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Impact of thermal ablation/cryoablation treatment on prognosis among patients with kidney cancer: a SEER database-based cohort study

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Abstract

Background Radiofrequency ablation (RFA) and cryoablation are minimally invasive treatments for renal cell carcinoma (RCC). However, their comparative efficacy remains under evaluation. This study aims to compare overall survival (OS) and cancer-specific survival (CSS) outcomes using data from the Surveillance, Epidemiology, and End Results (SEER) database.

Methods This retrospective cohort study included patients diagnosed with T1a-bN0M0 RCC from the SEER database (2004–2018). Propensity score matching was used to control for confounders, including age, sex, and tumor characteristics. Cox proportional hazards regression was applied to assess OS and CSS.

Results A total of 3768 patients were analyzed, including 3499 with T1a and 269 with T1b tumors. Patients aged > 65 years and those with T1b tumors exhibited significantly lower OS and CSS ($P < 0.001$). RFA was associated with reduced OS compared to cryoablation ($P = 0.012$). Multivariate analyses further confirmed that elderly patients, particularly those with T1b tumors, experienced worse OS ($P = 0.0104$) and CSS ($P = 0.008$) following RFA compared to cryoablation. Subgroup and competing risk analyses consistently demonstrated lower cumulative mortality in the cryoablation group.

Conclusions Cryoablation offers superior survival outcomes compared to RFA for T1a and T1b RCC, particularly in elderly patients. These findings support cryoablation as the preferred minimally invasive treatment for early-stage kidney cancer.

Keywords Kidney cancer, SEER database, Radiofrequency ablation, Cryoablation, Propensity score matching, Survival analysis

Background

The primary malignant tumors originating in the kidney include renal cell carcinoma (RCC), renal pelvis carcinoma, and Wilms tumor, with RCC accounting for 85 to 90% of kidney malignancies, comprising approximately 2.4% of all adult cancer cases. It ranks as the second most prevalent malignancy of the urinary system, and there is a notable annual increase in the

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incidence of RCC by about 2.5% [1]. Currently, the median age for RCC onset is about 65 years and the disease predominantly affects males, with a male-to-female ratio of 2:1 [2, 3]. However, due to the complex biological process of aging, the functional reserve, tolerance to invasive procedures, and comorbidities were significantly different among the young and the old cancer patients [4], 65 years is regarding a landmark for increased risk of cancer and associated mortality [5], therefore, age should be considered as an important factor for the treatment selection and outcome evaluation [6]. Although partial nephrectomy (PN) was widely used and achieved great performance for the treatment of RCC, recent developments in image-guided ablation has emerged as a leading treatment for solid tumors, including kidney cancer [7–10]. This method is particularly beneficial for patients with renal insufficiency or those who are ineligible for surgical interventions, with current guidelines favoring ablative therapy over nephron-sparing PN.

Specifically, radiofrequency ablation (RFA) and cryoablation are both minimally invasive treatments for renal cell carcinoma (RCC) [11]. Cryoablation is distinguished by its ability to allow real-time visual monitoring of the freezing process, enhancing the accuracy of the procedure [12]. Although commonly used for T_{1a} RCC, cryoablation's effectiveness in T_{1b} cases is questionable due to its recurrence rate, which varies in different studies and can reach up to 34.5% for cT_{1b} tumors [11, 13]. The risk of disease progression increases by 32% for each centimeter increase in tumor size, highlighting the importance of tumor size as a key factor in treatment outcomes [3]. While RFA is another minimally invasive technique that uses high-frequency electrical currents to produce heat, inflicts thermal damage on targeted tissues. In the context of kidney cancer, RFA is optimally used for small, localized tumors (predominantly T_{1a}), aiming to destroy cancer cells while sparing adjacent healthy kidney tissue [14, 15]. The advantages of RFA include reduced recovery times and fewer complications compared to conventional surgery, although its effectiveness might be compromised for larger tumors or those situated near vital structures. For clinical T_{1b} tumors, reported 5-year disease-free survival (DFS) rates after RFA range between 74.5 and 81% [16]. Comparing these two techniques, RFA is advised for tumors no larger than 3 cm, while cryoablation can be applied to tumors up to 4 cm in diameter [17], moreover, no significant difference in cancer-specific survival between RFA and cryoablation for T_{1a} RCC, which made the clinical selection of RFA or cryoablation more difficult [18].

