Radiology

ORIGINAL RESEARCH • VASCULAR AND INTERVENTIONAL RADIOLOGY

Percutaneous Cryoablation for Stage 1 Renal Cell Carcinoma: Outcomes from a 10-year Prospective Study and Comparison with Matched Cohorts from the National Cancer Database

John Morkos, BS • Kori A. Porosnicu Rodriguez, BA • Alice Zhou, BS • Andrew R. Kolarich, MD • Constantine Frangakis, PhD • Ronald Rodriguez, MD, PhD • Christos S. Georgiades, MD, PhD

From the Department of Radiology (J.M., K.A.P.R., A.Z., A.R.K.), Department of Biostatistics (C.F.), and Department of Vascular and Interventional Radiology (C.S.G.), Johns Hopkins University, 1800 Orleans St, Zayed 7203, Baltimore, MD 21231; and Department of Urology, University of Texas Health Sciences Center, San Antonio, TX (R.R.). Received October 17, 2019; revision requested November 14; final revision received March 31; accepted April 15. **Address correspondence to** C.S.G. (e-mail: *g_christos@hotmail.com*).

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

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Background: Percutaneous cryoablation (PCA) is an increasingly utilized treatment for stage I renal cell carcinoma (RCC), albeit without supportive level I evidence.

Purpose: Primary objective was to determine the 10-year oncologic outcomes of PCA for stage I RCC in a prospective manner. Secondary objectives were to compare outcomes after partial nephrectomy (PN) and radical nephrectomy (RN) from the National Cancer Database (NCDB), to determine long-term renal function, and to determine the risk of metachronous disease.

Materials and Methods: In this institutional review board–approved prospective observational study (2006–2013), study participants with single, sporadic, biopsy-proven RCC were included to calculate the 10-year overall survival, recurrence-free survival, and disease-specific survival after PCA. Results were compared with matched PN and RN NCDB cohorts. Overall and recurrence-free survival probabilities were estimated by using nonparametric maximum likelihood estimator. Disease-specific survival was estimated by using the redistribution-to-right method. Age at diagnosis was stratified as a risk for survival. The effect on estimated glomerular filtration rate, serum creatinine level, and the risk for hemodialysis and metachronous disease were calculated.

Results: One hundred thirty-four patients (46% men) with single, sporadic, biopsy-proven RCC (median size ± standard deviation, 2.8 cm ± 1.4) were included. Overall survival was 86% (95% confidence interval [CI]: 80%, 93%) and 72% (95% CI: 62%, 83%), recurrence-free survival was 85% (95% CI: 79%, 91%) and 69% (95% CI: 59%, 79%) (improved over surgery), and disease-specific survival was 94% (95% CI: 90%, 98%) at both 5 years and 10 years (similar to surgery), respectively. The 10-year risk of hemodialysis was 2.3%. Risk of metachronous RCC was 6%. Charlson/Deyo Combined Comorbidity score analysis showed decreasing overall survival with increasing comorbidity index. The PCA cohort outperformed both RN- and PN-matched subgroups in all Charlson/Deyo Combined Comorbidity score categories.

Conclusion: Percutaneous cryoablation yielded a 10-year disease-specific survival of 94%, equivalent to that reported after radical or partial nephrectomy. Overall survival probability after percutaneous cryoablation at 5 years and 10 years was longer than for radical or partial nephrectomy, especially for patients at higher risk (Charlson/Deyo Combined Comorbidity score ≥2).

Percutaneous cryoablation (PCA) is an increasingly utilized treatment option for stage I renal cell carcinoma (RCC). The American Urologic Association included ablation in its treatment guidelines for stage I RCC in 2009, albeit with cautionary references to increased risk for local recurrence compared with surgery (1). The National Comprehensive Cancer Network added ablation to its own guidelines in 2018 (2). These recommendations were based on meta-analyses of mostly small retrospective studies (3,4). Notwithstanding the lack of definitive evidence, patients with small renal masses are increasingly referred for ablation. The impetus behind the increasing utilization of PCA is mainly due to the changing epidemiologic landscape of RCC.

The expected number of RCC in the United States in 2019 is 74 000, with an increasing lifetime risk currently standing at 1.7%, and comprising 4.2% of all cancers (5). Furthermore, the proportion of patients diagnosed with stage I RCC continues to increase (currently 65%–75%) as well (6). This migration toward lower clinical stage is partly due to increase in incidental detection (utilization of cross-sectional imaging) and recognized risk factors, mainly obesity and smoking (7). These trends are emulated by European statistics on the epidemiology of RCC (8). The growth in (both relative and absolute) numbers of patients with RCC diagnosed at stage I is making nephron-sparing surgery (the current standard of care) and ablation increasingly important. Despite the mounting number of published studies supporting the use of ablation for small renal masses, most have limitations that include small number of patients, lack of histologic proof, retrospective design, and/or short follow-up time.

