



Research Article

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Characteristics Associated with Outcomes of Small Renal Mass Thermal Ablation

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Abstract

Purpose: This study aimed to evaluate which treatment, tumor, and patient characteristics are associated with treatment outcomes in patients with renal tumors treated with percutaneous cryoablation or microwave ablation (MWA).

Materials and methods: This single-center retrospective cohort study included patients age 18 and older who underwent CT-guided percutaneous renal tumor MWA or cryoablation for primary renal malignancy between 3/1/2010 and 1/31/2021 with at least two years of contrast-enhanced cross-sectional imaging follow-up. Patient demographics, procedure details, pre- and post-procedure imaging, and tumor characteristics were collected. Negative outcome was defined as recurrent or residual tumor nodularity at the treated tumor site. Categorical characteristics and event status were analyzed using Chi Square and Fisher's exact tests. Kaplan Meier curves were used to analyze event-free survival. Cox proportional hazard models and log rank tests were used to analyze survival probability between the two initial treatment technique groups.

Results: Of the 24 patients, 9 patients received cryoablation and 15 received MWA. The majority (87.5%) had renal cell carcinoma and 75% were at least partially exophytic. Statistically significant difference was identified in recurrence-free survival between patients who had exophytic and non-exophytic tumors ($P = 0.03$). Patients with exophytic tumors had a significantly reduced risk of nodularity recurrence by 76%, based on a hazard ratio of 0.24 (95% CI 0.06-0.93; $P = 0.04$).

Conclusion: Exophytic tumor status demonstrated a statistically significant association with recurrence-free survival. This suggests that tumor exophytic status may be helpful in guiding clinical approach to the treatment of renal tumors.

Level of evidence: Level 3, Cohort Study

Keywords

Renal ablation, Cryoablation, Microwave ablation, Interventional oncology, Renal mass

Introduction

The incidence of renal masses has increased over recent years due to increased incidental findings during imaging studies. Instead of being found when the patient is symptomatic with hematuria or a palpable mass, they are now asymptomatic and earlier staged tumors [1-3]. The management of small renal masses has evolved over the recent years with the advent of new treatments. Partial nephrectomy has revolutionized management of these methods by providing a nephron-sparing approach without compromising oncologic outcome and is now the standard of care for amenable renal masses.

More recently, percutaneous ablative techniques, such as microwave ablation (MWA) and cryoablation, have become an option for management of these masses. They provide

a treatment that is less invasive than partial nephrectomy and can be utilized for patients with more co-morbidities. Ablation therapy for T1 tumors has shown similar efficacy when compared to partial nephrectomy while having less of an effect on estimated glomerular filtration rate (eGFR) postoperatively [4-6]. Percutaneous thermal ablation offers a minimally invasive approach to treatment with

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generally acceptable oncologic outcomes while sparing renal parenchyma. This provides a possible treatment method for patients who would not tolerate a partial nephrectomy.

Urologists tasked with recommending treatment for small renal masses generally have four options: observation, percutaneous thermal ablation, partial nephrectomy, or radical nephrectomy. The urologist must weigh several factors, such as tumor characteristics, patient preferences, and risk, to determine the best route of treatment. Tumor complexity scoring systems such as the radius exophytic/endophytic nearness anterior/posterior location (RENAL) score and the preoperative aspects and dimensions used for anatomic (PADUA) score have historically helped urologists determine whether masses may be amenable to partial nephrectomy [7,8]. Novel scoring systems have also been developed for percutaneous ablation but have not been reliably validated. As percutaneous thermal ablation continues to improve and expand in use, the need for a reliable nomogram for predicting successful ablation still exists. This study aimed to review small renal masses that were ablated using MWA and cryoablation in order to explore patient and procedure related factors that affect outcomes.

Materials and Methods

Institutional Review Board granted approval for the execution of this study. This single-center retrospective cohort study included patients who underwent CT-guided percutaneous renal tumor MWA or cryoablation for primary renal malignancy between 3/1/2010 and 4/30/2020. Patients were excluded if they were under the age of 18, lacked at least two-years of post-procedural cross sectional imaging, or had a diagnosis of von Hippel-Lindau or non-primary renal malignancy.