While these figures appear lower than those for surgical methods, direct comparisons are often skewed by inherent biases. Some non-comparative studies suggest that tumor ablation may improve long-term survival, but the absence of control groups in these studies invites skepticism. The use of the US Surveillance, Epidemiology, and End Results (SEER) database helps overcome these biases by offering a controlled setting to assess the efficacies of different treatments across a diverse group of patients, providing a more accurate evaluation of ablation therapies' impact on kidney cancer management.

In this analysis, we aimed to compare the minimally invasive techniques (RFA and cryoablation) for treating early-stage kidney cancer in different age groups (≤ 65 and > 65 years) using the SEER database. Employing propensity score matching (PSM) to ensure balanced comparisons, we examine both overall survival (OS) and cancer-specific survival (CSS) among patients undergoing either thermal ablation or cryoablation. This methodology affords a thorough insight into the relative effectiveness of these interventions.

Methods

The demographic and clinical data for this study were obtained from the SEER database, with follow-up data updated through December 31, 2018. Data extraction was performed using SEER*Stat software (version 8.4.0), including variables such as age, sex, race, year of diagnosis, tumor grade, T stage, pathological classification, treatment modality, survival duration, and vital status. Since the median age for RCC onset is about 65 years, RCC patients > 65 years were defined as the older group, while patients ≤ 65 years were defined as the younger group.

The inclusion criteria were as follows: (1) a confirmed diagnosis of isolated primary renal cell carcinoma (ICD-O-3 site code: C64.9) based on pathological biopsy, recorded between January 1, 2004, and December 31, 2018; (2) classification as stage T_{1a}-bN0M0 according to the 8th edition of the AJCC Cancer Staging Manual; and (3) treatment with thermal ablation techniques (including RFA and microwave ablation, MWA) or cryoablation. Patients were excluded if they (1) had a history of malignancies in addition to renal cell carcinoma; (2) presented with bilateral kidney cancer or incomplete data on the contralateral kidney in cases of unilateral cancer; or (3) had incomplete medical records.

As a retrospective cohort study utilizing publicly available SEER data, this investigation did not require informed consent. Ethical approval for the study was waived by the Ethics Committee of Ruijin Hospital, affiliated with Shanghai Jiao Tong University School of Medicine.

Statistical analysis

Statistical analyses were conducted using R software, version 4.0.3 (Institute for Statistics and Mathematics, Vienna, Austria; www.r-project.org). We employed Pearson's χ^2 test to evaluate the distribution of demographic characteristics and clinicopathological features between the thermal ablation and cryoablation groups. The primary endpoints of this study were CSS and OS among patients with renal cancer. Survival curves for OS and CSS were plotted using the Kaplan–Meier method, and differences between curves were assessed with the log-rank test. We used both univariate and multivariate Cox proportional hazards regression models to identify prognostic factors that impact OS and CSS. Additionally, the effects of various ablation techniques on survival outcomes were examined in subgroup analyses; these findings, including hazard ratios (HRs), 95% confidence intervals (CIs), and P-values, were presented in forest plots. To minimize bias and ensure a balanced comparison of baseline characteristics across groups, propensity score matching was implemented in a 1:2 nearest-neighbor ratio with a caliper width of 0.05, based on factors such as age, gender, race, year of diagnosis, tumor location, histological type, and tumor grade. Statistical significance was established at a two-sided P-value of less than 0.05.

Results

Clinical baseline features

An analysis of the SEER database (Fig. 1) identified 3768 patients diagnosed with T1a-bNOMO renal carcinoma. Among these, 3499 patients were classified as stage T1a and 269 as stage T1b. Thermal ablation was performed on 983 patients (26.09%), with 910 (92.57%) belonging to the T1a subgroup and 73 (7.43%) to the T1b subgroup. Conversely, cryoablation was chosen for 2785 patients (73.91%), including 2589 (92.96%) in the T1a subgroup and 196 (7.04%) in the T1b subgroup.