Abbreviations

CI = confidence interval, eGFR = estimated glomerular filtration rate, NCDB = National Cancer Database, PCA = percutaneous cryoablation, PN = partial nephrectomy, RCC = renal cell carcinoma, RN = radical nephrectomy, sCr = serum creatinine

Summary

This 10-year prospective observational study in patients with biopsy-proven renal cell carcinoma showed that percutaneous cryoablation was associated with a high disease-specific survival (94%) and better overall survival compared with partial or radical nephrectomy.

Key Results

- For stage I renal cell carcinoma, 10-year overall survival was longer after percutaneous cryoablation compared with both partial and radical nephrectomy (72% vs 49% and 43%; $P <$ .001). This benefit was noted across all ages and all comorbidity levels.
- The 10-year disease-specific survival was 94% and was comparable to that reported for surgical interventions.
- Percutaneous cryoablation was associated with a low rate of complications (8%), as well as a low 10-year risk of hemodialysis (2%).

The primary objective of our study was therefore to define the 10-year oncologic outcomes of percutaneous cryoablation for biopsy-proven stage I RCC in a prospective manner. Secondary objectives were to compare outcomes to those after partial nephrectomy (PN) and radical nephrectomy (RN) by using matched cohorts from the National Cancer Database (NCDB), and to assess long-term effects of PCA on renal function and the risk of metachronous disease.

Materials and Methods

This was a single-center, institutional review board–approved, Health Insurance Portability and Accountability Act–compliant prospective study. Informed consent was obtained from all patients. All patients referred for PCA for an organ-confined RCC less than 7 cm were considered for inclusion. Inclusion criteria were biopsy-proven RCC and stage I disease. Exclusion criteria were inability to suspend anticoagulation, uncorrectable bleeding diathesis (international normalized ratio >1.7 or platelet count <50 000), life expectancy less than 1 year, active infection, or target mass inaccessible percutaneously.

Recruitment ran from February 2006 through May 2013, and data analysis was performed in November 2018. The same cohort of patients was previously analyzed, and the results of a 5-year interim analysis on technical efficacy and perioperative safety for PCA were published in 2014 (9), whereas this analysis reports on the 10-year oncologic outcomes. For patients who transferred their care to regional institutions, the Chesapeake Regional Information System was utilized for patients, which allows for interinstitutional sharing of electronic patient files. Additionally, an NCDB Participant User File (identification no. 2016.7) with nationwide data on patients with RCC was provided, the use of which received institutional review board exemption. Matched cohorts from the NCDB provided comparative outcomes to those from this single-arm study.

Patient Preparation

All patients were seen in the Urology and Interventional Radiology clinic, and were counseled on all treatment options, including PN, RN, and surveillance. A biphasic contrast material–enhanced CT or MRI examination including the kidneys was reviewed to ensure the RCC was stage I and accessible percutaneously. Patients whose adrenal gland was within 1 cm of the RCC were premedicated with α- and β-blockers for 5 days prior to the procedure. The coagulation status was optimized as per exclusion criteria above. Nonsteroidal anti-inflammatory medications and clopidogrel were suspended 5 days prior to each procedure.

Procedure

All ablations were performed with moderate sedation (midazolam and fentanyl) under CT guidance. Procedures were performed by a single operator (C.S.G., with 8 years of experience at the time). Biopsy was planned at the time of ablation unless the patient had a prior diagnostic biopsy. Technical objective was to generate an ice ball extending greater than or equal to 5 mm beyond the tumor margin. With the patient prone, baseline noncontrast CT was obtained. If a nontarget organ was within the ice ball, then a 22-gauge spinal needle inserted between the RCC and that organ provided air and/or hydrodissection. Cryoablation protocol consisted of a 10-minute freeze, an 8-minute thaw, and a 10-minute refreeze. Cryoablation needles used were either manufactured by Galil Medical (Yokneam, Israel) or Endocare (Irvine, Calif). The needles were removed and a noncontrast CT was obtained for immediate complications. Patients recovered for 3 hours and then were discharged to home. Patients were observed overnight in case of complications or symptoms such as nausea or pain requiring intravenous medications.

Follow-up

Patients were followed up in clinic with laboratories and with a biphasic intravenous contrast enhanced abdominal CT or MRI at 3-, 6-, 9-and 12-months, and thereafter annually. This fulfilled the minimum guidelines set by the American Urologic Association (9). Residual disease was defined as persistent or new nodular enhancement and/or continuously increasing size at subsequent imaging, in line with the American Urologic Association's definition of "treatment failure or local recurrence" (10). For patients with an estimated glomerular filtration rate (eGFR) less than 30 mL/min, complete ablation was defined as continuous size reduction of the target RCC on all subsequent nonenhanced CT or MR images. Imaging examinations were interpreted by board-certified diagnostic radiologists. Median follow-up was 7.4 years (50% interquartile range, 5.5–9.2 years) (range, 0.6–12.25 years).

Statistical Analysis

Oncologic outcomes.—Over the follow-up period, the probability of overall survival, recurrence-free survival, and disease-specific survival were estimated. For the first two, the probabilities were

estimated by using the nonparametric maximum likelihood estimator for interval-censored survival (11), a Kaplan-Meier analog with interval censoring. The disease-specific survival for patients for whom both the time and the cause of death are missing cannot be handled by a usual Kaplan-Meier estimator, because the latter does not distinguish between causes of death. To account for patients with unknown cause of death, time to disease-specific mortality was estimated by using the Efron redistribution-to-the-right method (12). The risk of developing a metachronous RCC was also estimated over the follow-up period.

