

Comparative outcomes of radio frequency ablation versus partial nephrectomy for T1 renal tumors: a systematic review

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Background: The role of radio frequency ablation (RFA) in small renal tumors remains controversial. This systematic review was performed to compare clinical outcomes of RFA versus partial nephrectomy (PN) for the treatment of T1 renal tumors.

Methods: A total of 11 studies including 2,397 patients were analyzed in this systematic review after searching the databases of PubMed, EMBASE and Web of Science. P value and odds ratio (OR)/hazard ratio (HR) with 95% confidence interval (CI) were used to evaluate the strength of the association.

Results: A total of six studies (2,056 patients) provided either survival curves or HR and its 95% CI, demonstrating that the majority of the patients with RFA treatment tended to exhibit a similar long-term survival rate to those with PN treatment. In addition, according to four studies, no differences were found in the overall rate of complications between the two groups. Furthermore, there were significant differences in glomerular filtration rate (GFR) change between the two methods in four studies but no differences were observed in other two.

Conclusions: Our systematic review indicated that RFA is an effective treatment option which could provide comparable oncologic outcomes to PN. Moreover, it may present obvious advantages in renal function preservation.

Keywords: Radio frequency ablation (RFA); partial nephrectomy (PN); T1 renal tumors; systematic review

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Introduction

Renal cell carcinoma (RCC), accounting for approximately 2-3% of all malignancies in adults, is considered as the seventh most common cancer in male and the ninth most common cancer in female (1). There are approximately 209,000 new cases and 102,000 deaths reported each year

worldwide (2). Recently, the detection rate of RCC has grown with the increasing use of cross-sectional imaging, resulting in a great number of accidentally diagnosed small RCCs with lower histological grades and lower possibility of metastases (3-6).

Traditional surgical treatment of renal tumors has



Figure 1 Flow diagram of the study selection process.

undergone a transformation in the past decade (7). Previously, partial nephrectomy (PN) was shown as a common surgical procedure for the treatment of T1 renal tumors (8,9). But in recent years, novel minimally invasive procedures [e.g., radio frequency ablation (RFA)] have been increasingly applied (10). The principle of RFA is to destroy the tumor tissues with heat and desiccation by radio frequency current, which can be performed through open incisions, laparoscopic or percutaneous routes under image guidance [i.e., ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT)] (11-13).

However, elderly patients with T1a stage (defined as a tumor 4 cm or less, confined to the kidney) or patients who cannot undergo a surgery are more appropriate for minimally invasive surgery of RFA to avoid unnecessary surgical complications (14). Furthermore, high temperature of RFA may bring about some side effects, such as inadvertent injury of non-target tissues. In consequence, the efficacy and safety of RFA in the treatment of T1 renal tumors remain controversial. Therefore, we performed a systematic review to compare outcomes (include longterm survival rates, complication events and renal function changes) of RFA versus PN in the treatment of T1 renal tumors.

This systematic review followed the PRISMA guidelines (15).

Methods

Search strategy

Several electronic databases were searched to identify relevant literature including PubMed, EMBASE and Web of Science with a deadline of March 30, 2019. Basically, only studies published in English were included in this systematic review. For the literature retrieval, the following key words were utilized: ("percutaneous ablation", or "radio frequency ablation"), ("partial nephrectomy", or "nephrectomy"), and ("T1 renal cell carcinoma", "T1 renal tumor", or "T1 renal masses"). In order to minimize the omission of the study, we manually screened the list of references for eligible studies to obtain more publications. A flow diagram of the study selection process is presented in *Figure 1*.

Inclusion and exclusion criteria

Eligible studies should meet the following criteria: (I) studies comparing the outcomes between RFA and PN in T1 renal tumors; (II) data obtained in different studies did not overlap. Instead, the exclusion criteria were displayed as follows: (I) studies consisted no usable data of outcomes of RFA versus PN in the treatment of T1 renal tumors; (II) studies had overlapped data; (III) reviews, abstracts or animal studies.

Data extraction

All useful data involved in eligible studies were extracted by two investigators (X Wei and X Ren) independently. The results were reviewed by a third investigator (Y Ding). The following elements were extracted from each selected study: (I) name of first author, publication year, study design, type of RFA and PN; (II) number of patients (case and control), follow-up period; (III) basic information of total patients; (IV) survival curves or hazard ratio (HR) and its 95% confidence interval (CI); (V) treatment complications; (VI) renal function changes.

Quality assessment

Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of articles included. All 11 studies were evaluated strictly and scored at least 7 points (*Table 1*).