Following PSM, baseline characteristics were balanced between the two treatment groups, ensuring comparability ($P > 0.05$). The matched dataset included 980 patients undergoing thermal ablation and 1931 receiving cryoablation, comprising 910 T1a and 70 T1b patients in the thermal ablation group and 1798 T1a and 133 T1b patients in the cryoablation group. Detailed demographic and clinical characteristics before and after PSM ($n = 3768$ pre-PSM; $n = 2911$ post-PSM) are presented in Table 1, confirming robust equivalence of key variables between cohorts. These balanced distributions are critical for reliable comparison of outcomes.

Univariate and multivariate analysis

Univariate and multivariate Cox regression analyses (Table 2) identified significant factors influencing OS

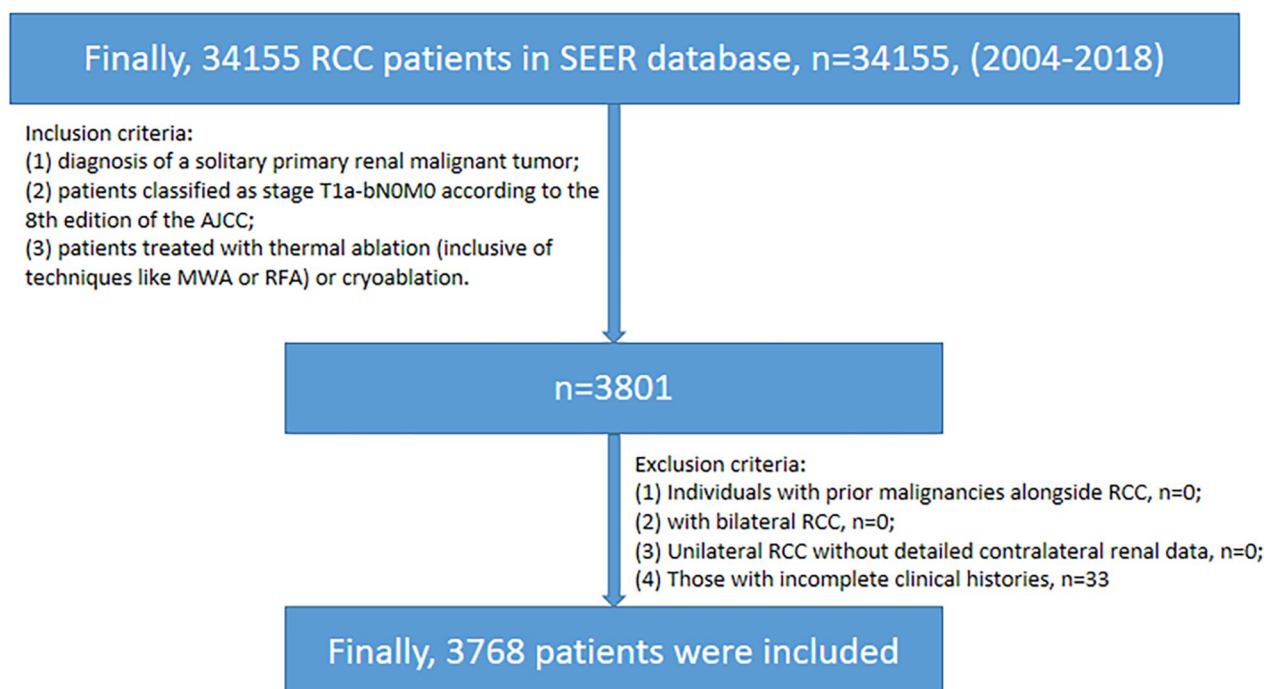


Fig. 1 The flowchart of the included population in the study

Table 1 Baseline characteristics

Variables	Original data set			After PSM		
	Cryosurgery, n = 2785	Thermal ablation, n = 983	P	Cryosurgery, n = 1931	Thermal ablation, n = 980	P
<i>Age (%)</i>						
> 65	1518 (54.5)	570 (58.0)	0.064	1128 (58.4)	569 (58.1)	0.886
≤ 65	1267 (45.5)	413 (42.0)		803 (41.6)	411 (41.9)	
<i>Sex (%)</i>						
Female	1060 (38.1)	398 (40.5)	0.192	760 (39.4)	396 (40.4)	0.612
Male	1725 (61.9)	585 (59.5)		1171 (60.6)	584 (59.6)	
<i>Race (%)</i>						
Black	278 (10.0)	127 (12.9)	0.012	229 (11.9)	125 (12.8)	0.762
Other	150 (5.4)	64 (6.5)		123 (6.4)	64 (6.5)	
White	2357 (84.6)	792 (80.6)		1579 (81.8)	791 (80.7)	
<i>Year of diagnosis (%)</i>						
2004–2008	421 (15.1)	139 (14.1)	< 0.001	277 (14.3)	139 (14.2)	0.988
2009–2013	914 (32.8)	260 (26.4)		506 (26.2)	259 (26.4)	
2014–2018	1450 (52.1)	584 (59.4)		1148 (59.5)	582 (59.4)	
<i>Grade (%)</i>						
G1/2	1354 (48.6)	451 (45.9)	0.257	892 (46.2)	451 (46.0)	0.308
G3/4	122 (4.4)	40 (4.1)		58 (3.0)	40 (4.1)	
Unknown	1309 (47.0)	492 (50.1)		981 (50.8)	489 (49.9)	
<i>Histology (%)</i>						
Renal cell	2272 (81.6)	797 (81.1)	0.764	1546 (80.1)	794 (81.0)	0.571
Other adenocarcinoma	513 (18.4)	186 (18.9)		385 (19.9)	186 (19.0)	
<i>T (%)</i>						
T _{1a}	2589 (93.0)	910 (92.6)	0.738	1798 (93.1)	910 (92.9)	0.858
T _{1b}	196 (7.0)	73 (7.4)		133 (6.9)	70 (7.1)	

