

Original Article

Outcome of radiofrequency ablation over partial nephrectomy for small renal mass (<4 cm): a systematic review and meta-analysis

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Abstract: Objective: A meta-analysis was undertaken to provide evidence-based clinical trials comparing radiofrequency ablation with partial nephrectomy for small renal mass. Methods: We searched through the major medical databases such as Pub Med, EMBASE, Medline, Science Citation Index, Web of Science and CNKI (Chinese National Knowledge Infrastructure Database) and Wangfang (Database of Chinese Ministry of Science & Technology) for all published studies without any limit on language from May 2007 until May 2015. The following search terms were used: partial nephrectomy, radiofrequency ablation, renal cell carcinoma, small renal tumor or mass. Furthermore, additional related studies were manually searched in the reference lists of all published reviews and retrieved articles. Results: We found there were no statistical differences between groups in 5y-DFS, recurrence rates, complications, but a less percentage decrease rate of GFR than PN, and RFA may be a better application for SRM (<4 cm).

Keywords: Meta-analysis, small renal mass, radiofrequency ablation, partial nephrectomy

Introduction

Partial nephrectomy is a well-established treatment modality for local renal tumor, but as minimal ablative techniques are developing so fast over the years, radiofrequency ablative techniques are progressing to an effective treatment with acceptable effectiveness and survivals. Thus, we conducted this meta-analysis to compare RFA with PN for small renal mass (SRM), defined as diameter <4 cm; the following outcomes were compared: the 5-year-disease-free-survival (DFS), local recurrence rate, surgical complications (SC) and the percentage change in GFR (PCG). We found there were no statistical differences between groups in 5y-DFS, recurrence rates, complications, but a less percentage decrease rate of GFR than PN, and RFA may be a better application for SRM (<4 cm).

Materials and methods

We searched through the major medical databases such as PubMed, EMBASE, Medline, Science Citation Index, Web of Science and CNKI (Chinese National Knowledge Infrastructure

Database) and Wangfang (Database of Chinese Ministry of Science & Technology) for all published studies without any limit on language from May 2007 until May 2015. The following search terms were used: partial nephrectomy, radiofrequency ablation, renal cell carcinoma, small renal tumor or mass, renal carcinoma. Furthermore, additional related studies were manually searched in the reference lists of all published reviews and retrieved articles ([Figure S1](#)).

Inclusion criteria were: (1) The studies must be published as a full paper without any limitation in language; (2) The trials had to cover the original outcomes of patients of both RFA and PN; (3) The mean size of renal mass was less than 4 cm. (4) The data of patients' clinical and pathological parameters. (age, sex, tumor differentiation and so on) were reported; (5) Availability of at least one of our outcomes: LR, 5y-DFS, SC and PCG. Exclusion criteria were: (1) Studies without full text articles or could not be obtained; (2) No initial data or only assessing parameter of either RFA or PN; (3) Patients with metastasis or with other tumors. (4) The study was not conducted on animals; (5) Experimental trials,

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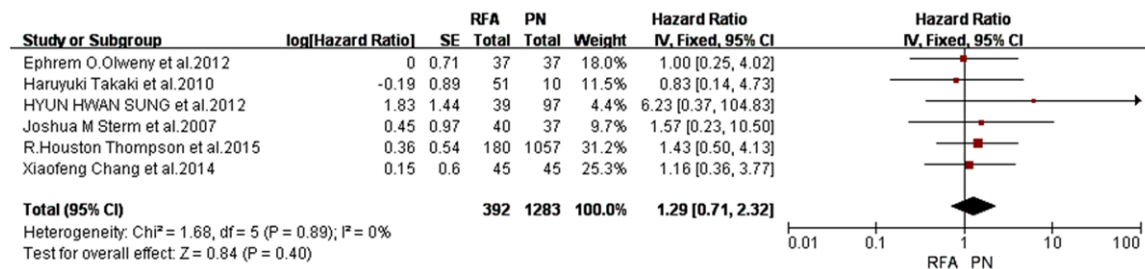


Figure 1. Forrest plot-analysis of 5-year disease free survival.