Effect of age at diagnosis.—For every observed age at diagnosis (index value), a "similar-age subgroup" was considered to be patients within plus or minus 7.5 years from that index age. For each similar-age subgroup, the survival probabilities were calculated. This calculation was performed for each index age and for all patients. The probabilities were plotted against index age to provide a representation of the probability of survival versus age at diagnosis. The same calculation was performed for the matched PN and RN groups (see the "NCDB Matching" section below). Statistical significance of the comparison of probability estimates between age groups was assessed by using Sun method (13).

Renal function outcomes.—The risk of new hemodialysis requirement (among those who were not undergoing hemodialysis prior to cryoablation) was calculated. The probability of this binary (yes or no) categorical outcome was estimated by using the nonparametric maximum likelihood estimator for interval-censored outcomes. Further calculated was the risk of a new hemodialysis requirement versus age at diagnosis. Baseline and eventual serum creatinine (sCr) level and eGFR were calculated for all patients, for those with normal baseline sCr level (≤1.2 mg/dL), and for those with abnormal baseline sCr level (>1.2 mg/dL). The equation used for eGFR was as follows: glomerular filtration rate (mL/min/1.73 m^2) = $175 \times (S_{cr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$.

NCDB matching.—The NCDB is a hospital-based national registry of patients with cancer, a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The NCDB Participant User File for RCC was received and filtered to include 118 773 patients with stage I RCC with a date of diagnosis from 2006 to 2013, to match the stage and period of our study. Patients who underwent treatments other than resection were excluded. The remaining patients were divided into two groups: those treated with PN and those treated with RN. Each was used to generate a subgroup that matched our current study population for the following variables: age, sex, relative proportions of stage IA/IB, and the Charlson/Deyo Combined Comorbidity, or CDCC, score (Table 1). Exact matches were found for sex, relative proportion of stage IA/IB, and CDCC score between 128 of our patients, 13 090 registry patients treated with PN, and 6645 registry patients treated with RN. For age at diagnosis, matches were exact for 104 and 103 patients, in the PN and RN groups, respectively, with the rest matched within 1–3 years. The overall survival probabilities at 5 years and 10 years for the matched subgroups were calculated by using the weighted Kaplan-Meier estimate. For example, for a male cryoablation patient aged 42 years at diagnosis, with a CDCC score of 1 and stage 1A disease, there were 34 exact matches in the matched PN NCDB group, thus each receiving a weight of one of 34. Standard errors were estimated with jackknife method.

Results

Among 246 consecutive patients who were treated with PCA for stage I RCC, the following were excluded: 57 of 246 (23%) patients lacking biopsy results or with nondiagnostic biopsy results, 43 of 246 (18%) patients whose histologic findings were benign, and 12 patients who were lost to follow-up. The 12 of 246 (5%) patients lost to follow-up were not available for even a first follow-up visit or any contact. Those with at least one follow-up were either censored or followed up to the end of the study. One hundred thirty-four patients (61 men and 73 women) with single sporadic RCC were included, with a median age of 68 years ± 11 (standard deviation) (range, 35–88 years) (Fig 1). Median tumor size was 2.8 cm ± 1.4 (range, 0.5–7.0 cm), with 115 of 134 (86%) being stage IA, and 19 of 134 (14%) being stage IB. Among 134 patients, 21 (15.6%) had to be admitted for either clinically significant symptoms or complications, whereas 84.6% were discharged after a 3-hour observation period. Two patients had residual disease at follow-up. One underwent repeat ablation without recurrent disease at follow-up, and the second refused further treatment. Fifteen percent required hydrodissection to protect a nontarget organ, and 15% required admission for clinically significant symptoms or complications, such as hemorrhage.

After biopsy, histologic classification was as follows: 100 of 134 (75%) clear cell carcinoma, 25 of 134 (18%) papillary carcinoma, and nine of 134 (7%) chromophobe renal cell carcinoma.

Survival Outcomes

For the PCA group, overall survival was 87% (95% confidence interval [CI]: 80%, 93%) and 72% (95% CI: 62%, 83%) at 5 years and 10 years, respectively. Recurrence-free survival was 85% (95% CI: 79%, 91%) and 69% (95% CI: 59%, 79%) at 5 years and 10 years, respectively, and disease-specific survival was 94% (95% CI: 90%, 98%) at both 5 years and 10 years. Survival outcomes are shown graphically in Figure 2. For stage IB disease, overall survival, recurrence-free survival, and disease-specific survival were 88% (95% CI: 73%, 100%), 89% (95% CI: 75%, 100%), and 94% (95% CI: 85%, 100%), respectively, at both 5 years and 10 years.

Risk for Metachronous RCC

During the follow-up period, eight of 134 patients (6%) were diagnosed with metachronous RCC. Median time to diagnosis was 48 months (mean, 46 months; range, 12–89 months).

