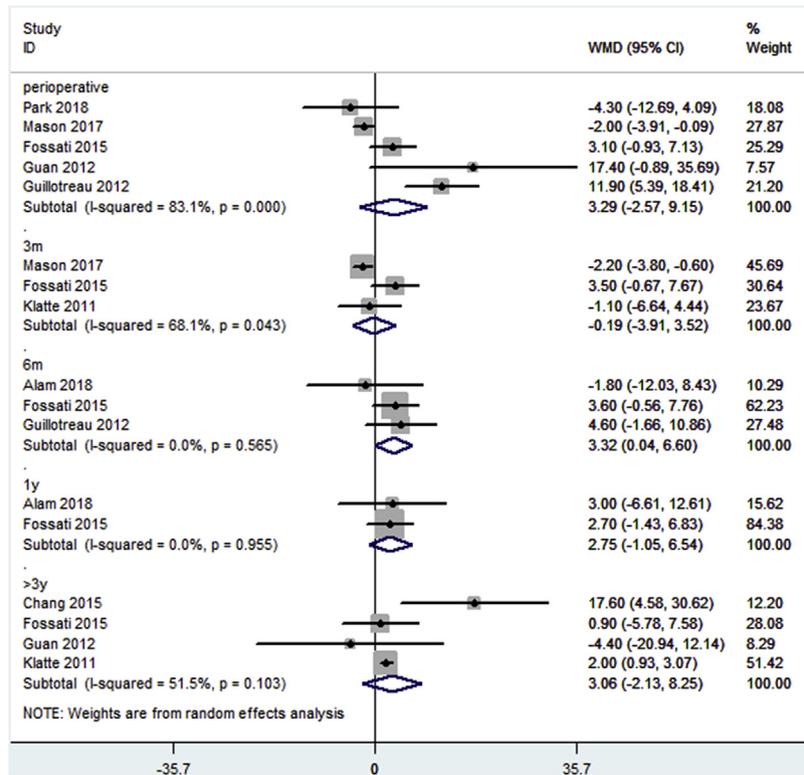


Fig. 4. Ablation versus PN for change in renal function of different periods.

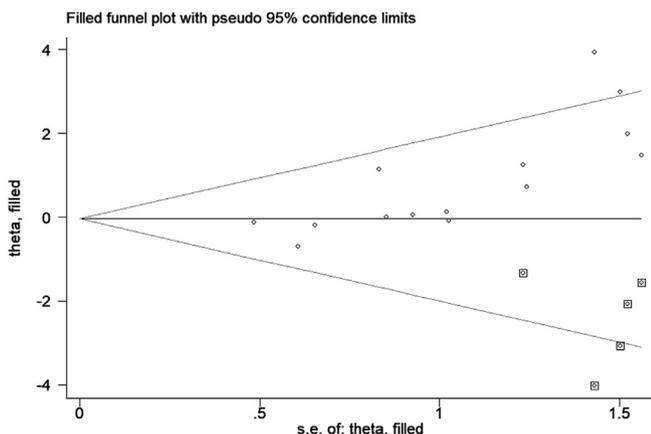


Fig. 5. Trim and fill method for publication bias indicating 5 hypothesized studies missing.

and the number of patients was small, so the accurate comparison between PN and ablation in survival outcomes is still unclear and need further prospective studies to evaluate.

The preservation of renal function has been another major focus. Decreased renal function is associated with cardiovascular events and mortality [45]. It is well established that radical nephrectomy (RN) has a greater impact on renal function than PN and is associated with an increased risk of developing chronic kidney disease (CKD) stage ≥ 4 [46,47]. However, when comparing ablation and PN, the differences of change in renal function between nephron-sparing therapies remains unclear. Reportedly, some studies have investigated the effect on renal function between two treatments and have had mixed results. Park et al. demonstrated renal function reduction of post-treatment in RFA was no less than in the robotic

PN [20]. But RFA group had a higher proportion of endophytic renal cell carcinoma (RCC) than PN, this discrepancy of tumor location may lead to an insignificant difference in renal function preservation. Alam et al. performed a multivariable mixed-effects linear regression to evaluate the relative change in renal function, and no significant difference between PN and ablation was revealed [33]. While, only 27 patients were enrolled in the ablation group and 231 patients in the PN group, which may have an effect. Conversely, Mason et al. observed a statistically greater decline at discharge and 3-month follow up in eGFR after percutaneous cryoablation compared with PN [21]. Fossati et al. showed that laparoscopic cryoablation was significantly associated with better renal function preservation at 6-month compared to PN (coefficient 4.68, 95% CI 0.06–9.30; $P = 0.047$) based on multivariate linear regression analysis [9]. In the following 2 years, renal function recovered, reaching a plateau approximately 3 years after surgery, when two treatments provided a comparable functional outcome. While Chang et al. observed that percentage decrease in GFR was significantly lower in the RFA group at the time of the last follow-up (>5 years, $P = 0.001$) [25]. Post-treatment renal function and appearance of CKD is associated with ischemia time [31]. Ablation can damage the tumor without unnecessary removal of the kidney tissue and could be a maximum nephron-sparing approach. Each minute of hilum clamping may influence the short- and long-term functional outcome [48]. And ablation does not need to require clamping of the renal vessels, which may reduce the damage by warm ischemia [23]. From our perspective, ablation had better renal function preservation at 6-month and potential benefit at long-term follow up compared with PN, while no significant difference at postoperative and 3-month was found. But enrolled studies of different periods were few and heterogeneity exist. Recently, a randomized clinical trial (NCT03390413) investigates robot-assisted PN compared to cryoablation in a number of

functional, oncological aspects. We hope that this clinical trial could provide us with some additional information.

Our study is not devoid of limitations. First, a majority of included studies were retrospective studies, increasing the risk bias and reducing the reliability of the results. Second, the approaches of PN and ablation are different, and some approaches are mixed, which may influence clinical outcomes. While in order to maximize the sample size, we did not perform subgroup analysis. However, a meta-analysis of 883 cases showed that cryoablation and RFA have similar efficacy and complication rates [49]. Third, missing statistical adjustment for some variables, for instance, patient's age, tumor location, and comorbidities, may have distorted our results. Fourth, enrolled patients ranged wide, from 1995 to 2016, equipment, concepts and operations surgical techniques changed, which may influence patients' outcome. Last, enrolled studies for analyses of OS, CSS, DFS, and change in renal function were few, which cannot evaluate the efficacy and safety powerfully.

Conclusion

Compared to PN, ablation may have a significantly lower OS and higher local recurrence rates in selected patients, while CSS and DFS were comparable between the two treatments. But the heterogeneity among studies and high risk of bias may contribute to a difference in OS and local control. On the other hand, ablation had a significantly decreased risk of perioperative complication and the potential advantage of long-term renal function preservation. More large randomized controlled trials are needed further to enhance the evidence of ablation in patients with small renal tumors. We believe that ablation is an attractive addition to the urologist's treatment options for small renal masses.

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Conflicts of interest

We declare that we have no conflicts of interest.

Authorship

Xu Hu, Yan Wang, and Xiang Li drafted the manuscript. Yan-Xiang Shao, Zhi-Qiang Yang and Xu Hu collected those medical data. Xu Hu, Yan Wang, Yan-Xiang Shao and Wei-Xiao Yang performed statistical analyses. Xu Hu, Yan Wang, and Xiang Li revised the manuscript. Xu Hu and Xiang Li designed the study.

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