Table 2 Multivariate Cox proportional hazard regression model for the OS and CSS

Treatment		Total/events	Model 1		Model 2	
			Uni_P	HR.CI95	P	mul_HR.CI95
OS	Cryoablation		Ref.	–	Ref.	–
	Therapy thermal ablation		0.017	1.23 (1.04–1.46)	0.0104	1.25 (1.05–1.49)
CSS	Cryoablation					
	Therapy thermal ablation		0.012	1.58 (1.1–2.27)	0.008	1.63 (1.14–2.34)

HR hazard ratio, CI confidence interval

Model 1: Crude adjusted

Model 2: Adjusted for age, sex, race, tumor grade, histological type, T stage, year of diagnosis

and CSS. Univariate analysis demonstrated that patients aged over 65 had significantly lower OS (HR=0.35, 95% CI 0.29–0.43, $P<0.001$) and CSS (HR=0.35, 95% CI 0.23–0.54, $P<0.001$). Similarly, T1b tumors were

associated with worse OS (HR=2.1, 95% CI 1.61–2.75, $P<0.001$) and CSS (HR=3.44, 95% CI 2.12–5.57, $P<0.001$) compared to T1a tumors. Patients treated with thermal ablation had inferior OS (HR=1.23, 95% CI

1.04–1.46, $P=0.017$) and CSS (HR=1.58, 95% CI 1.1–2.27, $P=0.012$) relative to those receiving cryoablation (Fig. 2). Notably, cryoablation demonstrated a significant survival benefit for patients with T1b tumors, improving both OS and CSS outcomes (Fig. 3).

Multivariate analysis, adjusted for potential confounders, reinforced these findings. Independent predictors of reduced OS and CSS included age over 65, T1b stage, and thermal ablation. Specifically, thermal ablation was associated with a modestly increased risk of lower OS (HR=1.25, 95% CI 1.05–1.49, $P=0.0104$) and CSS (HR=1.63, 95% CI 1.14–2.34, $P=0.008$), underscoring the significant impact of treatment modality on survival outcomes in kidney cancer.

Subgroup and competitive risk analysis

As shown in Fig. 4, significant differences were observed in cumulative mortality between the thermal ablation and cryoablation groups, both before and after PSM (Gray's test, $P=0.011$ and $P=0.012$, respectively). Over time, the cumulative mortality rate consistently remained lower in the cryoablation group compared to the thermal ablation group. When accounting for competing risks (e.g., death from other causes), cryoablation maintained a survival advantage, highlighting its potential as a more effective management strategy for kidney cancer relative to thermal ablation.

