Image-guided Cryoablation for Sporadic Renal Cell Carcinoma: Three- and 5-year Outcomes in 220 Patients with Biopsy-proven Renal Cell Carcinoma

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Conflicts of interest are listed at the end of this article.

See also the editorial by Georgiades in this issue.

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Purpose: To evaluate the long-term efficacy of image-guided cryoablation of sporadic clinical T1 (cT1) biopsy-proven renal cell carcinoma (RCC) and the technical success and safety of all cryoablation treatments.

Materials and Methods: For this retrospective single-institution study, 433 patients (median age, 68 years; range, 19–90 years), of whom 293 were men (median age, 69 years; range, 19–90 years) and 140 were women (median age, 68 years; range, 30–89 years), who had 484 cT1 renal masses (mean size, 33 mm) and who were treated between 2007 and 2016 were identified from a prospectively maintained tumor registry. Treatment efficacy for all treated lesions and complication rates of all procedures were computed. Oncologic outcomes for a subset of 220 patients with sporadic biopsy-proven RCC were analyzed. The Kaplan-Meier method was used to estimate local recurrence–free survival (LRFS), metastasis-free survival (MFS), and overall survival (OS) rates.

Results: Of the 484 treated cT1 renal masses, 474 were imaged subsequently, with a primary treatment efficacy of 96% (453 of 474), increasing to 98% (465 of 474) after secondary ablation, and a major complication rate (Clavien-Dindo grade ≥ III) of 4.9% (23 of 473 procedures). The estimated LRFS and MFS rates, respectively, for the 220 patients with biopsy-proven RCC were 97.2% (95% confidence interval [CI]: 92.6%, 99.0%) and 97.7% (95% CI: 93.3%, 99.1%) at 3 years and 93.9% (95% CI: 85.8%, 97.4%) and 94.4% (95% CI: 86.7%, 97.7%) at 5 years. The estimated OS of all 433 patients was 91.7% (95% CI: 87.5%, 94.5%) and 78.8% (95% CI: 71.1%, 84.6%) at 3 and 5 years, respectively.

Conclusion: Five-year oncologic outcomes after image-guided cryoablation for clinical T1 renal cell carcinoma are competitive with those of resection at a lower complication rate.

The incidence of renal cell carcinoma (RCC) is increasing, with an estimated 65 340 new cases in the United States in 2018 and 14 970 estimated deaths (1). This growth is largely driven by the incidental detection of small renal masses at cross-sectional imaging, as well as increasing patient age. As a result, there has been a trend toward early stages at presentation, with 57.1% stage 1 tumors in 2004 (up from 43.0% in 1993), with a decrease in the mean diameter of stage 1 tumors (to 3.6 from 4.1 cm) (2). This stage migration reflects a relatively indolent disease process largely affecting older patients; however, in practice, optimal and current management of small RCCs remains finely balanced between active surveillance, partial nephrectomy, and thermal ablation.

Thermal ablation techniques involving image guidance have evolved considerably over the past 2 decades. This evolution resulted in a limited accrual of sound outcome data for a standardized approach to renal tumor ablation. As a result, guidelines for the management of small renal tumors issued by the American Urological Association (AUA) and the European Association of Urology (EAU) continue to recommend relatively invasive partial nephrectomy as the standard of care for T1a tumors, with thermal ablation techniques as a conditional recommendation (AUA evidence level C) (3). The EAU guidelines also highlight the low quality of the available data to draw definitive conclusions regarding the morbidity and oncologic outcomes of thermal ablation techniques (EAU level of evidence 3) and therefore recommend thermal ablation for elderly patients and/or patients with comorbidities (4). However, accumulating evidence has suggested that thermal ablation is an acceptable treatment option in selected patients with clinical T1 (cT1) RCC, and this is what has been recommended in the most recent National Comprehensive Cancer Network kidney cancer guidelines (5).

Cryoablation as a surgical tool has also evolved considerably in recent years and benefits from the characteristics of real-time imaging assessment and uniformity of the ablation zone. There are well-established efficacy and complication rates for partial nephrectomy (6,7), but renal tumor ablation data remain compromised by small numbers, lack of biopsy proof, and variable techniques. In our single-institution study of renal tumor cryoablation, we set out to prospectively record both technical and oncologic outcomes using a consistent procedure and imaging technique with diligent radiologic follow-up. A clinical practice

Abbreviations

AUA = American Urological Association, CI = confidence interval, cT1 = clinical T1, LRFS = local recurrence–free survival, MFS = metastasis-free survival, OS = overall survival, RCC = renal cell carcinoma

Summary

This study provides 3- and 5-year outcome data for a large cohort of patients with biopsy-proven renal cancer treated with image-guided cryoablation, which should help further inform treatment guidelines for renal cell carcinoma.