Table 1: Test and NCDB Patient Characteristics before and after Matching

	Before Matching			After Matching		
	Study	NCDB		Study	NCDB	
Characteristic	PCA	PN	RN	PCA	PN	RN
No. of patients	134	44 274	37 357	128*	13 090	6645
Age	67 (11)	59 (12)	62 (12)	67 (11)	67 (11)	67 (11)
Sex						
Female	73 (54)	17 005 (38)	14 900 (40)	71 (55)	7261 (55)	3686 (55)
Stage						
IA	115 (86)	35 741 (81)	16 590 (44)	110 (86)	11 249 (86)	5711 (86)
IB	19 (14)	8533 (19)	20 767 (56)	18 (14)	1841 (14)	934 (14)
CDCC						
0	29 (22)	30 633 (69)	24 464 (66)	29 (23)	2966 (23)	1505 (23)
1	28 (21)	10 237 (23)	9028 (24)	28 (22)	2863 (22)	1454 (22)
2	39 (29)	2559 (6)	2670 (7)	36 (28)	3682 (28)	1869 (28)
3	37 (28)	815 (2)	1195 (3)	35 (27)	3579 (27)	1817 (27)
Unknown	1 (1)	…	…	…	…	…

Note.—Data are numbers, with percentages in parentheses. NCBD = National Cancer Database, PCA = percutaneous cryoablation, PN = partial nephrectomy, RN = radical nephrectomy.

* Six patients from the study group were diagnosed outside the date range provided by the NCDB and were therefore excluded from matched analysis.

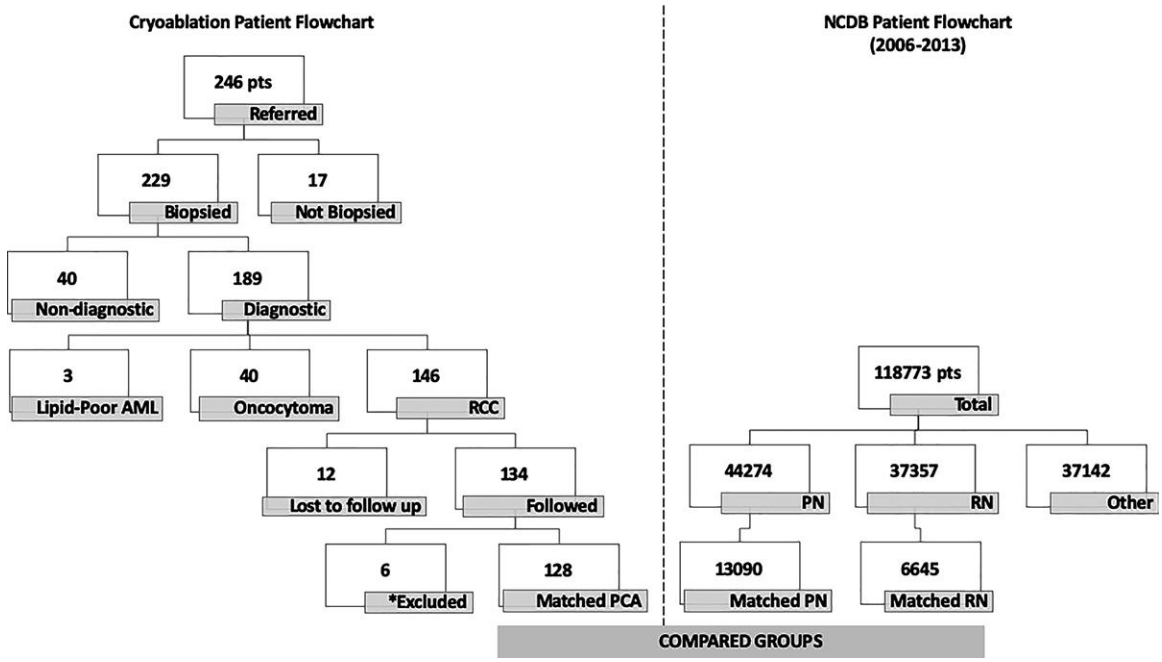


Figure 1: Image shows patient inclusion flowchart. Among initial 246 patients (pts) with stage I renal cell carcinoma (RCC) referred from urology for percutaneous cryoablation (PCA), 134 were eventually included in our study (left). From National Cancer Database (NCDB) (right), among total 118 773 patients with stage I RCC treated between 2006 and 2013, 44 274 (37%) were treated with partial nephrectomy (PN), 37 357 (32%) were treated with radical nephrectomy (RN), and 37 142 (31%) were treated otherwise (percutaneous, laparoscopic, or open ablation). After matching, three comparison groups were PCA (128 patients), PN (13 090 patients), and RN (6645 patients). ∗ = Among 134 study patients, five were excluded because they were treated before 2006 and one due to lack of Charlson/Deyo Combined Comorbidity score. AML = angiomyolipoma.