Results

Characteristics of included studies

A total of 11 relevant studies (16-26) were finally included in this systematic review, including 2,397 patients with the average age of 59.07. The characteristics of patients receiving RFA or PN treatment are displayed in *Table 1*. The summary results indicated that most patients in the RFA group were visibly older (16,18,21,22,24). Five studies showed smaller tumor size in RFA group than those in the PN group (16,18,20-22), while two studies show larger tumor size (23,25). However, no statistical differences were observed in gender (16,17,19,21-25).

Long-term survival rates

A total of 6 studies (1,700 patients) provided either survival curves or HR and its 95% CI. As indicated in *Table 2*,

the HR of overall survival for RFA compared with PN were provided in three articles [Chang 2015: HR =1.00 (0.81–1.24); Chang 2015: HR =0.86 (0.49–1.50); Thompson 2015: HR =1.99 (1.62–2.45)]. The results from Chang *et al.* and Chang *et al.* (20,21) showed no significant survival advantage for RFA, while the advantage of PN could be observed in Thompson's research (22). In addition, three studies consistently exhibited insignificant differences in recurrence-free survival time [Chang 2015: HR =1.02 (0.67–1.56); Sung 2012: HR =1.06 (0.84–1.31); Stern 2007: HR =1.08 (0.53–2.22)].

Overall complication events

Six studies (559 patients) reported the overall complication events, including urine leak, urinary retention and delay bleeding. Complications were classified by the Clavien-Dindo classification system. As is displayed in *Table 3*, a total of 48 complication events were observed, in which minor complications accounted for more than 80% of all complications. According to four studies (19,21,24,25), there were no obviously differences in the incidence of total complications between two groups (P=1, P=0.241, P=1, and P=0.47).

Pre/post-GFR and GFR change

Nine studies (1,083 patients) provided either pre/post-GFR or change in GFR. Detailed differences in pre/post-GFR between the two group are summarized in *Table 4*. According to the results from Zhu *et al.* (17), Pantelidou *et al.* (18), Huang *et al.* (19) and Sung *et al.* (24), the decline in GFR was smaller in the RFA group than in the PN group (P<0.001, P<0.0001, P=0.048, P=0.013, respectively). However, no significant differences were found in studies of Park *et al.* (16), Cooper *et al.* (23) and Takaki *et al.* (25) (P=0.395, P=0.8959, P=0.34, respectively).

Discussion

With the advancement of nephron-sparing technology, traditional surgical procedures have been challenged by new minimally invasive ablation, such as RFA, microwave ablation and cryoablation (27,28). Several previously published studies have demonstrated that RFA was an alternative treatment for T1 RCC with acceptable midterm results and lower risk of complications (29). Nonetheless, there were still several studies revealing that RFA had the

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Name of firs	; ; 		No. of	Stage of			Follow-up (months, m modia	period lean or	Age (years,	, mean or r	nedian)	Sex (m	ale/femal	(e)	Tumor size (c	cm, mean ± ¦ nedian)	SD or	Tu histolo	gy (clear	SON
author	Year Stur	dy design r	atients	renal cell	Type of RFA	Type of PN	PILIA	- 										20		
				carcinoma			RFA	N	RFA	N	P value	RFA	NA	P /alue	RFA	N	P value	RFA P	N P value	8
Park (16)	2019 Retr	ospective study	115	T1a	Laparoscopic	Laparoscopic	60	88	58	53	0.023	45/17	40/13 (.725	2.14	2.75	0.00	49	37 0.294	ø
Zhu (17)	2017 Retr	ospective study	200	T1a	Laparoscopic	Laparoscopic	12	12	56.5	54	0.176	71/29	68/32 (.795	2.8	3.1	0.906	78	74 0.498	ø
Pantelidou (18)	2016 Retr	ospective study	126	F	Percutaneous	Robotic	47.5	18.5	61	54	<0.0001	63	63	Į.	2.11±0.19	2.88±0.13	0.0003	48	54 -	2
Huang (19)	2016 Rar clir	ndomized ical trial	89	T1a	Laparoscopic	Laparoscopic	12	12	51	52	0.406	34/10	28/17 (0.123	2.65	3.0	0.215	29	31 -	2
Chang (20)	2015 Retr	ospective study	268	T1a	Laparoscopic or percutaneous	Open or laparoscopic	66.4±15.7 6	7.0±15.0	56.6±14.6	53.9±11.5	0.117	98/36	81/53 (0.027	3.6±1.5	4.0±1.2	0.004	115 1	20 0.574	ø
Chang (21)	2015 Retr	ospective study	56	T1b	Laparoscopic or percutaneous	Open or laparoscopic	65.9±17.9 7	0.2±11.7	64	56.9	0.001	18/9	18/11 (0.720	4.7±0.5	5.2±0.6	0.001	24	24 1	ø
Thompson (22)	2015 Retr	ospective [.] study	1,237	F	Percutaneous	I	43.2	62.4	70.7	60.1	<0.001	114/66 6	47/410 (0.46	2.1	2.5	<0.001	73 8	36 0.019	ω
Cooper (23)	2015 Retr	ospective study	18	F	Percutaneous	I	I	I	51	53	I	5/4	5/4	4	078±1.739 2	722±0.931.	<0.0001	ω	। ठ	7
Sung (24)*	2012 Retr	ospective study	150	F	Percutaneous	Open	36.6±16.8 3	7.4±15.6	59.8	53.4	0.005	33/7	78/32 (0.152	2.44±1.27	2.23±1.02	0.299	I	I I	œ
Takaki (25)	2010 Retr	ospective study	61	T1a	Percutaneous	Open or laparoscopic	34.0±23.2 2	6.0±16.9	69.4	64.0	60.0	36/15	8/2 (1.71	2.4±0.7	1.9±0.7	0.03	I	I	ω
Stern (26)	2007 Retr	ospective study	22	T1a	Laparoscopic or percutaneous	Open or laparoscopic	29.8	46.7	60.5	56.4	0.63	40	37	I	2.41±0.70	2.43±0.80	0.45	24	23 0.47	ω
*, including (5 patients of	T2 stage. F	3FA, radic	o frequency	/ ablation; PN, par	rtial nephrectom	y; SD, stand	ard deviation	n; RCC, ren	al cell carc	inoma; NO	S, Newca	stle-Otta	va Scale						