Discussion

Our comprehensive analysis of the SEER database, encompassing 3,768 patients diagnosed with T1a-bNOM0 renal carcinoma, revealed critical differences in clinical outcomes between thermal ablation and cryoablation. By utilizing propensity score matching,

we achieved a balanced comparison across patient groups, minimizing potential confounding factors. This analysis identified key predictors of reduced OS and CSS, including age over 65, the use of thermal ablation, and a diagnosis of stage T1b renal cancer. Furthermore, competitive risk analysis highlighted the distinct advantages of cryoablation over thermal ablation, with significantly lower cumulative mortality rates, even when accounting for deaths from other causes. These findings emphasize the importance of tailoring treatment strategies to individual patient characteristics, particularly age and tumor stage. Notably, cryoablation demonstrated a pronounced survival benefit in specific subgroups, making it a preferred minimally invasive treatment option for renal cell carcinoma. This distinction is essential for optimizing treatment approaches and improving patient outcomes in clinical practice.

Current clinical guidelines suggest thermal ablation as an alternative to nephron-sparing surgery (NSS) for patients with conditions such as hypertension, diabetes, or renal insufficiency, or for those who are unsuitable for surgical interventions [19]. With advancements in medical treatment, the proportion of elderly patients with kidney cancer and those unable to undergo surgery due to various intolerances is on the rise [20–22]. Research indicates that the efficacy of ablation for T1a RCC can rival that of surgery, offering maximal preservation of renal function and minimizing complications associated with surgical procedures, such as infections at the surgical site and intestinal obstruction [23, 24]. Despite these advancements, there remains a significant gap in comparative research concerning the clinical effectiveness and prognosis of

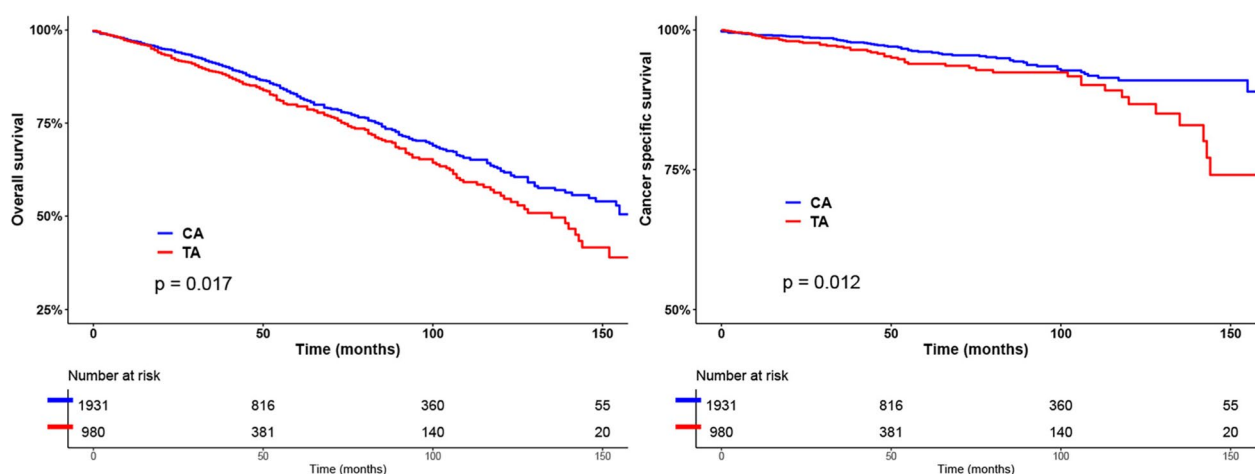


Fig. 2 Survival outcomes by stage in renal cell carcinoma patients. Kaplan–Meier curves for OS and CSS, displaying lower survival rates for T_{1b} compared to T_{1a} RCC patients over 150 months, with statistical significance ($p < 0.0001$). Hazard ratios (HR) reflect increased risk for T_{1b} stage