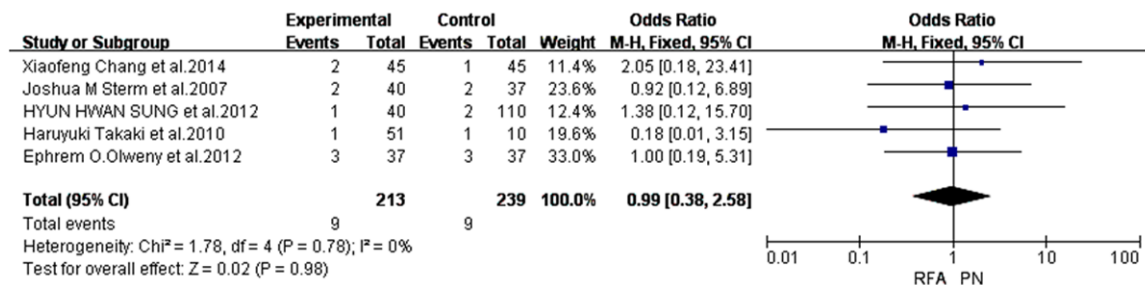


Figure 2. Forrest plot-analysis of local recurrence.

case report, letters, and comments were also excluded.

Data extraction and study quality assessment: Studies selection from the included trails were conducted independently by two authors, and any disagreement was resolved by consensus. The main extracted data included: first author, year of publication, institution, study design, inclusion and exclusion criteria, matching criteria, sample size (cases and controls or cohort size) and outcomes of interest. The Newcastle-Ottawa Scale (NOS) was applied to assess the quality of the studies, and a study with ≥ 7 awarded stars was considered as a high-quality study (Table S1).

Statistical analysis

We used the Review Manager software (Rev-Man 5.3, Cochrane Collaboration) to carry out the meta-analysis. 5y-DFS was calculated on the log-hazard scale and expressed as hazard ratio (HR) as recommended for time-to-event outcomes [1]; for LR and SC, the RR was estimated as the common measure of association across trials, along with the 95% confidence intervals (95% CI). Moreover, The Cochrane chi-square test and inconsistency (I²) were used to evaluate the heterogeneity which indicates the percentage of variation across trails contribut-

ing to heterogeneity not to chance. We pooled the effect estimates from the quality studies using a random effects model, which considered both within- and between-study variations, yielding less fixed-effect model than conservative results. The I² was below 50%, the fixed-effect model was conducted such as 5y-FDS, LR and SC and I² was above 50% of PDG, the random-effects (RE) model was reported; and Funnel plots were applied to assess publication bias, meanwhile sensitivity analysis was conducted by excluding the heterogeneity-causing studies. The pooled effects were determined by the Z-test, and a P value <0.05 was considered to be statistically significant.

Results

Description of eligible studies: Using the search strategy, we selected more than 800 abstracts which were published before May 2015. After carefully reviewing, we identified 8 eligible studies for analyses from May 2007 to May 2015, and this resulted in a total number of 1813 patients. 470 patients in the RFA group and 1343 in the PN group. All were retrospective trials. In addition, four studies [2-5] were conducted in USA, two [6, 7] in Korea, one [8] in China and one [9] in Japan. The quality of all the studies was satisfactory. All patients follow up after RFA and PN included periodic history, physical,

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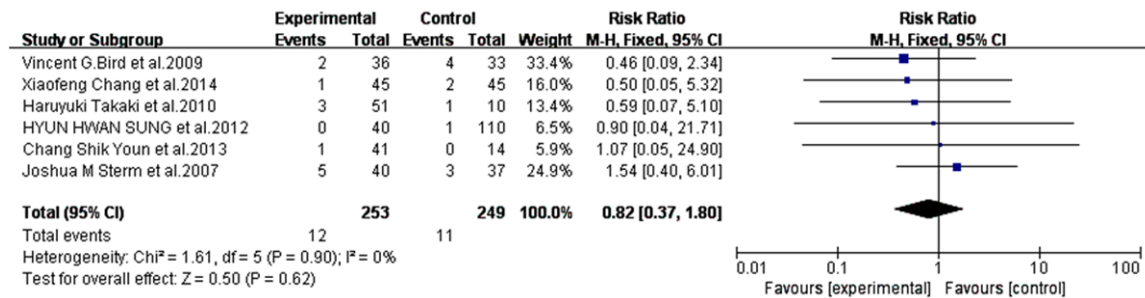


Figure 3. Forrest plot-analysis of surgical complications.