Translational Andrology and Urology, Vol 8, No 6 December 2019

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Name of first author	Year	No. of patients	Methods	HR (PN vs. RFA)	95% CI	
Chang (20)	2015	90	Overall survival rate	1.00	0.81–1.24	
Chang (21)	2015	56	Overall survival rate	0.86	0.49–1.50	
Thompson (22)	2015	1,237	Overall survival rate	1.99	1.62–2.45	
Chang (20)	2015	90	Recurrence-free survival rate	1.02	0.67–1.56	
Sung (24)	2012	150	Recurrence-free survival rate	1.06	0.84–1.31	
Stern (26)	2007	77	Recurrence-free survival rate	1.08	0.53–2.22	

Table 2 Summary results of long-term survival between RFA and PN treatment group

RFA, radio frequency ablation; PN, partial nephrectomy; HR, hazard ratio; CI, confidence interval.

Table 3 Summary results of complication events between RFA and PN treatment group

Nome of first suther	Veer	No. of potients	Compl	ication		05% 01	Divoluo
Name of first author	rear	No. of patients	RFA	PN	- OK	95% CI	P value
Pantelidou (18)	2016	126	5	11	0.41	0.13–1.25	-
Huang (19)	2016	89	4	5	0.80	0.20–3.20	1
Chang (21)	2015	56	7	3	3.03	0.70–13.23	0.241
Sung (24)	2012	150	0	1	0.90	0.04–22.58	1
Takaki (25)	2010	61	3	1	0.56	0.05-6.03	0.47
Stern (26)	2007	77	5	3	1.62	0.36–7.31	-

Urinary complications and bleeding were the primary complication, including urine leak, urinary retention and delay bleeding. RFA, radio frequency ablation; PN, partial nephrectomy; OR, odds ratio; CI, confidence interval.

Table 4 Summary results of GFR change between RFA and PN in renal tumor

Nome of		No. of	Pre-GFR	(mL/min/1.7	3 m²)	Post-GFF	R (mL/min/1.73	3 m²)	Change in GFF	R (mL/min/1.73 r	m² or %)
first author	Year	patients	RFA	PN	P value	RFA	PN	P value	RFA	PN	P value
Park (16)	2019	115	94.2	97.5	0.499	84.3	91	0.092	9.85	6.53	0.395
			(35.82–193)	(30.2–155)		(18.4–138)	(41.9–133.7)		(-26.7 to 47.9)	(-62.8 to 90.3)	
Zhu (17)	2017	200	36.30±9.18	38.31±8.29	0.107	32.41±8.19	31.32±7.04	0.314	-9.41±13.82	-17.13±15.19	<0.001
Pantelidou (18)	2016	126	-	-	_	-	-	-	-0.8±9.6	-16.1±19.5	<0.0001
Huang (19)	2016	89	-	-	-	-	-	-	4.5	-11.1	0.048
Chang (20)	2015	268	97.2±30.0	105.7±27.7	0.017	82.7±34.2	78.8±29.8	0.311	-14.5	-26.9	-
Chang (21)	2015	56	78.8±28.9	86.4±29.3	8 0.318	71.6±25.4	76.9±25.0	0.437	-7.2	-9.5	-
Cooper (23)	2015	18	52.44±12.41	56.67±7.73	8 0.7401	50.78±17.13	55.33±10.30	0.7319	1.66±7.58	1.33±2.69	0.8959
Sung (24)	2012	150	75.2±22.1	89.7±12.8	3 0.001	73.0±24.4	82.2±15.1	0.041	2.3±8.6	7.4±10.9	0.013
Takaki (25)	2010	61	49.2	68.6	0.01	49.8	65.1	0.02	3.2	7.0	0.34
			(39.3–63.6)	(57.2–79.6))	(35.5–61.0)	(52.6–74.0)		(–3.6 to 8.2)	(–7.8 to 11.5)	