Patient demographics, and clinical, treatment, and imaging information was collected and managed using RED Cap (Research Electronic Data Capture) electronic data capture tools [9]. Demographic and clinical data collected included age, gender, ethnicity, race and pathologic diagnosis. Treatment

information collected included type of treatment (MWA vs. cryoablation), watts, minutes performed, and type and number of probes used. Baseline and post-treatment imaging of the tumor was assessed, including laterality, location, and size of the tumor, presence of tumor enhancement, distance from renal sinus, distance from skin, and location relative to polar line (entirely above, entirely below, crosses polar line, > 50% across polar line, crosses axial renal midline or entirely between polar lines). Contrast-enhanced CTs and MRIs were used to evaluate imaging. The kidneys had to be fully visible in the imaging studies for them to be included. Outcomes were grouped into five categories: Renal tumor surgical intervention, tumor enhancement, recurrence of nodularity, repeated ablation, and death.

Demographics and baseline imaging tumor characteristics were reported by initial ablation technique that patients received, including mean and standard deviation for continuous variables, and frequencies and percentages for categorical variables. Survival and progression-free survival analyses were conducted to evaluate the associations between characteristics and the outcomes of percutaneous ablation of renal tumors. Chi-square or Fisher's exact tests were performed to examine the association between categorical characteristics and event status. Kaplan Meier curves were used to visualize patient survival after receiving initial treatment, stratified by demographics and baseline imaging tumor characteristics. Log-rank tests were used to examine differences in patient survival by baseline features and recurrence of tumor or nodularity by baseline features. Lastly, univariable Cox proportional hazard models were fit to explore relationships between patient survival and recurrence of nodularity, and those features. A significance level of 0.05 was used for all tests. All statistical analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Twenty-four patients met inclusion and exclusion criteria. Cryoablation treatment was used in nine patients (37.5%) while MWA was used in 15 patients (62.5%). Table 1

Table 1: Summary of demographics.

	Cryoablation (N = 9)	MWA (N = 15)	All (N = 24)
Age (years), mean (SD)	65.4 (8.1)	70.1 (9.6)	68.3 (9.2)
Male, n (%)	7 (77.8%)	10 (66.7%)	17 (70.8%)
Non-Hispanic/Latino, n (%)	6 (66.7%)	14 (93.3%)	20 (83.3%)
Race, n (%)			
American Indian/Alaskan Native	1 (11.1%)	0	1 (4.2%)
Black	1 (11.1%)	3 (20.0%)	4 (16.7%)
White	6 (66.7%)	11 (73.3%)	17 (70.8%)
Unknown	1 (11.1%)	1 (6.7%)	2 (8.3%)
BMI (kg/m ²), mean (SD)	33.5 (9.5)	33.6 (8.9)	33.5 (8.9)
Number of treatments performed on largest tumor, n (%)			
1	4 (44.4%)	10 (66.7%)	14 (58.3%)
2	2 (22.2%)	5 (33.3%)	7 (29.2%)
3	3 (33.3%)	0	3 (12.5%)

summarizes the patient demographics. Patients were mostly male (70.8%), non-Hispanic (83.3%), and White (70.8%). The average age was 68.3 years (SD = 9.2) with an average BMI of 33.5 (SD = 8.9). Patients who received cryoablation as their initial treatment received more repeated treatments than patients who received MWA (55.6% vs. 33.3%).

The baseline imaging characteristics for each treatment group are included in Table 2. Renal cell carcinoma was diagnosed in 87.5% of patients. In the population, 75% had tumors that were at least partially exophytic, 55.6% had tumors that were > 50% exophytic. In the cryoablation group, 44.4% of patients had exophytic tumors and none of them had tumors that were greater than 50% exophytic, while 93.3% of the microwave ablation population had exophytic tumors with 71.4% of the group had tumors that were greater than 50% exophytic.

No significant difference was identified in time between baseline imaging and initial ablation, time between initial ablation and event, or time between initial ablation and first

recurrence of nodularity. There was a significant difference in median survival time for patients receiving MWA (4.6 years) versus those who received cryoablation (2.5 years) (log-rank test P = 0.03) as seen in Figure 1. Cryoablation increases the hazard of event by a factor of 4.30, or 330% as compared to MWA (95% confidence interval [CI] 1.06-17.42; Cox model Wald test P = 0.04). There was marginal significance (log-rank or Cox model Wald test P < 0.10) between median survival time and ethnicity, exophytic status, and tumor size, see Table 3.

A statistically significant difference was identified in recurrence-free survival between patients who had exophytic and non-exophytic tumors (P = 0.03) seen in Table 4. Patients with exophytic tumors had a significantly reduced risk of nodularity recurrence by 76%, based on a hazard ratio of 0.24 (95% CI 0.06-0.93; Cox model P = 0.04).