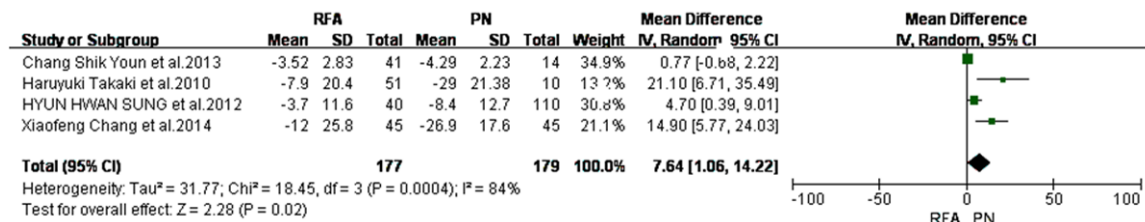


Figure 4. Forrest plot-analysis of the percentage decrease of GFR.

chest radiograph, contrast-enhanced abdominal CT or MRI, serum chemistries, and liver function tests [10]. We extracted all the information that we needed from the studies included for our meta-analysis.

In this meta-analysis, there were no statistical differences between groups in 5y-DFS [HR=1.29, 95% CI (0.71, 2.32), P=0.40], local recurrence rate [OR=0.99, 95% CI (0.38, 2.58), P=0.98] and surgical complications [RR=0.82, 95% CI (0.37, 1.80); P=0.62] between RFA and PN. However, RFA has a lower rate of percentage decrease of GFR [MD=7.64, 95% CI (1.06, 14.22), P=0.02] than PN. All of the outcomes, except for percentage decrease of GFR, had no observed heterogeneity (Figures 1-4). Meanwhile, sensitivity analysis was performed by omitting one study at a time, generating the pooled estimates and comparing with the original estimates. The results between studies was stable in LR, SC and 5y-DFS; the heterogeneity was not significantly reduced by the sensitivity analysis in PCG (Chi²=16.32, P=0.0003, I²=88). And the funnel plots (Figure S2) showed there were no significant publication bias.

Discussion

Partial nephrectomy is a well-established treatment modality for local renal tumor with proven

safety and efficacy and remains the gold standard for the treatment of patients with T1a renal tumors [11]. However, surgical procedures are being challenged as minimal ablative techniques become available. Articles in the recent literature have demonstrated that radiofrequency ablative techniques are effective treatments with acceptable effectiveness and risks, including a generally low risk of complications and change in GFR. Thus, we conducted this meta-analysis to compare RFA with PN for small renal mass in our interested outcomes: 5-year-DFS, recurrence rate, surgical complications, and the percentage change of decrease rate in GFR. We anticipate what this meta-analysis could provide an evidence-based basis for clinical trials for comparing treatment for SRM.

To our knowledge, this meta-analysis is the first study to systematically estimate the effectiveness and safety of RFA and PN in the treatment of small renal mass, through a review of published comparative studies. In total, there were 8 eligible studies and 1813 patients were included in our study.

We demonstrated that there were no statistical differences between groups in 5y-DFS, recurrence rates, complications between RFA and PN. As for the survival, PN is known to offer

excellent long-term oncologic cure; and a retrospective review from Memorial Sloan Kettering [12] evaluated 252 patients who had either nephrectomy or PN for renal masses of <4 cm. The DFS for the PN group at 3 and 5 years was 96%. Compared with high rate survival of PN, renal ablative surgery is a newer technology, but abstracted intermediate follow-up data appear to mirror the outcomes seen with PN in contemporary series [13]. Olweny [3] reported their comparative 5-year oncologic outcomes for RFA vs PN in patients with clinical T1a RCC. They concluded that the respective 5-year OS was 97.2% vs. 100% ($P=0.31$), CSS was 97.2% vs. 100% ($P=0.31$), DFS was 89.2% vs. 89.2% ($P=0.78$), local RFS was 91.7% vs. 94.6% ($P=0.96$), and MFS was 97.2% vs. 91.8% ($P=0.35$). Increasing matched analysis confirmed that there was no significant difference in the survival rates between RFA and PN cohorts, which was similar to our finding. From the anatomic point, PN separates the tumor from normal renal tissue, thus patients can be permanently cured. However, RFA causes coagulation necrosis within the tumor [14, 15]. When electrical current from the uninsulated RF electrode is delivered to the tumor, ionic agitation occurs in the tissue, resulting in heat energy. This results in the tumor clotting and necrosis [16, 17]. We found that the recurrence rate was not significantly different between the two techniques [OR=0.99, 95% CI (0.38, 2.58), $P=0.98$]. Stern JM [9] recently reported their experience with 37 patients that the recurrence-free probability for RFA and PN was 93.4% and 95.8% ($P=0.674$), respectively. In the series reported by Chang [8], a total of 90 patients (RFA45; PN45) were included in the final study after being matched by propensity scores, and the result of 5-year recurrence-free survival (95% CI) was 95.4% (89.3-98.1) vs. 97.7% (93.3-99.2). RFA should have fewer surgical complications over PN [18, 19], but unfortunately, these available data in our meta-analysis do not get the point.