Implications for Patient Care

- Image-guided renal cancer cryoablation demonstrated a high treatment efficacy rate of 98% in 474 treated and imaged patients with a low major complication rate of 5%.
- In 220 patients with solitary sporadic biopsy-proven renal cell carcinoma, the local recurrence–free survival rate was 97% and 94% at 3 and 5 years, respectively.

may include a diverse group of patients with occasional benign tumors, multifocal cancer, inheritable renal cancer syndromes, previous contralateral disease, and even, occasionally, poorly appreciated metastatic disease at the time of treatment. This heterogeneous group of tumors confounds listed outcomes in small studies and limits the quality of the available evidence for guideline recommendation (4). Our study set out to analyze the long-term efficacy of image-guided percutaneous cryoablation of sporadic cT1 biopsy-proven RCC and the treatment efficacy and safety of all renal cryoablation treatments.

Materials and Methods

After consultation with our local Ethics Committee, institutional review board approval and the requirement to obtain informed consent were waived for this retrospective service evaluation study. The authors declare no financial support for this study. The authors had control of all data in the study and of the information submitted for publication.

Patient Selection

All patients were discussed at a multidisciplinary Urology team meeting and underwent formal Urology consultation before a treatment pathway was determined. Primary clinical indications for image-guided renal cryoablation included contraindications to surgery, major comorbidities, and patient preference where there was believed to be treatment equipoise in terms of procedure tolerance. Data regarding all treated patients and outcomes were recorded prospectively in a registry database from May 2007 to December 2016. Patient demographic data and tumor characteristics are detailed in Table 1.

Procedure

Our institution undertook a complete conversion to image-guided cryoablation in 2007, with no overlap or variable use of radiofrequency ablation in view of improved intraprocedural treatment visualization with cryoablation (8). All tumors were treated with the goal of complete ablation in a single session by using an iterative image-guided technique. Two experienced interventional radiologists (D.J.B., with 23 years of experience, and A.J.K., with 5 years of experience) oversaw almost all tumor ablations. The cryoablations were performed with general anesthesia and with the patient in a prone-oblique position ("swimmer's position"). One, and, in the vast majority, two or more 18-G core biopsy samples were taken from the tumor either at a prior procedure with US guidance or at the time of tumor ablation with CT guidance.

Cryoablation was performed by using the Galil Medical/BTG cryoablation system (Galil Medical, Arden Hills, Minn). Cryoprobes (17 G) were placed around the tumor, with four probes (median) used for a mean tumor size of 33 mm. Retroperitoneal contrast material–tinted saline hydrodissection was used to displace any thermally sensitive related structures such as the bowel and pancreatic tail in 239 (47.0%) of procedures.

CT monitoring was performed during the double freeze-thaw cycle treatment (10 minutes freeze, 8 minutes thaw, 10 minutes freeze) at approximately 4-minute intervals to confirm extension of the ice ball at least 5 mm beyond the tumor margin, as accepted by the Working Group on Image-Guided Tumor Ablation (9).

Patients were routinely admitted for overnight observation and combined care with the Urology service.

Follow-up

Patients returned for postprocedural assessment with CT at approximately 4 weeks, with their studies reviewed by D.J.B. and/or A.J.K. This was performed routinely with thin-section volumetric CT and injection rates of 4 mL/sec, including unenhanced and late arterial phases, and additionally with dual-energy iodine mapping since 2011, after the installation of a new CT scanner. A determination of treatment adequacy and the presence or absence of complications, both radiologic and clinical, was made. If there was any uncertainty about marginal treatment adequacy at 1 month, the patient returned for final-adjudication imaging at 3 months. This uncertainty often reflects the presence of benign enhancement secondary to tissue repair at the ablation margin, which diminishes with time, whereas residual disease is often asymmetric and persists or enlarges at subsequent CT studies. Patients with any residual disease at this stage underwent completion treatment. Any enhancing disease recurrence appreciated at subsequent imaging performed at 6 months or annually thereafter was regarded as a treatment failure and was logged as a "late local recurrence." Whole-body CT was performed to include the chest and pelvis annually out to 5 years earlier in our experience. Because of the low rate of late local recurrence and the usually minor and indolent nature of these small nodular lesions, the frequency of CT surveillance has been lowered since 2012 to studies at 1, 3, and 5 years. Urologic surgery clinic follow-up was also performed initially at 4 weeks, with subsequent follow-up annually to 5 years.

Treatment efficacy was defined as a complete response with no residual enhancing tumor by 3 months, with the nonenhancing ablation zone more than encompassing the previous tumor and subsequent slow involution of the ablated tumor over time. Treatment efficacy was assessed for treatment of all tumors to assess the efficacy of cryoablation. Late local recurrence was defined as any nodular or growing enhancement within the ablation zone or ablation bed at follow-up imaging; most patients with late local recurrence underwent completion/secondary cryoablation treatment.

Complications were recorded prospectively and were all reviewed in one session and graded in consensus by D.J.B. and A.J.K. according to the Clavien-Dindo classification, with grades of III or greater considered to indicate major complications (10). Access to full medical records was available at the time of grading.

Statistical Analysis

Statistical analyses were performed according to a predefined statistical analysis plan.