Effect of Age at Diagnosis

The 5- and 10-year overall survival (Fig 3a) and recurrence-free survival (Fig 3b) curves exhibit divergence with advanced age, notably above 80 years ($P = .01$ and $P = .03$, respectively). Additionally, both the 5- and 10-year curves for disease-specific survival peak at 100% for patients who were aged 85 years at diagnosis (Fig 3c).

When stratified by age at diagnosis and compared with matched NCDB PN and RN cohorts, PCA resulted in a longer 5- and 10-year overall survival at nearly every index age (Fig 4).

Renal Function Outcomes

Risk for hemodialysis.—Two patients who were undergoing hemodialysis prior to PCA were excluded. During the follow-up period, five patients (five of 132, 3.8%) transitioned to hemodialysis, three of whom had normal sCr level prior to PCA. Overall, the dialysis-free probability was calculated to be 98% (95% CI: 95%, 100%) at 5 years, and 95% (95% CI: 89%, 100%) at 10 years. There was no difference in the dialysis-free probability between patients with stage IA and IB. For patients with sCr level greater than 1.2 mg/dL, both the 5- and 10-year probability of being dialysis-free was 94% (95% CI: 84%, 100%). For patients with normal baseline sCr level, the 5- and 10-year hemodialysis-free probability was 99% (95% CI: 97%, 100%) and 95% (95% CI: 88%, 100%), respectively. The unadjusted hemodialysis risk for patients with normal baseline renal function was 2.3% over 10 years.

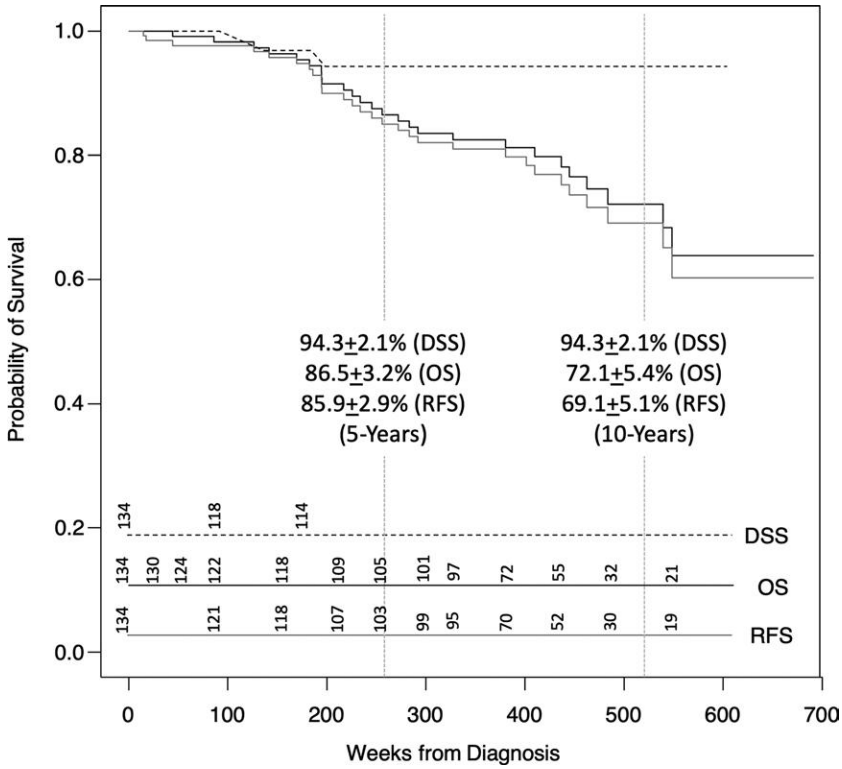


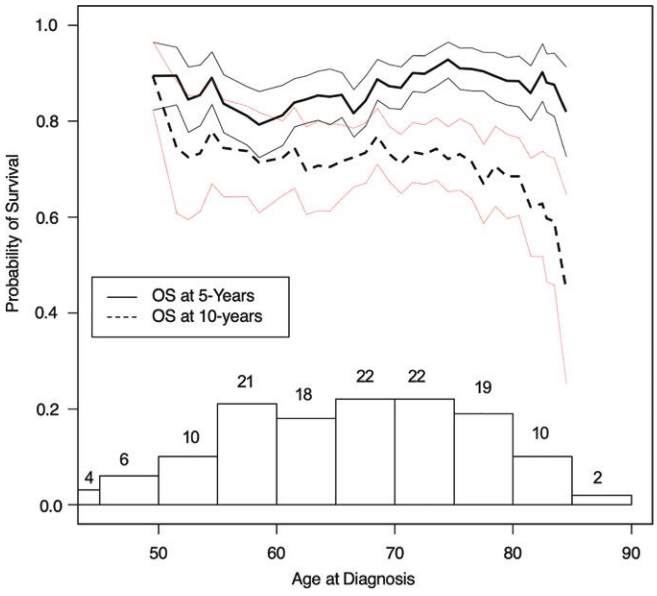
Figure 2: Graph shows survival curves for 134 patients with stage I renal cell carcinoma (RCC) treated with cryoablation. Disease-specific survival (DSS) was 94.3% ± 2.1 at both 5 years and 10 years after diagnosis. Recurrence-free survival (RFS) was calculated at 85.9% ± 2.9 and 69.1% ± 5.1 at 5 years and 10 years, respectively. This suggests that even in rare instance of documented recurrence after 5 years (n = 2, 1.5%), RCC is unlikely to be cause of patient's mortality. Overall survival (OS) was 86.% ± 3.2 and 72.1% ± 5.4 at 5 years and 10 years, respectively. This did not differ significantly from RFS as number of disease recurrence was low (n = 5, 3.7%). Numbers at risk for each curve are indicated in lower portion of graph area.