Discussion

The aim of this study was to identify correlations between patient and renal tumor characteristics and ablation

Table 2: Summary of baseline imaging tumor characteristics.

	Cryoablation (N = 9)	MWA (N = 15)	All (N = 24)
Pathologic diagnosis, n (%)			
Renal cell carcinoma	9 (100.0%)	12 (80.0%)	21 (87.5%)
Other	0	3 (20.0%)	3 (12.5%)
Laterality, n (%)			
Left	7 (77.8%)	6 (40.0%)	13 (54.2%)
Right	2 (22.2%)	9 (60.0%)	11 (45.8%)
Tumor enhancement, n (%)			
Yes	5 (55.6%)	10 (66.7%)	15 (62.5%)
No	2 (22.2%)	2 (13.3%)	4 (16.7%)
Unknown	2 (22.2%)	3 (20.0%)	5 (20.8%)
Tumor size (cm), mean (SD)	2.2 (0.8)	2.8 (1.3)	2.6 (1.2)
Tumor distance from renal sinus (cm), mean (SD)	0.9 (2.1)	1.1 (0.9)	1.0 (1.4)
Tumor distance from skin (cm), mean (SD)	11.0 (5.0)	9.7 (5.0)	10.2 (4.9)
Location, n (%)			
Upper pole - anterior	1 (11.1%)	1 (6.7%)	2 (8.3%)
Mid pole - anterior	0	2 (13.3%)	2 (8.3%)
Lower pole - anterior	4 (44.4%)	2 (13.3%)	6 (25.0%)
Upper pole - posterior	1 (11.1%)	3 (20.0%)	4 (16.7%)
Mid pole - posterior	3 (33.3%)	4 (26.7%)	7 (29.2%)
Lower pole - posterior	0	3 (20.0%)	3 (12.5%)
Exophytic, n (%)	4 (44.4%)	14 (93.3%)	18 (75.0%)
Exophytic: > 50%, n (%)	0	10 (71.4%)	10 (55.6%)
Tumor is entirely above polar line, n (%)	3 (33.3%)	4 (26.7%)	7 (29.2%)
Tumor is entirely below polar line, n (%)	1 (11.1%)	4 (26.7%)	5 (20.8%)
Tumor crosses polar line, n (%)	5 (55.6%)	7 (46.7%)	12 (50.0%)
Tumor is > 50% across polar line, n (%)	3 (33.3%)	6 (40.0%)	9 (37.5%)
Tumor crosses axial renal midline, n (%)	2 (22.2%)	6 (40.0%)	8 (33.3%)
Tumor is entirely between polar lines, n (%)	0	0	0