Local recurrence–free survival (LRFS) was defined as the interval between the date of first cryoablation and the date of the first local recurrence, with censoring at the last CT or MRI examination date for patients who did not have a local recurrence. Metastasis-free survival (MFS) was defined as the interval between the date of the first cryoablation and the first date of metastases being detected, with censoring at the last CT or MRI examination date for patients who did not develop metastases. Overall survival (OS) was defined as the interval between the date of the first cryoablation and the date of death, with censoring at the date a patient was last known to be alive for patients who had not died. LRFS, MFS, and OS rates were estimated by using the Kaplan-Meier method. Treatment efficacy and complication rates of all procedures were computed. Univariable and multivariable logistic regression analyses of both primary treatment efficacy and complications were performed. Also, univariable and multivariable Cox regression analyses of LRFS and MFS were performed. Variables assessed in the univariable analyses with $P < .1$ were entered in a multivariable regression model, and then a backward elimination procedure was implemented such that factors with $P < .1$ remained in the multivariable analysis. $P < .05$ was considered to indicate a statistically significant difference.

Statistical analyses were performed by using SAS (SAS Institute, Cary, NC) versions 9.3 and 9.4.

Table 1: Demographic Data and Tumor Characteristics in All Treated Patients and in an RCC Subpopulation with 3 or More Months of Follow-up

Parameter	Entire Treated Population (n = 433)	RCC Subpopulation with ≥ 3 Months of Follow-up (n = 220)
Age at first cryoablation procedure (y)		
Mean ± standard deviation	67.2 ± 11.81	66.1 ± 12.19
Median and range	68 (19–90)	68 (19–88)
Sex		
Male	293 (67.7)	147 (66.8)
Female	140 (32.3)	73 (33.2)
Tumor characteristics		
No. of tumors	484	221
Size		
Mean ± standard deviation (cm)	3.3 (1.05)	3.4 (0.97)
Median and range (cm)	3.2 (0.9–6.7)	3.4 (1.3–6.2)
No. of tumors ≤ 4 cm	375 (77.5)	166 (75.1)
No. of tumors > 4 cm	109 (22.5)	55 (24.9)

Note.—Unless otherwise specified, data are numbers of patients or tumors, with percentages in parentheses. RCC = renal cell carcinoma.

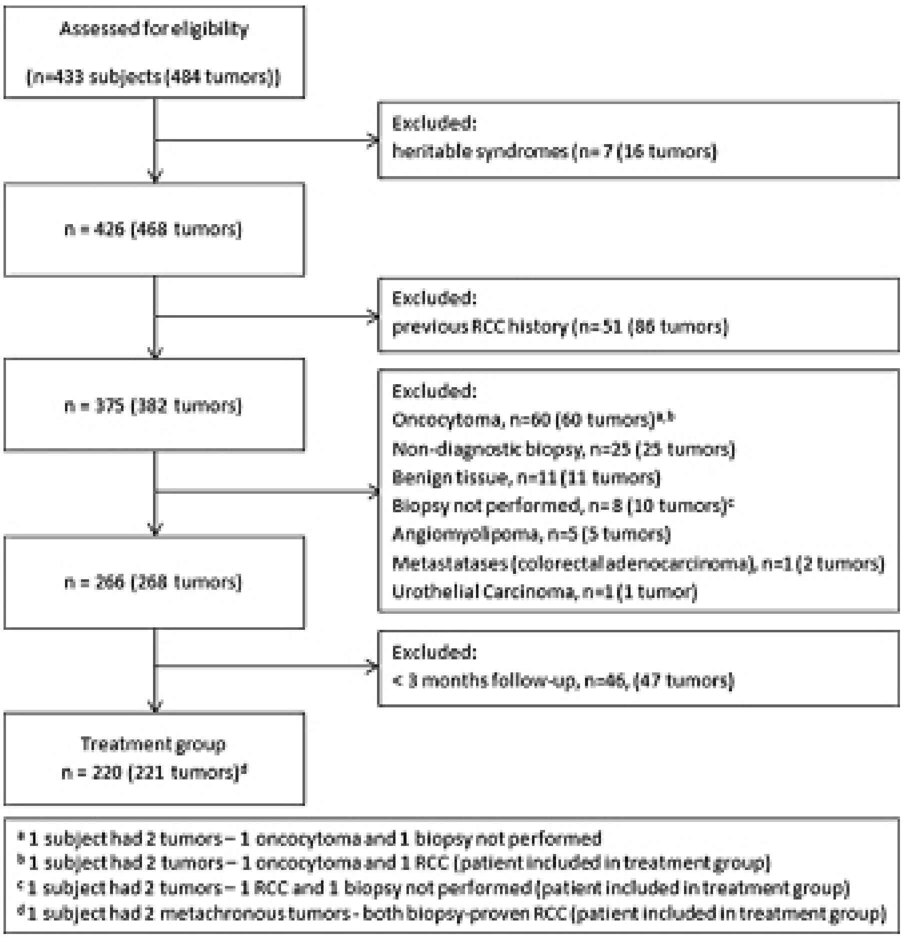

Figure 1: Flowchart of patient selection in treatment group. Eligible patients were identified from the tumor database from May 2007 to December 2016 (inclusive). RCC = renal cell carcinoma.