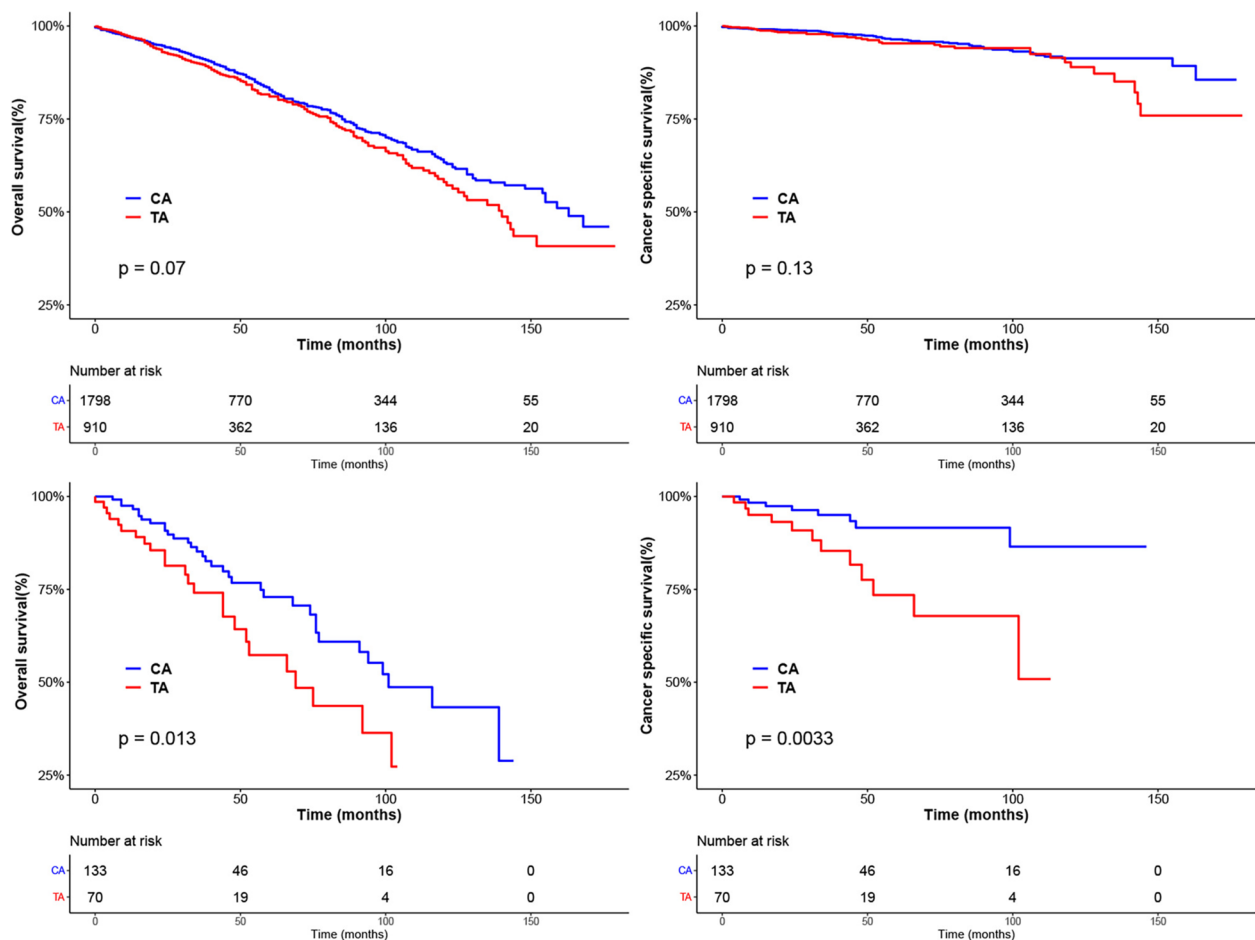


Fig. 3 Survival analysis comparing cryoablation (CA) versus thermal ablation (TA) in patients with renal cell carcinoma (RCC). The upper panels illustrate Kaplan–Meier survival curves for the T1a patients, with overall survival (OS) on the left ($p=0.07$) and cancer-specific survival (CSS) on the right ($p=0.13$). The lower panels are dedicated to patients with T1b stage tumors, displaying OS ($p=0.013$) and CSS ($p=0.0033$) on the left and right, respectively. Notably, for T1b patients, CA significantly enhances survival outcomes as evidenced by both OS and CSS measures, suggesting a potential therapeutic advantage in this subgroup