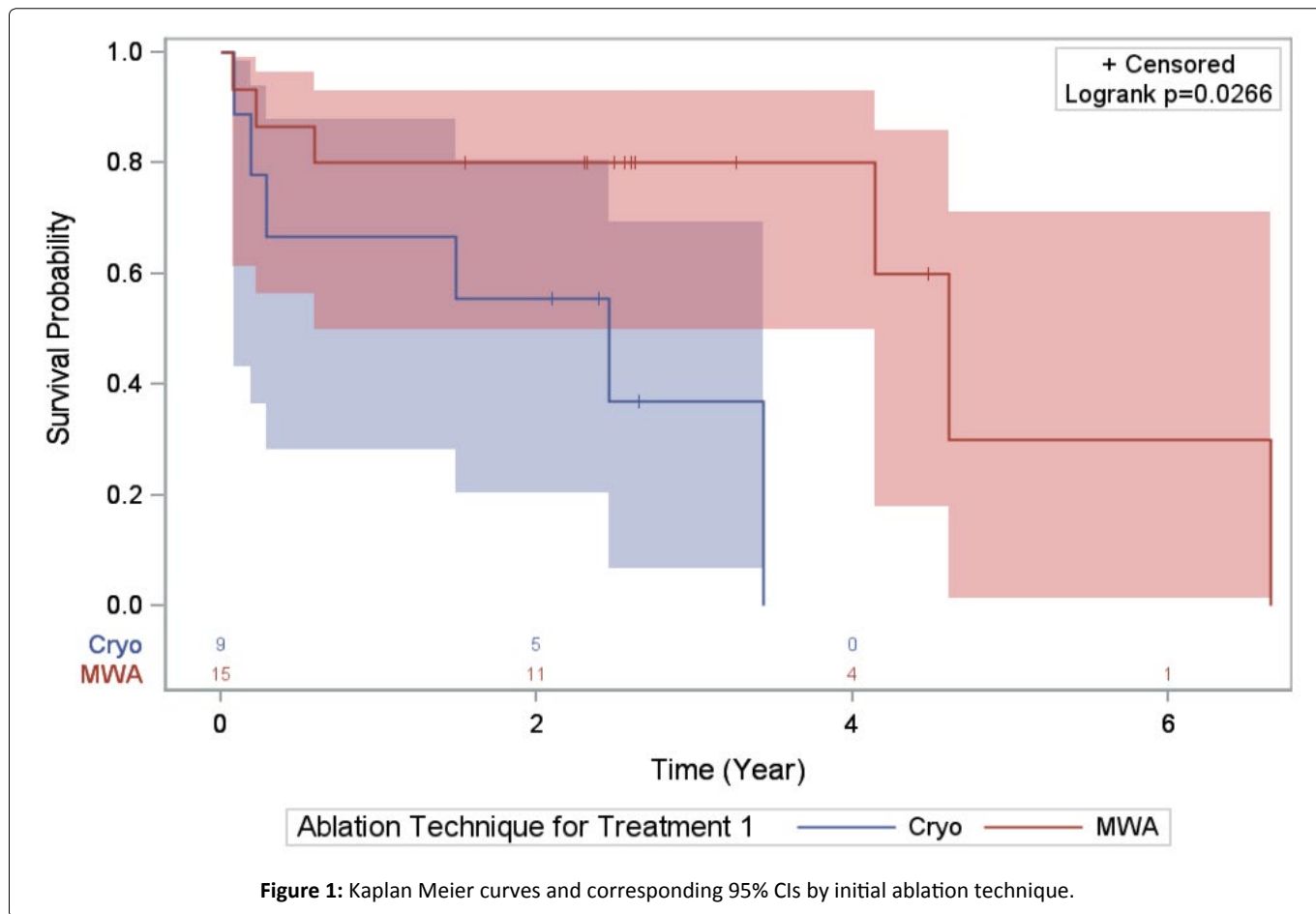


Table 3: Survival analysis.

Characteristics	Log-Rank Test P	Cox Proportional Hazards Model			
		Comparison	Estimate (Std Err)	P	Hazard Ratio (95% CI)
Age (years)	N/A	N/A	-0.07 (0.04)	0.1120	0.94 (0.86-1.02)
Sex	0.3469	Male Vs. Female	-0.60 (0.65)	0.3540	0.55 (0.15-1.95)
Ethnicity	0.0532	Hispanic Vs. Non-Hispanic	-1.33 (0.74)	0.0716	0.26 (0.06-1.12)
		American Indian/Alaskan native Vs. Unknown	16.10 (2482.16)	0.9948	9813679 (N/A)
Race	0.4516	Black Vs. Unknown	15.94 (2482.16)	0.9949	8357575 (N/A)
		White Vs. Unknown	15.07 (2482.16)	0.9952	3490225 (N/A)
BMI (kg/m ²)	N/A	N/A	0.01 (0.04)	0.8300	1.01 (0.94-1.09)
Pathologic diagnosis	0.2399	Renal cell carcinoma Vs. Other	16.26 (2885.56)	0.9955	11502048 (N/A)
Laterality	0.8727	Left Vs. Right	-0.10 (0.65)	0.8724	0.90 (0.25-3.20)
Tumor enhancement	0.9842	Yes Vs. No	0.02 (0.89)	0.9843	1.02 (0.18-5.85)
Location	0.6509	Upper pole-anterior Vs. Lower pole-posterior	-0.72 (1.23)	0.5573	0.49 (0.04-5.40)
		Mid pole - anterior Vs. Lower pole - posterior	-1.94 (1.38)	0.1583	0.14 (0.01-2.13)
		Lower pole - anterior Vs. Lower pole -posterior	-1.64 (1.09)	0.1310	0.19 (0.02-1.63)
		Upper pole posterior Vs. Lower pole -posterior	-0.83 (1.02)	0.4130	0.43 (0.06-3.20)
		Mid pole - posterior Vs. Lower pole - posterior	-1.13 (0.97)	0.2457	0.32 (0.05-2.17)