Table 2: Results of Logistic Regression Analysis of Entire Treated Population (n = 433) in Terms of Primary Treatment Efficacy and Occurrence of Complications

	Treatment Efficacy of Primary Ablation				Occurrence of Any Complications			
	Univariable Analysis		Multivariable Analysis		Univariable Analysis		Multivariable Analysis	
Variable and Category	Odds Ratio	*P* Value	Odds Ratio	*P* Value	Odds Ratio	*P* Value	Odds Ratio	*P* Value
Age (linear 10-year difference)	0.82 (0.56, 1.21)	.315	…		0.91 (0.69, 1.20)	.477	…	
Sex								
Female	0.32 (0.13, 0.78)	.014	0.21 (0.07, 0.67)	.009	0.98 (0.44, 2.15)	.948	…	
Male	1				1			
No. of probes (linear one-probe difference)	0.75 (0.54, 1.05)	.092	…		1.00 (0.75, 1.32)	.990	…	
Largest tumor size (mm)								
≤40	3.38 (1.36, 8.38)	.010	2.83 (0.91, 8.78)	.070	1.54 (0.69, 3.43)	.278	…	
>40	1				1			
Pole of kidney								
Interpolar	1	.718	…		1	.932	…	
Lower pole	0.65 (0.23, 1.89)				1.15 (0.48, 2.76)			
Upper pole	0.75 (0.24, 2.34)				1.13 (0.46, 2.80)			
Location								
Anterior	0.74 (0.30, 1.81)	.498	…		1.70 (0.80, 3.59)	.156	…	
Posterior	1				1			
Location								
Exophytic	2.91 (1.15, 7.36)	.025	2.95 (0.90, 9.67)	.073	0.50 (0.23, 1.07)	.071	2.52 (0.80, 7.95)	.108
Central	1				1			
Hydrodissection								
Used	0.28 (0.09, 0.89)	.032	…		1.43 (0.67, 3.04)	.336	…	
Not used	1				1			
Pyeloperfusion or ureteric stent placement								
Used	0.12 (0.03, 0.51)	.005	0.14 (0.03, 0.71)	.018	5.94 (1.61, 21.86)	.010	0.19 (0.04, 0.78)	.024
Not used	1				1			

Note.—Data in parentheses are 95% confidence intervals.

Results

A total of 433 patients (293 [67.7%] men and 140 [32.3%] women) with a total of 484 tumors with mean and median sizes of 33 and 32 mm, respectively, were treated in 473 separate cryoablation procedures. The median patient age was 68 years (range, 19–90 years), with a median age of 69 years (range, 19–90 years) for the male patients and a median age of 68 years (range, 30–89 years) for the female patients (Table 1). In some patients, more than one tumor was treated in one procedure, and in other patients, a tumor may have been re-treated in a separate procedure because of primary technical failure or recurrence. A total of 375 (77.5%) of the 484 tumors were 40 mm or smaller (T1a), and 109 (22.5%) were larger than 40 mm (T1b) in maximum tumor diameter.

Inclusion criteria for the cT1 RCC subset analysis included all patients with biopsy-proven RCC and more than 3 months of follow-up CT imaging. Patients with any history of ipsilateral, contralateral, or metastatic RCC disease; inheritable renal cancer syndromes; inadequate biopsy; or benign or indeterminate histologic findings were excluded, as demonstrated in Figure 1.

A total of 221 (45.7%, in 220 patients) of the 484 tumors were biopsy-proven sporadic RCC with at least 3 months of imaging follow-up. Ten tumors were lost to initial follow-up (4-week CT) and were excluded from the assessment of treatment efficacy and subsequent follow-up.

Treatment Efficacy

Complete response was achieved at the first treatment in 453 of 474 tumors (95.6%; 95% confidence interval [CI]: 93.3%, 97.1%) and with secondary cryoablation in 465 of 474 tumors overall (98.1%; 95% CI: 96.4%, 99.0%). In the remaining nine tumors (1.9%) with trace residual disease, a clinical decision was made to pursue no further treatment, and in one patient, a salvage nephrectomy was performed for a hilar-lip tumor remnant.

Univariable and multivariable logistic regression analyses of primary treatment success are summarized in Table 2. In the multivariable analysis, the following variables were significant: Female patients were less likely to experience primary treatment success (odds ratio, 0.21; 95% CI: 0.07, 0.67; P = .009), and patients who underwent pyeloperfusion or stent placement were also less likely to experience primary treatment success (odds ratio, 0.14; 95% CI: 0.03, 0.71; P = .018).