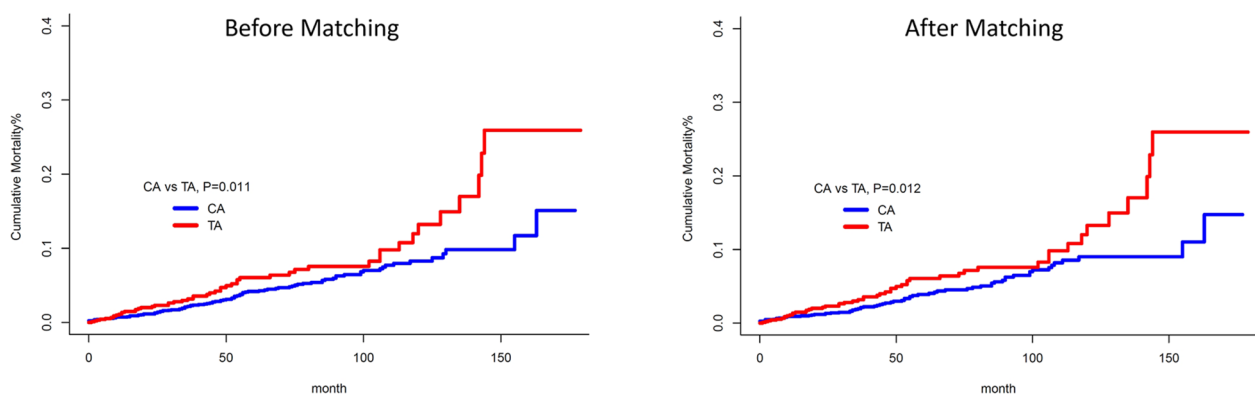


Fig. 4 Cumulative mortality rates in RCC patients: cryoablation vs. thermal ablation pre- and post-PSM. This figure compared cumulative mortality rates for patients receiving cryoablation (CA) versus thermal ablation (TA) in renal cell carcinoma (RCC) treatment, both before (left panel) and after (right panel) propensity score matching (PSM). The X-axis indicates time in months, while the Y-axis shows the cumulative mortality rate. Statistical analysis indicates a significant difference in mortality rates post-PSM ($p=0.012$) favoring CA, suggesting a survival benefit after accounting for confounding variables

different ablation techniques, especially for minimally invasive approaches in treating T2b-stage RCC.

In the SEER database, methods like RFA and MWA are collectively categorized under "thermal ablation." This study seeks to explore the outcomes associated with thermal ablation and cryoablation across various age groups and stages of RCC, utilizing a robust real-world dataset from the United States [25]. For the treatment of RCC, numerous studies have highlighted the outstanding therapeutic benefits of both thermal and cryoablation, Pandolfo et al. reported that MWA, cryoablation, and RFA were all safe and effective treatment options, they also reported that MWA could offer low complication rate [26], Aveta concluded that RFA and cryoablation showed comparable rates regarding recurrence rates and suggested surveillance post-treatment [11]. However, these studies did not perform an age-specific analysis, and studies have shown that increased age is often related to poor-risk biology and reduced tolerance to cancer treatment [27, 28]. In the present study, after adjusting for age, sex, race, tumor grade, histological type, and other factors, results showed that cryotherapy had better survival outcomes over patients receiving thermal ablation, the subgroup analyses further confirmed these findings among those aged 65 years and older. A rigorous evaluation involving RFA, cryoablation, and MWA demonstrated an absence of local recurrence, metastatic progression, or mortality related to RCC within a 2-year follow-up period for patients receiving any of these treatments [29]. Andrews et al. [30] undertook a retrospective analysis involving 1055 T1a RCC patients treated with partial PN, 180 with RFA, and 187 with cryoablation, alongside 324 and 52 T1b patients treated with PN and cryoablation respectively. The five-year CSS rates for T1a patients were notably high at 99% for PN, 96% for RFA, and 100% for cryoablation. For T1b patients, these rates were 98% and 91% respectively. Further, a study from the National Cancer Database (NCDB) [23] indicated that in the cT1a RCC cohort, patients undergoing cryoablation typically experienced longer OS compared to those undergoing thermal ablation. However, among patients with tumors measuring ≤ 2 cm in diameter, no significant difference in postoperative survival rates was observed between the two ablation techniques. Shapiro et al. [31] performed MWA on stage T_{1b} renal cell carcinoma, and the CSS was 100% for 5 years. Guo et al. [5] reported the treatment results of MWA in T_{1b} renal cell carcinoma, with OS of 95.2%, 85.7%, and 71.4% at 1, 2, and 3 years. Gunn et al. [32] conducted a retrospective analysis of 37 T_{1b}RCC patients treated with cryoablation. The relapse-free survival rates at

1, 2, and 3 years were 96.5%, 86.1%, and 62.6%. 1-, 2-, and 3-year CSS were 100%. OS of years 1, 2, and 3 were 96.7%, 91.8%, and 77.6%.