RFA, radio frequency ablation; PN, partial nephrectomy; GFR, glomerular filtration rate.

605

risk of perforation, fistula and stenosis (30). They suggested that these risks can be avoided by non-ablative treatment. Therefore, the safety and long-term tumor efficacy of RFA remained controversial. Compared with individual studies, systematic reviews can provide comprehensive and reliable results and help explain controversial conclusions. For this reason, we conducted a systematic review to explore whether RFA has significant benefits for small renal tumors compared with PN.

The primary limitation of individual studies is lack of observation concerning long-term prognosis of RFA, including local recurrence rate and long-term survival rate. Our results demonstrated that RFA played a positive but similar role in long-term survival compared with PN. Nonetheless, the overall survival rate of PN group was obviously higher in Thompson's research possibly because of the selection bias (22). In their study, patients treated with PN were significantly younger (P<0.001) and had lower Charlson scores (P<0.001) than those treated with RFA. Furthermore, Sung et al. reported that since the ablation edge of RFA is unclear on unenhanced CT, it is difficult to determine whether the tumor edge is sufficiently ablated during RFA surgery (24). They suggested that if the surgery is performed by less experienced operators, it may result in postoperative residual and recurrence. As a result, the operator experience might have a certain impact on the recurrence-free survival of RFA.

In our study, the complication rate in RFA group was equivalent to that described in PN group. Urinary complications and bleeding were the primary complications of RFA. The goal of RFA is to induce temperatures between 50 and 100 °C throughout the tumor tissue. Irreversible cell damage resulting from high temperatures in RFA treatment may lead to the injury of urinary tract, microvasculature and arterioles, causing the above-mentioned complications. Previous studies revealed that the use of renal pelvis perfusion might reduce the risk of ureteral injury (31). Nevertheless, it might cause inadvertent damage to nerves simultaneously.

It is well known that renal function preservation is another important goal for patients with small renal tumors. Our results indicated that most patients had a smaller decline in renal function after RFA compared with PN method (17-19,24), while another three studies concluded that RFA had a similar benefit as PN in renal function preservation (16,23,25). In these three studies, the mean tumour size (2.14, 4.078, 2.4 cm) treated by RFA were significantly larger than those (2.75, 2.722, 1.9 cm) treated by PN. The researchers failed to match for tumour size in their study. As mentioned previously, tumor size was regarded as a significant indicator of the outcomes of patients with RFA. Therefore, lack of matching tumor size may reduce the accuracy of the results to a certain extent. Furthermore, retained renal parenchyma and warm-ischemia time (WIT) play important roles in affecting postoperative renal function (32). Krokidis *et al.* (33) revealed that RFA did not require clamping the main renal artery, thus eliminating the WIT required for all types of surgical removal of the kidney mass. Therefore, RFA therapy might be superior to PN in preserving renal function.

Admittedly, there are still several limitations in our review. First, we only enrolled 11 articles which focused on the outcomes between RFA and PN in T1 renal tumors. With an increasing number of clinical studies being published, more high-quality studies could be enrolled to strength our conclusion. Second, our systematic review was composed of 11 individual articles with different contents, which might result in limited statistical validity and scattered results. Third, other information besides tumor size and histology (e.g., tumor location and ethnicity) was not available in most studies. Fourth, Sung's study (24) included five RCC patients of stage T2, which might cause a slight bias. However, due to limited number of studies comparing these two methods, they were also included in this analysis. More studies with high-quality are required in the future to get more accurate results.

In conclusion, RFA is an effective treatment option which requires enough training and sufficient experience. Despite of its postoperative complications, the advantages of RFA are evident. For patients with T1 renal tumors, it could provide comparable long-term oncologic outcomes to PN and promote renal function preservation. Nevertheless, further studies are required to draw a more accurate conclusion.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Translational Andrology and Urology, Vol 8, No 6 December 2019

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Wei et al. RFA versus PN in T1 renal tumors

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