Exophytic?	0.0762	Yes Vs. No	-1.06 (0.62)	0.0884	0.35 (0.10-1.17)
Exophytic: > 50% or < 50%	0.0565	> 50% Vs. < 50%	-1.88 (1.13)	0.0953	0.15 (0.02-1.39)
Location relative to polar line					
Entirely above	0.9024	Yes Vs. No	-0.08 (0.69)	0.9025	0.92 (0.24-3.57)
Entirely below	0.6469	Yes Vs. No	-0.36 (0.80)	0.6487	0.70 (0.15-3.32)
Crosses polar line	0.6218	Yes Vs. No	0.30 (0.61)	0.6231	1.35 (0.41-4.43)
> 50% across polar line	0.8105	Yes Vs. No	-0.15 (0.63)	0.8106	0.86 (0.25-2.96)
Crosses axial renal midline	0.4179	Yes Vs. No	-0.55 (0.68)	0.4234	0.58 (0.15-2.20)
Entirely between polar lines	N/A	N/A	N/A	N/A	N/A
Tumor size (cm)	N/A	N/A	-0.54 (0.32)	0.0900	0.58 (0.31-1.09)
Tumor distance from renal sinus (cm)	N/A	N/A	0.14 (0.16)	0.3755	1.15 (0.84-1.57)
Tumor distance from skin (cm)	N/A	N/A	-0.04 (0.07)	0.5431	0.96 (0.84-1.09)
Initial ablation technique	0.0266	Cryoablation Vs. MWA	1.46 (0.71)	0.0412	4.30 (1.06-17.42)

Table 4: First recurrence of nodularity analysis.

Characteristics	Log-Rank Test P	Cox Proportional Hazards Model			
		Comparison	Estimate (Std Err)	P	Hazard Ratio (95% CI)
Age (years)	N/A	N/A	-0.05 (0.04)	0.2555	0.95 (0.88-1.03)
Sex	0.7883	Male Vs. Female	-0.19 (0.71)	0.7886	0.83 (0.21-3.33)
Ethnicity	0.0821	Hispanic Vs. Non-Hispanic	-1.21 (0.74)	0.1010	0.30 (0.07-1.27)
		American Indian/Alaskan native Vs. Unknown	15.84 (2419.68)	0.9948	7556297 (N/A)
Race	0.5310	Black Vs. Unknown	15.89 (2419.68)	0.9948	7944431 (N/A)
		White Vs. Unknown	15.05 (2419.68)	0.9950	3436828 (N/A)
BMI (kg/m ²)	N/A	N/A	0.01 (0.04)	0.8034	1.01 (0.93-1.10)
Pathologic diagnosis	0.2771	Renal cell carcinoma Vs. Other	16.25 (3111.30)	0.9958	11436082 (N/A)
Laterality	0.7669	Left Vs. Right	-0.21 (0.71)	0.7673	0.81 (0.20-3.27)
Tumor enhancement	0.7048	Yes Vs. No	0.41 (1.10)	0.7067	1.51 (0.17-13.10)
Location	0.6784	Upper pole - anterior Vs. Lower pole - posterior	-1.04 (1.27)	0.4102	0.35 (0.03-4.22)
		Mid pole - anterior Vs. Lower pole - posterior	-1.45 (1.31)	0.2716	0.24 (0.02-3.10)
		Lower pole - anterior Vs. Lower pole - posterior	-1.39 (1.03)	0.1787	0.25 (0.03-1.89)
		Upper pole - posterior Vs. Lower pole - posterior	-1.29 (1.23)	0.2928	0.27 (0.03-3.05)
		Mid pole - posterior Vs. Lower pole - posterior	-1.48 (1.05)	0.1581	0.23 (0.03-1.78)
Exophytic?	0.0263	Yes Vs. No	-1.41 (0.68)	0.0390	0.24 (0.06-0.93)
Exophytic: > 50% or < 50%	0.1859	> 50% Vs. < 50%	-1.41 (1.16)	0.2226	0.24 (0.03-2.35)
Location relative to polar line					
Entirely above	0.6516	Yes Vs. No	-0.37 (0.81)	0.6535	0.69 (0.14-3.44)
Entirely below	0.9671	Yes Vs. No	-0.03 (0.81)	0.9674	0.97 (0.20-4.70)
Crosses polar line	0.6622	Yes Vs. No	0.29 (0.68)	0.6632	1.34 (0.36-5.07)
> 50% across polar line	0.6591	Yes Vs. No	-0.32 (0.72)	0.6603	0.73 (0.18-2.99)
Crosses axial renal midline	0.2798	Yes Vs. No	-0.86 (0.82)	0.2928	0.42 (0.08-2.10)
Entirely between polar lines	N/A	N/A	N/A	N/A	N/A

Tumor size (cm)	N/A	N/A	-0.74 (0.41)	0.0679	0.48 (0.22-1.06)
Tumor distance from renal sinus (cm)	N/A	N/A	-0.01 (0.27)	0.9593	0.99 (0.58-1.68)
Tumor distance from skin (cm)	N/A	N/A	0.03 (0.07)	0.7019	1.03 (0.90-1.17)
Initial ablation technique	0.0774	Cryoablation Vs. MWA	1.23 (0.74)	0.0960	3.41 (0.80-14.47)

techniques to help guide future treatments. This study found that patients who underwent MWA had a better median survival time. However, no statistically significant difference in residual or recurrent tumor nodularity was observed between the MWA and cryoablation treatment groups. Additionally, those with exophytic tumors demonstrated better recurrence free survival.