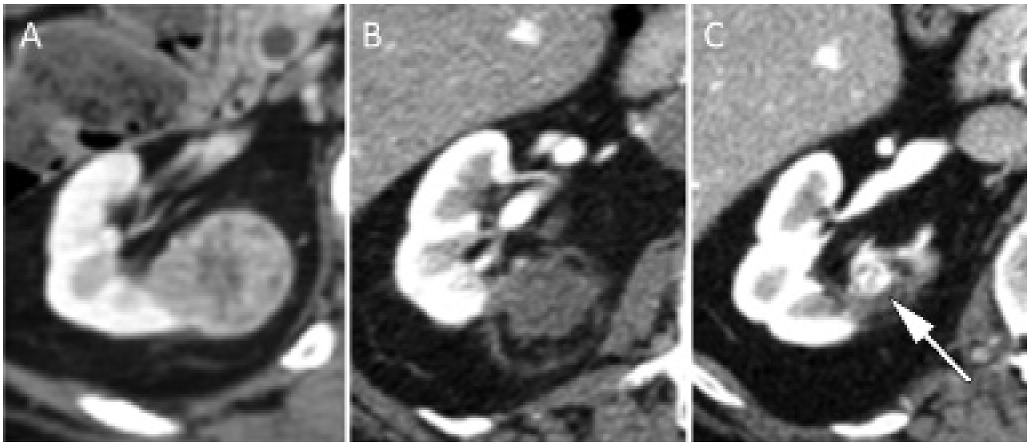

Figure 2: A–C, Axial CT images through the right kidney acquired at the level of the tumor in the late arterial phase (iodinated contrast material delivery rate, 4 mL/sec) in a 67-year-old man treated for a 32-mm right posterior interpolar region renal cell carcinoma. A, Image obtained before cryoablation. B, Image obtained 1 year after cryoablation shows an involuting ablation zone with no residual enhancing tumor. On, C, image obtained 3 years after cryoablation, a 10-mm enhancing nodule is seen at the margin of the ablation zone (arrow).

LRFS Results

Of the 433 patients treated—not counting those with indeterminate biopsies, inheritable cancer syndromes, and metastatic disease at outset—220 (50.8%) had biopsy-proven sporadic, solitary RCC and follow-up of at least 3 months, with one patient having two metachronous biopsy-proven RCCs. Five patients had residual disease and did not undergo a secondary ablation because of a multidisciplinary or patient decision for no further treatment or for salvage nephrectomy; data in these patients were therefore excluded from the LRFS analysis.

Of the 220 patients with 221 tumors with follow-up beyond 3 months, median follow-up was 31 months (range, 3–99 months). There were four local recurrences by 3 years and six recurrences by 5 years. These were typically small, brightly enhancing nodules of around 5–10 mm in diameter at the margin of the ablation zone (Fig 2), and all were treated with completion cryoablation with complete response. Of note, these occasional nodular recurrences tended to be appreciated at 3–4 years after treatment. Kaplan-Meier estimates of LRFS rates were 97.2% (95% CI: 92.6%, 99.0%) at 3 years and 93.9% (95% CI: 85.8%, 97.4%) at 5 years. Figure 3 shows the Kaplan-Meier curve for LRFS for this subgroup.

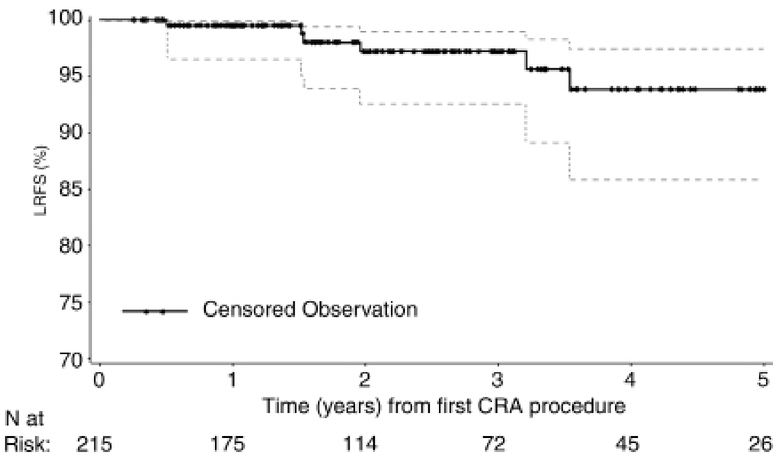

Figure 3: Kaplan-Meier curve shows local recurrence–free survival (LRFS) in patients with biopsy-proven sporadic solitary renal cell carcinoma and follow-up of at least 3 months. Dashed lines = 95% confidence intervals. Tick marks = censored data. Estimated LRFS rates of 97.2% at 3 years and 93.9% at 5 years are comparable to those after partial nephrectomy. CRA = cryoablation.

Univariable Cox regression analyses identified no statistically significant effect of patient age, sex, or tumor size on the LRFS rate, as demonstrated in Table 3. Kaplan-Meier curves for LRFS according to tumor size for this RCC subgroup are shown in Figure 4.

Overall and Cancer-specific Survival

The median OS was not reached, with a median duration of follow-up for the 433 patients of 24.3 months and a maximum follow-up of 120 months. Kaplan-Meier estimates of the OS rates in these 433 patients at 3 and 5 years were 91.7% (95% CI: 87.5%, 94.5%) and 78.8% (95% CI: 71.1%, 84.6%), respectively. For the 220 patients with sporadic, solitary biopsy-proven RCC, the estimated OS rates at 3 and 5 years were 93.2% (95% CI: 87.5, 96.4) and 84.8% (95% CI: 75.3%, 90.9%), respectively, as shown in Figure 5.