sCr Level and eGFR.—For patients who had a new hemodialysis requirement, the last sCr measurement prior to hemodialysis was used for analysis. For all patients, the baseline mean sCr level was 1.13 mg/dL ± 0.33 and eGFR was 75 mL/min ± 22. At the end of the follow-up period, mean sCr level was 1.29 mg/dL ± 0.44 and eGFR was 59 mL/min ± 20. For the subgroup with baseline sCr level greater than 1.2 mg/dL, mean baseline sCr level and eGFR were 1.54 mg/dL ± 0.27 and 55 mL/min ± 10, respectively. The corresponding ending mean values were 1.9 mg/dL ± 0.25 for sCr level, and 40 mL/min ± 5 for eGFR. For patients with normal baseline sCr level (≤1.2 mg/dL), mean baseline sCr level was 0.96 mg/dL ± 0.18 and eGFR was 89 mL/min ± 17, transitioning to 1.10 mg/dL ± 0.23 and 70 mL/min ± 14 in the long term (Table 2).

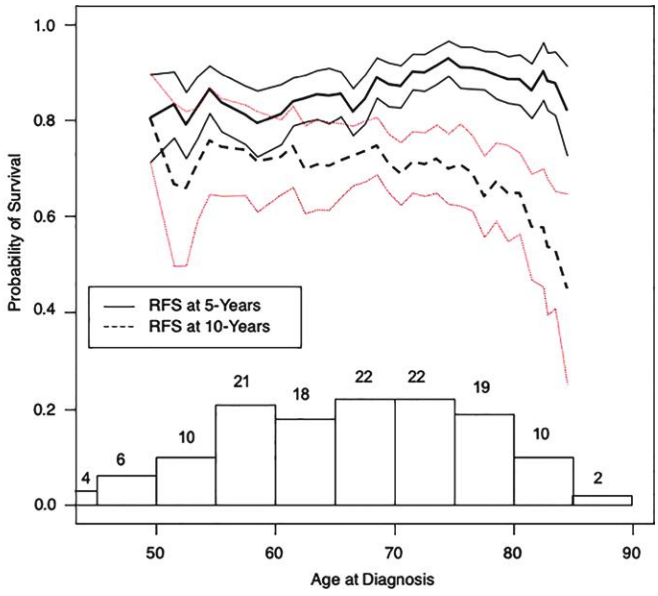
NCDB cohorts.—The NCDB does not provide information on cause of death; therefore, the recurrence-free survival and disease-specific survival could not be estimated. After matching the two subgroups (PN and RN) with our cohort, the 5- and 10-year overall survival for PN was estimated to be 78% (95% CI: 74%, 81%) and 49% (95% CI: 41%, 57%), and for RN 67% (95% CI: 63%, 71%) and 43% (95% CI: 38%, 49%), respectively. Stratification by increasing CDCC score showed a decreasing overall survival. In terms of overall survival, the PCA group outperformed both the PN and RN subgroups in all CDCC score categories and at both the 5- and 10-year marks (Table 3).

Discussion

Our study showed a disease-specific survival of 94% (95% confidence interval [CI]: 90%, 98%) at both 5 years and 10 years after percutaneous cryoablation (PCA) for stage I renal cell carcinoma (RCC). Several secondary conclusions can be drawn. PCA was associated with longer overall survival compared with partial nephrectomy (PN) and radical nephrectomy (RN), a trend becoming more pronounced for patients with comorbidities (Charlson/Deyo Combined Comorbidity score ≥2). This finding suggests that surgical interventions may have long-term detrimental effects on patients at higher risk. The risk of metachronous disease in our population was approximately 6% at 10 years. The 10-year risk of transitioning to hemodialysis for patients with normal baseline sCr level was 2.3%, comparable to that reported in the literature for surgical treatments, which ranges between 2.5%–2.7% (14,15). Finally, based on the age-at-diagnosis analysis, it appears that cryoablation (or any treatment, for that matter) in patients with stage I RCC older than 80 years is unlikely to confer a survival benefit. These reassuring long-term oncologic outcomes after PCA are underpinned by a low rate of perioperative complications, reported at 6%.



a.