When taking a closer look at each study, we could find that RFA had a less percentage decrease rate of GFR than PN. According to Lucas [21], they reported that RFA is superior to PN in terms of preserving renal function in patients with SRM with short follow up time. In nephron-sparing surgery, warm ischemia to the kidney leads to increase injury renal function. At the same time, resection of partial kidney

also leads to a loss of parenchyma. In contrary, RFA was signed as a less invasive approach without blocking the blood flow of kidney and keeping as much more as nephron, and renal function is protected in uttermost. At this point, RFA might be recommended to the patients with chronic renal diseases. And this is in accordance with most clinical trials.

The present meta-analysis carries few limitations that must be taken into account. The main limitation is that our meta-analysis contain only retrospective data, all the studies included were observational, and the small number of cases in several studies also decreased the reliability of the results. Although we compared the study groups with respect to all variables known to affect the primary outcome, there are certainly variables unaccounted and confounders for that may affect the results. Second, the studies included in the analysis were mostly conducted at varied major institutions. It was not possible to match all patient groups for age, BMI, preoperative therapy, and previous abdominal history. All these factors may have contributed to a high heterogeneity between studies. Because of these limitations, a randomized control trial could confirm these results.

Conclusion

Considering RFA's relatively minimal invasiveness, excellent preservation of renal function, and acceptable effectiveness and side effects, RFA may be a better application for SRM (<4 cm). We expected a randomized control trial to confirm these results.

Acknowledgements

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Disclosure of conflict of interest

None.

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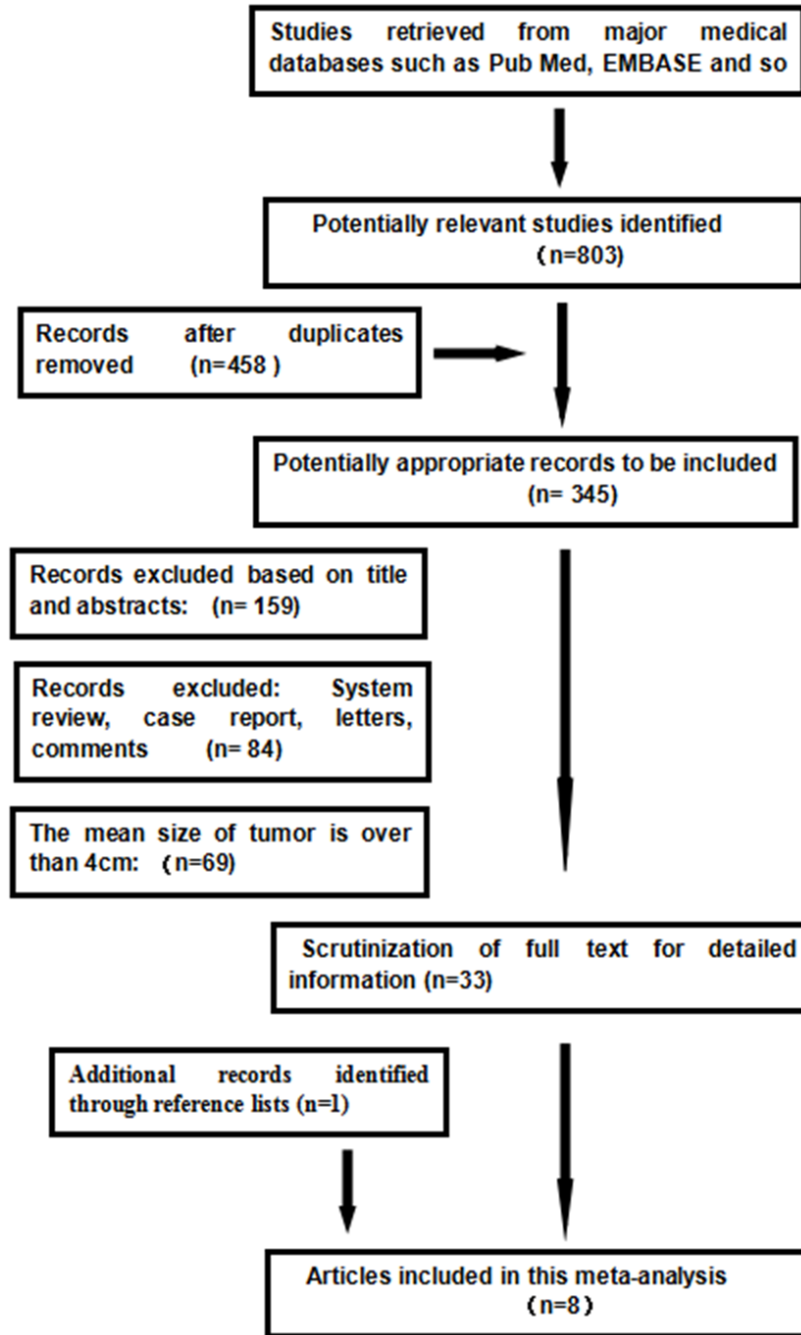