In the 220 patients with sporadic, solitary biopsy-proven RCC, the Kaplan-Meier estimates of MFS rates at 3 and 5 years were 97.7% (95% CI: 93.9%, 99.1%) and 94.4% (95% CI: 86.7%, 97.7%), as shown in Figure 6. Univariable Cox regression analyses of MFS are summarized in Table 3 and showed no significant variable affecting MFS rate.

Complications and Hospital Stay

Almost all patients were observed overnight after the ablation treatment, with occasional day cases. The median hospital stay was 1 day (range, 0–8 days). The longest stays were in patients who subsequently developed pneumonia and cerebrovascular accident. For the 433 patients included in this analysis, the major complication rate (Clavien-Dindo grade ≥ III) was 23 (4.9%) of 473 procedures. The nature of these complications is summarized in Table 4. There was one death at 5 days of pulmonary embolism after discharge. There was only a single patient with procedure-related hemorrhage that required coil embolization. Pneumothorax was the prevalent complication, with 10 events (2.3%) requiring therapeutic chest drain insertion, and was identified and treated at time of cryoablation procedure. At univariable analysis, no tumor or procedural feature (age, sex, number of probes, tumor size > 40 mm) proved significant in anticipating complications (Clavien-Dindo grade ≥ III). Multivariable analysis (Table 2) showed that patients who underwent pyeloperfusion or ureteric stent placement were less likely to have a complication (odds ratio, 0.19; 95% CI: 0.04, 0.78; P = .024).

Table 3: Results of Cox Regression Analysis of LRFS and MFS in Patients with Biopsy-proven Sporadic Solitary RCC and Follow-up of at Least 3 Months

Variable and Category	Univariable Analysis for LRFS: Hazard Ratio	Univariable Analysis for LRFS: P Value	Univariable Analysis for MFS: Hazard Ratio	Univariable Analysis for MFS: P Value
Age (linear 10-year difference)	0.66 (0.39, 1.10)	.110	2.01 (0.84, 4.77)	.115
Sex				
Female	0.32 (0.04, 2.68)	.293	0.39 (0.05, 3.32)	.387
Male	1		1	
Largest tumor size				
≤40 mm	0.52 (0.10, 2.77)	.446	0.55 (0.10, 3.03)	.491
>40 mm	1		1	

Note.—Multivariable analyses were not performed because none of the parameters included in the univariable analyses had a P value of less than the prespecified cutoff of .1 to allow inclusion in the multivariable analysis. Data in parentheses are 95% confidence intervals. LRFS = local recurrence–free survival, MFS = metastasis-free survival, RCC = renal cell carcinoma.

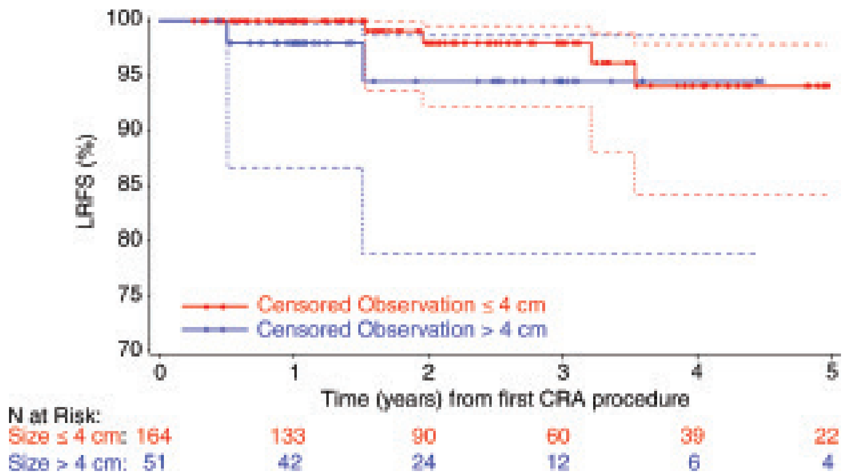

Figure 4: Kaplan-Meier curve of local recurrence–free survival (LRFS) according to tumor size in patients with biopsy-proven sporadic solitary renal cell carcinoma and follow-up of at least 3 months. Dashed lines = 95% confidence intervals. Tick marks = censored data. No difference in LRFS is seen between clinical T1a (≤4 cm) and clinical T1b (>4 cm) tumors (P = .446). CRA = cryoablation.

Discussion

The appropriate clinical management of incidental small RCCs remains finely balanced between active surveillance, partial nephrectomy, and image-guided ablation. Small RCC (T1a, ≤ 40 mm) is a largely indolent disease in an older population, with treatment decisions hinging on tumor size and location and patient comorbidities. Recent meta-analyses have increasingly acknowledged the statistically similar cancer-specific survival rates across these management strategies. However, among the treatment options, there are small critical differences in renal functional outcomes, complications, and progression-free survival rates (11,12). These differences create uncertainty in regard to treatment recommendations and grades in specialist guidelines, and, ironically, the available ablation data and outcomes are limited by these guidelines (3,4,13,14). Even with the most recent acceptance of thermal ablation techniques in the National Comprehensive Cancer Network 2018 guidelines, the recommendation is that patients are adequately counseled in view of a reported high local recurrence rate (5). This recommendation is based on an early AUA 2009 guideline and a 2008 meta-analysis of studies that were heavily weighted toward laparoscopic cryoablation and percutaneous radiofrequency ablation (15,16).