The findings from this study may be useful in developing a scoring system similar to RENAL and PADUA but specific to percutaneous thermal ablation. Scoring systems have been previously applied to percutaneous thermal ablation with reasonable success [10,11]. Adaptations to RENAL have also been made in effort to tailor the scoring system for application in percutaneous thermal ablation by adjusting the radius category. While the RENAL nephrometry and PADUA scores have been applied to percutaneous ablation, they fall short of providing insight optimized to the treatment. For example, tumor characteristics applied to the RENAL scoring system may not influence outcomes for percutaneous thermal ablation and vice versa. This study's results showing that exophytic tumor status influences survival and progression may play a role in developing a nomogram for percutaneous ablation treatments.

Recurrence free survival was better in patients who had exophytic tumors compared to non-exophytic tumors in this study. Exophytic tumor status in other studies has demonstrated that incidence of residual of tumor is lower compared to non-exophytic tumors [12]. Additionally, exophytic tumors are more likely to be treated with a single ablation [13]. Together, this evidence supports the idea that exophytic tumor status may be a valuable prognostic factor when considering treatment with percutaneous ablation.

Although our study demonstrated a difference in median survival time between cryoablation and MWA, other studies have found no difference between these two treatment types. Hasegawa demonstrated that there was no difference in tumor progression rate and overall survival between cryoablation and MWA in their retrospective cohort [14]. In the retrospective cohort done by Thompson, no difference was found in local recurrence free survival and overall survival between MWA and cryoablation groups [15]. Additionally, De Cobelli found in their retrospective cohort that there was no significant difference in overall survival between cryoablation and MWA in T1a and T1b masses [16]. The conclusions from this data are reflected in the AUA guidelines which state that for patients who elect thermal ablation treatment, there is no significant difference in complications, metastatic progression and cancer-specific survival between radiofrequency and cryoablation and with an evidence level of grade C [17]. It is possible due to the small sample size of this study that there

was heterogeneity between the two treatment groups leading to a confounding bias. This difference in this study may also be due to the fact that patients with exophytic tumors had better response to ablation techniques, and the vast majority (93.3%) of the patients treated with MWA had tumors that were at least partially exophytic while only 44% of patients of cryoablation patients had at least partially exophytic tumors. An additional contrast between this study and previous studies is that other studies have found that tumor size is an important prognostic factors in progression-free survival [11,13]. However, our study did not find that tumor size showed any correlation with progression-free survival. This may also be due to low sample size.

The patient population eligible for the study was limited due to lack of two-year post procedure contrast imaging follow up. This requirement eliminated the majority of patients who would have otherwise been eligible for the study. Usage of contrast imaging may be limited in this patient population due to the nephrotoxicity associated with contrast. The American College of Radiology appropriateness criteria lists computed tomography (CT) abdomen with/without contrast, CT abdomen with contrast and magnetic resonance imaging (MRI) abdomen with contrast as "usually appropriate" for post-ablative follow up imaging modality for renal cell carcinoma. However, CT and MRI abdomen without contrast are listed as "may be appropriate" for follow up imaging for post-ablative renal cell carcinoma. Future studies with shorter follow up periods, allowing non-contrast imaging may increase the eligible patient population and the power of the study.

Limitations of this study include its small sample size. Future studies should explore outcomes between cryoablation and MWA with a larger sample size. Randomized control trials would be able to control for differences in patient and procedure related characteristics that this study was unable to do. Future studies should also explore tumor exophytic status and the role it may play in determining the best treatment approaches.

Conclusion

The goal of the study was to evaluate whether there was any correlation between patient and tumor characteristics and renal ablation outcomes. We found that those that underwent MWA had a better median survival time and that exophytic tumor status had a reduced risk of nodularity recurrence by 76%. This suggests that tumor exophytic status may be helpful in guiding clinical approach to the treatment of renal tumors.

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