In this study, we conducted an initial comparison of OS and CSS among patients who underwent thermal ablation versus those treated with cryoablation. The findings indicated that both OS and CSS were significantly improved in the cryoablation group as compared to the thermal ablation group. Subsequent analyses focusing on RCC stages T1a and T1b showed that both OS and CSS were higher in stage T1a, suggesting that patients with this stage of RCC have a more favorable prognosis following either treatment modality, relative to those in stage T1b. However, partial PN was still the preferred surgical method for T1 RCC [33], and studies have shown that partial PN was related with a lower cancer specific mortality when comparing to cryoablation [3], while RFA and cryoablation were independent predictors of recurrence [34], but pitifully in this study, and partial PN was not included. Subsequent comparisons within the T1a and T1b subgroups showed that, in the T1a category, the OS and CSS rates for cryoablation were marginally higher than those for thermal ablation, although the differences were not statistically significant. Additionally, a multicenter study involving 23 patients each undergoing RFA and cryoablation for T1b tumors indicated a better response rate to cryoablation compared to RFA. However, the 5-year OS rates were similar between the two methods (78% for cryoablation vs. 82% for RFA; $P=0.82$) [35], highlighting comparable long-term outcomes between these ablation techniques. In this study, a distinct difference in efficacy between thermal ablation and cryoablation was observed within the T1b subgroup, with the latter showing superior outcomes. This suggests that cryoablation may be a more effective interventional therapy option for patients with T1b renal cell carcinoma, diverging slightly from conclusions drawn in earlier, smaller-scale studies.

However, this study still possessed several limitations, first, this study aggregated diverse thermal ablation techniques into a single category, and patients who received PN treatment was not included for analysis; second, we only included SEER database before 2019, the 2018–2021 data was not added to the analysis due to short follow-up time, also, the SEER database only includes cancer-related data from U.S. regions, while previous research already showed that significant disparities in treatment decision-making were found for patients with kidney cancer [36], which could impair the generalization ability of this study; third, it lacks specific details on ablation procedures (such as equipment settings, postoperative complications, or the level of expertise of the medical staff involved, such as

equipment settings, postoperative complications, or the level of expertise of the medical staff involved), detailed tumor information (including tumor localization, size specificity, and local recurrence rates post-treatment), follow-up information (loss of follow-up details), and only a PSM method was performed in this study, these variability complicates the standardization of procedural details across different healthcare facilities; finally, there were several socioeconomic issues, the price of other methods would also affect the clinical outcomes, these confounding factors were not included for analysis in the present study.

Conclusion

In summary, our analysis of the SEER database showed that T1a and T1b renal cell carcinoma patients receiving cryotherapy had better survival outcomes than patients receiving thermal ablation, especially those aged 65 years and older. However, these findings should be further evaluated using a large-scale prospective cohort or randomized controlled trial before clinical application.

Abbreviations

RFA	Radiofrequency ablation
RCC	Renal cell carcinoma
OS	Overall survival
CSS	Cancer-specific survival
NSS	Nephron-sparing surgery

Acknowledgements

Not applicable.

Author contributions

Ziyin Wang and Yuyue Jiang carried out the studies, participated in collecting data, and drafted the manuscript. Wei Huang and Xiaoyu Liu performed the statistical analysis and participated in its design. Qungang Shan, Zhuozhuo Wu and Ziyu Yang participated in acquisition, analysis, or interpretation of data and draft the manuscript. All authors read and approved the final manuscript.

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None.

Data availability

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

Given the retrospective cohort study design and the public availability of the SEER data, this investigation did not necessitate informed consent. Accordingly, the Ethics Committee of Ruijin Hospital, affiliated with Shanghai Jiao Tong University School of Medicine, provided an exemption from review for this study. I confirm that all methods were performed in accordance with the relevant guidelines. All procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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