Figure S1. Preferred reporting items for meat-analysis flow of study selection.

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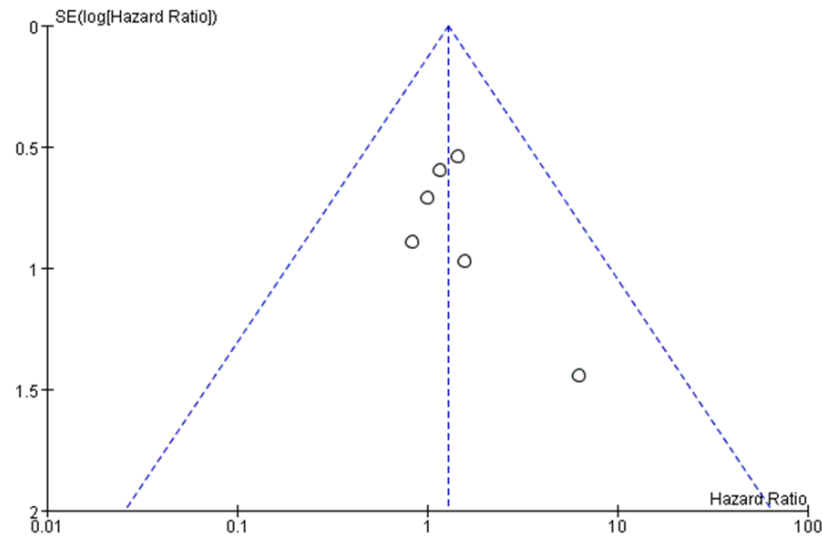


Figure S2. Funnel plots of studies to detect publication bias.

Table S1. Characteristics and quality assessment of the included studies

Reference	Country	Period	Sample		Age (year)		Gender (M/F)		Tumor Size (mean: cm)		Follow Up (month)	Quantity
			RFA	PN	RFA	PN	RFA	PN	RFA	PN		
Xiaofeng Chang et al. 2014	China	2005-2009	45	45	52.9	52.8	38/7	34/11	3.0	3.0	50	*****
Chang Shik Youn et al. 2013	Korea	2007-2012	41	14	52.9	53.9	27/14	8/6	2.3	2.4	34	*****
Haruyuki Takaki et al. 2010	Japan	2007-2012	51	10	69.4	64.0	36/15	8/2	2.4	1.9	46	*****
Joshua M Stern et al. 2007	USA	1996-2004	40	110	59.8	53.4		NA	2.4	2.4	72	*****
Ephrem O.Olweny et al. 2012	USA	1998-2005	37	37	63.8	54.8	24/13	20/17	2.1	2.5	37	*****
HYun H Sung et al. 2012	Korea	2006-2008	40	110	59.8	53.4	33/7	78/32	2.4	2.2	27	*****
Vincent G.Bird et al. 2009	USA	2002-2007	36	33	59.8	57.8	22/13	18/15	2.8	3.1	48	*****
R.Houston Thompson et al. 2015	USA	2000-2011	180	1057	70.7	60.1	14/66	647/410	1.9	2.4		*****

NA: Not mentioned.