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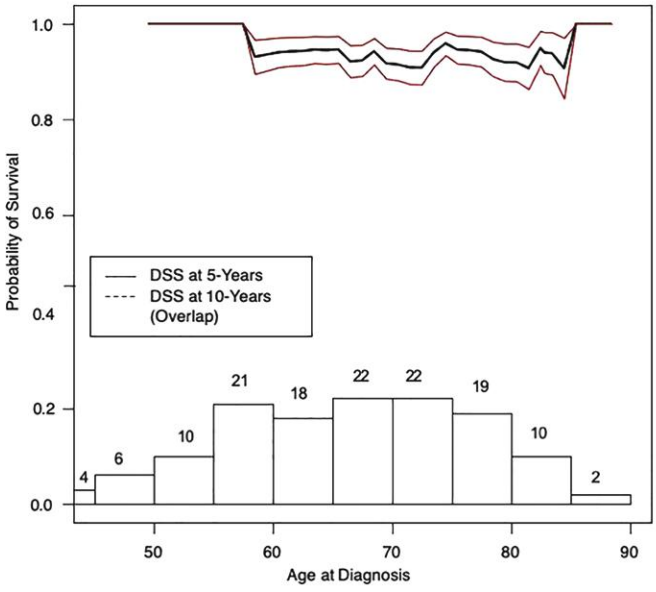

c.

Figure 3: Plots show 5-year (solid lines) and 10-year (dashed lines) **(a)** overall survival (OS), **(b)** recurrence-free survival (RFS), and **(c)** disease-specific survival (DSS) probabilities by age at diagnosis of all 134 patients in percutaneous cryoablation group. Whereas 5-year curves are relatively stable, 10-year curves dip with advancing age, notably above 80 years. This suggests cryoablation is beneficial at any age, provided life expectancy of octogenarians is at least 5 years. (Number above bars are number of patients used in calculation for that age range. Bracket curves represent standard error).

Patients with stage I RCC are increasingly treated with ablative modalities that include radiofrequency ablation, microwave ablation, and PCA. Introduced in the mid-1990s, ablative options accounted for 1% of stage I RCC treatments in 1993 and reached nearly 10% in 2017 (16–18). Anticipating nearly 74 000 new cases in 2019 (of which approximately 45 000 will be stage I), more than 4500 patients are expected to be treated with ablation during the same year. This increased utilization of ablative treatments has drawn critical investigations with conflicting conclusions. Some newer studies suggest that ablation yields similar oncologic outcomes to surgery with a 5-year disease-specific survival around 95%, an improved risk profile, and better renal functional outcomes. Others confirm the superiority of nephron-sparing surgery (19–21). In a review of the Surveillance, Epidemiology, and End Results Program or SEER database, Yan et al (22) concluded that cryoablation was equivalent to PN for RCC up to 2 cm, with PN showing better disease-specific survival for tumors larger than 2 cm. Similar outcomes were reported by Andrews et al (23), who showed a 5-year disease-specific survival of 99% for PN and 100% for PCA for stage IA. For stage IB disease, PN resulted in an improved 5-year disease-specific survival compared with PCA, 98% and 91%, respectively. In a more recent study, again using the SEER database, Xing et al (24) showed that there was no statistically significant difference in 9-year disease-specific survival between thermal ablation and PN or RN. Most authors presenting PCA outcomes acknowledge limitations including retrospective nature, lack of biopsy, and/or lack of long-term follow-up. The latter is especially critical for RCC, as its mean doubling time is approximately 1.4 years, and its annual volumetric growth rate is 0.7–1.3 cm^3 per year (25,26). In addition, there is emerging evidence that cryoablation is associated with better disease-specific survival compared with thermal ablation (microwave ablation or radiofrequency ablation), especially for larger (≥3 cm) masses (27). Our study was designed to address those limitations. It was prospective, included only patients with biopsy-proven RCC, utilized only PCA, and provided 10-year oncologic outcomes.

The main limitation of our study was its single-arm design, partially mitigated by comparing outcomes to those of matched