In the past 2 decades, there has been a rapid evolution of ablative technologies and image guidance, which raises further questions as to how renal tumor

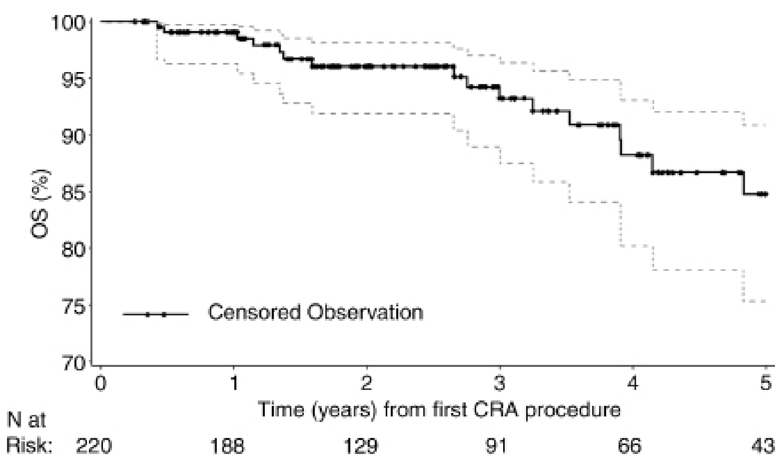

Figure 5: Kaplan-Meier curve of overall survival (OS) in patients with biopsy-proven sporadic solitary renal cell carcinoma and follow-up of at least 3 months. Dashed lines = 95% confidence intervals. Tick marks = censored data. The estimated OS rates of 93.2% and 84.8% (at 3 and 5 years, respectively) are lower than the local recurrence–free survival and metastasis-free survival rates, reflecting treatment in a largely older population with comorbidities. CRA = cryoablation.

ablation should be performed. Recent analyses have begun to indicate that among ablative technologies, cryoablation may deliver more consistent results in terms of local progression-free survival (17,18), certainly for tumors larger than 40 mm (19,20), although this may prove difficult to demonstrate in a randomized setting (21).

Much of the available ablation outcome data are compromised not only by major medical comorbidities but also by previous histories of renal cancer, multifocal disease, and a high proportion of solitary kidneys. This analysis of renal cryoablation has therefore sought to particularly analyze oncologic outcomes (LRFS, MFS, and OS) in a clearly defined cohort of patients with solitary, sporadic, biopsy-proven RCC (who had notably been declined for surgery) to help inform future treatment guidelines. This yielded a cohort of 220 patients with cT1 RCC and assessment of oncologic outcomes at 3 and 5 years.

These 220 patients with a median follow-up of 31.1 months had LRFS rates of 97.2% (95% CI: 92.6%, 99.0%) at 3 years and 93.9% (95% CI: 85.8%, 97.4%) at 5 years. This is clearly slightly lower than the reported LRFS rate for partial nephrectomy (10), but does not manifest as a difference in cancer-specific survival in multiple case series (22). Our reported LRFS rates are similar to those in other recent studies by Thompson et al (23) and Georgiades and Rodriguez (24) and should bear on future treatment guidelines.

Multivariable analysis of all treated tumors did not show tumor location (anterior, posterior, polarity, or endophycity) as a significant factor in treatment efficacy. Similarly, tumor size in the RCC subcohort of tumors larger than 40 mm (T1b tumors) failed to show a significantly lower LRFS or complication rate when compared with T1a tumors. This again alludes to the superior oncologic efficacy of cryoablation versus radiofrequency ablation in the setting of T1b disease (25).

Of note, the time (range) in this series to local tumor progression was 6–61 months, although local recurrence was relatively uncommon, with an estimated LRFS rate of 93.9% at 5 years. This indolence suggests that surveillance at the 3- and 5-year marks remains important to cryoablation in terms of long-term local efficacy. A high level of radiologic scrutiny was performed in this series, with the majority of local recurrences being represented by small, briskly enhancing foci, usually at the edge of the involuted ablation zone. In most patients, these were not possible to confirm as tumors by means of biopsy but proved straightforward to treat. There is no evidence from our experience that these would necessarily bear out as harbingers of compromised cancer-specific survival.

Technical efficacy and safety of image-guided cryoablation was assessed for all treated tumors (474 tumors in 433 patients over 473 cryoablation procedures). The primary ablation efficacy of all tumors was 95.6%, increasing to 98.1% after a secondary completion ablation. All patients who underwent a secondary ablation experienced complete response, with the remaining 1.9% not undergoing completion ablation because of clinical or patient decision.