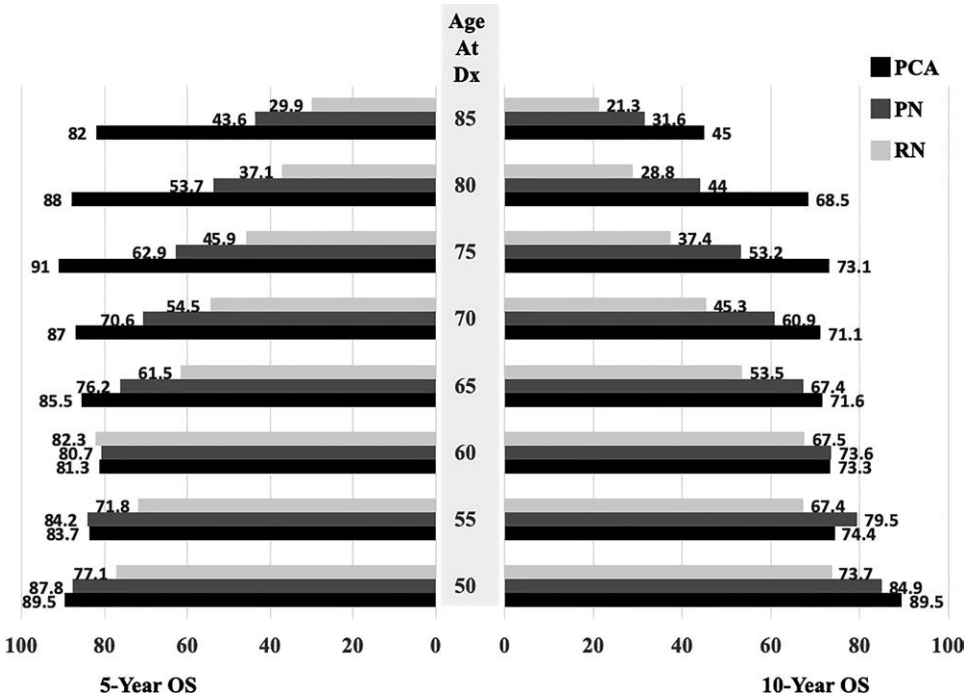

Figure 4: Graph shows 5-year (left) and 10-year (right) overall survival (OS) after percutaneous cryoablation (PCA), partial nephrectomy (PN), and radical nephrectomy (RN) stratified according to patient age at diagnosis (Dx).

Table 2: Changes in sCR Level and eGFR after Cryoablation for Stage 1 Renal Cell Carcinoma

	sCr Level				eGFR			
Parameter	Baseline (mg/dL)	End (mg/dL)	Rate of Change per Year (mg/dL)	Annual Increase (%)	Baseline (mL/min)	End (mL/min)	Rate of Change per Year (mL/min)	Annual Decline (%)
All Patients (n = 132)	1.13 ± 0.33	1.29 ± 0.44	0.021	1.8	75 ± 22	59 ± 20	−2.2	−2.9
Baseline sCr level >1.2 mg/dL (n = 35)	1.54 ± 0.27	1.9 ± 0.25	0.049	3.1	55 ± 10	40 ± 5	−2.1	−3.8
Baseline sCr level ≤1.2 mg/dL (n = 97)	0.96 ± 0.18	1.10 ± 0.23	0.019	1.9	89 ± 17	70 ± 14	−2.6	−2.9

Note.—Unless otherwise specified, data are means ± standard deviation. eGFR = estimated glomerular filtration rate, sCR = serum creatine.

Table 3: Overall Survival Rates for Patients with Stage I Renal Cell Carcinoma Treated with PCA

	5-Year Overall Survival					10-Year Overall Survival				
		PN		RN			PN		RN	
CDCC Score	PCA (%)	Percentage	*P* Value	Percentage	*P* Value	PCA (%)	Percentage	*P* Value	Percentage	*P* Value
0	93 (5) [84, 100]	89 (2) [86, 93]	.48	83 (3) [77, 89]	.07	83 (11) [61, 100]	69 (7) [55, 84]	.32	66 (4) [58, 74]	.16
1	88 (7) [74, 100]	81 (2) [77, 85]	.36	74 (3) [69, 80]	.07	70 (14) [42, 97]	52 (7) [39, 65]	.25	47 (5) [37, 57]	.14
2	89 (5) [79, 100]	77 (3) [72, 82]	.03	63 (4) [56, 70]	<.01	67 (15) [38, 96]	45 (8) [30, 60]	.18	38 (5) [28, 47]	.05
3 or greater	78 (8) [63, 95]	66 (5) [57, 76]	.22	54 (4) [46, 62]	.01	55 (10) [35, 75]	33 (11) [11, 54]	.13	28 (6) [16, 41]	.02
All CDCC scores	87 (3) [80, 93]	78 (2) [74, 81]	.02	67 (2) [64, 71]	<.01	72 (5) [62, 83]	49 (4) [41, 57]	.001	43 (3) [38, 49]	<.001

Note.—Unless otherwise specified, data in parentheses are standard errors, with 95% confidence intervals in brackets. Partial nephrectomy (PN) and radical nephrectomy (RN) data were calculated by using matched subgroups from the National Cancer Database. Cryoablation was associated with longer overall survival compared with both PN and RN at every Charlson/Deyo Combined Comorbidity (CDCC) grade.

cohorts from the NCDB. Matching with NCDB may be imperfect. The NCDB does not include data on cause of death, information on experience of treating centers, or availability of treatment options. PCA outcomes from our study were extracted from a single high-volume center performed by experienced operators with multidisciplinary support. Some of the NCDB outcomes were undoubtedly partly based on data from small centers with variable experience. Referral bias may be another limitation. Referring urologists may have preselected for "ablatable" tumors with intend to cure, that is, smaller, percutaneously accessible, and not in contact with other organs. Finally, the strict follow-up protocol may have afforded earlier and more effective treatment for metachronous tumors and other incidentally detected disease.

In summary, data from our 10-year prospective observational study in patients with stage I renal cell carcinoma (RCC) showed that percutaneous cryoablation (PCA) provides an excellent disease-specific survival, at least equivalent to that of surgery. Overall survival was longer after PCA for stage I RCC, especially for patients at higher risk (Charlson/Deyo Combined Comorbidity score $\geq$2) when compared with partial nephrectomy (PN) and radical nephrectomy (RN). Additionally, PCA exhibited an improved perioperative risk profile compared with PN or RN, and conferred the same or lower long-term risk for transitioning to hemodialysis.

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