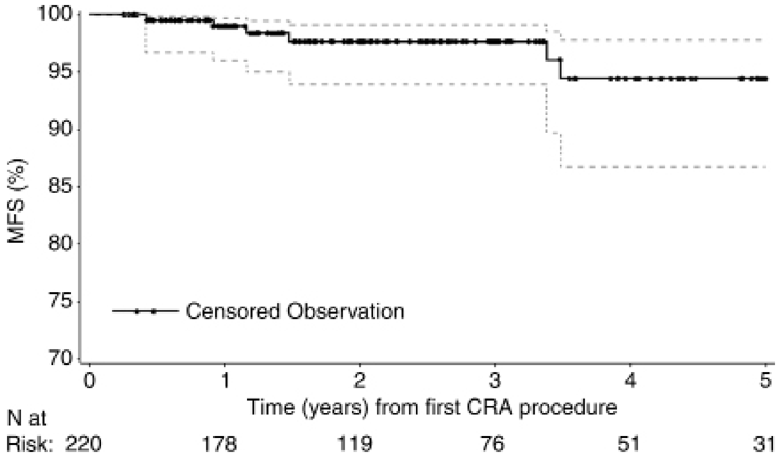

Figure 6: Kaplan-Meier curve of metastasis-free survival (MFS) in patients with biopsy-proven sporadic solitary renal cell carcinoma and follow-up of at least 3 months. Dashed lines = 95% confidence intervals. Tick marks = censored data. Estimated MFS was 97.7% at 3 years and 94.4% at 5 years, with no difference seen between clinical T1a (≤4 cm) and clinical T1b (>4 cm) tumors (P = .491). CRA = cryoablation.

Table 4: Complications (Clavien-Dindo Grade ≥ III) as a Percentage of the 473 Procedures Performed

Clavien-Dindo Grade and Complication	Total No.
Grade III	20 (4.2)
Pneumothorax (treated with chest drain)	10 (2.1)
Pelvicalyceal or ureteric injury (treated with ureteric stent)	4 (0.8)
Ureteric obstruction due to clot (treated with ureteroscopy with or without stent placement)	3 (0.6)
Hematuria and clot retention (treated with bladder irrigation)	2 (0.4)
Hemorrhage (treated with embolization)	1 (0.2)
Grade IV	2 (0.4)
Myocardial infarction (treated with coronary stent placement)	1 (0.2)
Cerebrovascular accident (treated with thrombolysis)	1 (0.2)
Grade V	1 (0.2)
Venous thromboembolism	1 (0.2)

Note.—Numeric data in parentheses are percentages.

In 433 patients with a median tumor size of 33 mm, there was a complication rate (Clavien-Dindo classification ≥ III) of 4.9% (23 of 473 procedures). Unusually, a considerable portion of these events (43.5% [10 of 23]) were related to small-to-moderate pneumothoraces. This was attributed to probe placement across the pleural reflection, a procedure that has subsequently been modified with more oblique probe placements and enhanced use of hydrodissection in recent years. This change in practice has negated the risk of pneumothorax in the treatment of upper-pole tumors, as described in our previous published series (26). Contrary to our previous published series, we experienced considerably fewer hemorrhagic complication rates, with only three events requiring transfusion and a single case of coil embolization. We suspect this may relate to the consistent use of 17-G cryoprobes rather than the 13-G probes provided by some manufacturers. The use of pyeloperfusion or ureteric stent placement was associated with suboptimal treatment efficacy (multivariable analysis P = .018), but we suspect that these adjunctive techniques were used only in patients with anticipated ablation treatment complexity. The use of these urothelial-protective techniques does lead to a lower complication rate (multivariable analysis P = .024) when these techniques are used (Table 2). Interestingly, regression analysis demonstrated that neither anterior-posterior location nor tumor centrality resulted in a significant difference in treatment efficacy.

The median hospital stay of 1.0 day (range, 0–8 days) was also notable in this series against a mean tumor size of 33 mm and median age of 68 years. This compares favorably with a median partial nephrectomy stay of 4 days (27).

Active surveillance remains a valid treatment pathway in a proportion of elderly patients but it is predicated on the risks posed by surgical resection (28,29). Image-guided ablation potentially provides a treatment paradigm for a substantial cohort of older patients with small renal tumors. A considerable proportion of incidental small renal tumors manifests in older patients with reasonable life expectancies, and renal cryoablation may represent a useful, less-invasive treatment option for many of these patients. In terms of cost efficacy, the authors of a Markov model cost-utility analysis (30) reviewed the relative efficacy of active surveillance, radiofrequency ablation, and cryoablation, coming down in favor of a period of active surveillance for growth trajectory followed by cryoablation as necessary. The low complication rate and high progression-free survival in this case series would appear to add further weight to this proposed treatment plan.

Our study had several limitations despite being based on a prospectively maintained registry. Because of the regional and supraregional nature of our service, some patients were lost to imaging follow-up. Patient performance status and renal functional outcomes were not recorded. Within our institution, registries of active surveillance and partial nephrectomy outcomes were not available for comparison purposes. The data contained herein represents single-institution data and outcome recording of a consistent image-guided renal tumor cryoablation protocol in a large-practice setting.

In conclusion, oncologic outcomes of image-guided renal cryoablation for RCC are competitive with those of partial nephrectomy and are associated with a low complication rate. These data add to the accruing evidence for percutaneous renal tumor cryoablation and should bear on upcoming treatment guidelines.

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