Efficacy and safety of percutaneous cryoablation for stage 1A & 1B Renal Cell Carcinoma: 5-Year outcomes

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Aims and objectives

Percutaneous ablation is an increasingly utilized treatment option for Renal Cell Carcinoma (RCC). In the few prospective studies that exist, the reported efficacy of percutaneous ablation for RCC ranges from 90% to 98% (1-4). In addition, oncologic outcomes after percutaneous ablation appear comparable, albeit slightly lower, than those of surgical treatments (5). The safety profile of the procedure is favorable with a reported major complication rate ranging from 3.2% to 8.6% (1, 6, 7, 8). It is similar to that of laparoscopic ablation (8) and lower than that of other surgical options, which range from 11.5% to 13.8% (9, 10, 11). However, the major drawback of ablative modalities is the lack of long-term follow up, with most studies reporting only short and intermediate term oncologic outcomes. Our objective was to perform a prospective study on the safety and efficacy of percutaneous, CT-guided cryoablation for stage 1 RCC and determine the 5-year efficacy and oncologic outcomes.
Methods and materials

Our Institutional Review Board approved this prospective study. The study included all patients with stage 1 RCC treated with percutaneous cryoablation over a 7 year period. Exclusion criteria were inability to suspend anticoagulation, lack of percutaneous access to the target lesion, inability to ensure non-target ablation, severe comorbid conditions/life expectancy <1 year, INR>1.7 or platelets<50K. Two risk factors were especially scrutinized on the baseline cross-sectional imaging to mitigate complications: 1. If the adrenal gland was at risk of being injured during cryoablation, the patient was pre-medicated with both alpha- and beta-blockers for at least 5 days prior to the procedure, and 2. If the target lesion was within 1.5 cm of the ureter, an internal double-J ureteral catheter was placed prior to the ablation. The catheter would remain in place for at least 1 month after the procedure and then removed.

All cases were performed under conscious sedation with versed and fentanyl and under CT guidance. After informed consent and with the patient prone on the CT table the appropriate flank was prepped and draped in a sterile manner. A baseline non-contrast CT was obtained. The overlying skin was anesthetized with lidocaine hydrochloride. All lesions were biopsied at the time of procedure except: 1. Lesions with a positive biopsy from another institution, 2. Patients who had a positive biopsy of a synchronous or metachronous lesion and the target lesion was new or growing. Biopsies were performed with a 16- or 18-gauge coaxial core biopsy needle. Under CT guidance the cryoprobes were placed into the tumor. The number and location of the cryoprobes depended on the size and geometry of the target lesion. We used both the Endocare and the Galil Medical systems and utilized their 2.4 mm cryoprobes exclusively. We considered the procedure technically successful if the following two requirements were met: 1. the visualized "ice-ball" covered the entire lesion plus a 5 mm margin (Figure 1); 2. the ablation protocol, which included a 10 minute freeze, an 8 minute thaw and a 10 minute re-freeze was completed. Hydro- or air-dissection was utilized if a non-target organ were to be within the 5 mm margin. At the end of the procedure a non-contrast CT was obtained to document any complications (such as hemorrhage, pneumothorax etc) and to help triage the patient to discharge or admission. Patients were observed for 4 hours and then discharged to home. They were kept overnight if there was a complication or symptoms requiring further observation or treatment or, if in the judgment of the treating physician, there was a substantial risk of complications at home (for example elderly patient with comorbidities and living alone). Multi-staged treatment (lesion treated in two sessions) was performed if tumors were larger than 5 cm and there was pre-existing cardio-pulmonary disease or advanced patient age (independent predictors of complications).

Patients were re-evaluated at 3, 6, 9, 12 months and then every year along with laboratory tests and contrast enhanced dual-phase. CT or MRI. Treatment efficacy was defined as the complete lack of enhancement of the previously enhancing tumor.
and a gradual decrease in the size of the treated lesion. The studies were read by experienced radiologists, not involved with treatment. We calculated the 1-, 2-, 3- and 5-year overall survival, cancer-specific survival and efficacy of the treatment. Complications were tabulated according to the Common Terminology Criteria for Adverse Events version 4 (CTCAE 4).
Fig. 1: Figure 1. Immediate post-operative CT image after CT-guided, percutaneous cryoablation for RCC. The "ghost" artifact of the removed probe (arrowhead) is seen traversing the target lesions (arrow). This is visible while the "ice-ball" is still frozen and the tissue uncollapsed. The "ice-ball" itself is clearly seen as a hypodense oval region (thin arrows) surrounding the target lesion.

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Results

Two hundred and sixty five renal tumors were ablated in 246 consecutive patients during the study period. Of these, 134 patients had biopsy proven RCC and at least one follow up session and thus included in the study (Figure 2). There were 61 males (46%) and 73 females (54%) with a mean age of 68±11 years (35-88).

Median RCC size was 2.8±1.4 cm (0.5-7.0), with 115/134 being stage 1A (<4cm) and 19/134 being stage 1B (4-7 cm). Four of the 19 (21%), stage 1B RCC were staged. Most RCC were of the clear or papillary cell type (93%) (Figure 3).

Efficacy: Two patients were found to have residual disease on follow up imaging, one of which refused re-ablation and remains alive with viable tumor. The other patient underwent re-ablation with no evidence of disease thus far. The 1-, 2-, 3-, 4- and 5-year efficacy of CT-guided, percutaneous cryoablation for RCC was calculated to be 99.2%, 99.2%, 98.9%, 98.5% and 97.0%, respectively and shown Table 1. All cause mortality during our study was 3 patients (none from RCC), yielding an overall 5-year survival of 97.8%. The cancer-specific 5-year survival was 100%. No patient developed metastatic disease during the follow up period.

Safety: The type and rate of complications of the procedure do not depend on the histology of the target lesion, therefore all ablation sessions (n=265) in all 246 patients were included in the safety analysis. A total of 742 cryoprobes (2.4 mm) were used [median 2.8±1 (1-6) per case]. In addition, 229 lesions were biopsied concurrently with the procedure using a 16- or 18-gauge core biopsy needle system. Thirty-eight patients (15.4%) had to be admitted, while 208 (84.6%) were treated as outpatients. We had to utilize hydro- and/or air dissection in 47 ablation sessions (18%) to avoid injuring a non-target organ, most commonly the colon (Figure 4). There was one 30-day mortality, unrelated to the procedure. Procedure-related mortality was 0%. The significant-complication rate according to CTCAE v.4.0 was 6% (Table 2). Specifically, there were four cases of hemorrhage requiring transfusion. Three of them occurred approximately 1 week post-ablation and in patients who restarted anticoagulation with warfarin. Two additional cases of hemorrhage-related complications were noted in patients with hematuria resulting in bladder outlet obstruction due to bladder clot. They were treated with continuous bladder irrigation. In both cases the bladder clot resolved and patients were able to be discharged on the same day as the procedure without further complications. Two pneumothoraces after intentional pleural transgression required chest tube drainage. Overall, we crossed the pleural in 41 sessions (up to 4 probes), which yields a rate of chest tube placement of 5% in this subgroup. There was one case of ureteral injury and hydronephrosis requiring nephrostomy tube placement. This patient did not receive an internal double-J ureteral catheter prior to ablation. As this was an early patient in the series, we immediately altered our protocol to include
stenting in all patients with ureters in close proximity to the ablation zone. Subsequently, we performed 27 ablations in which the ureter was adjacent to the target lesion. An internal double-J ureteral catheter was placed prior to ablation and kept for at least one month post-ablation. None of these patients developed ureteral stricture. One patient developed a peri-renal abscess requiring drainage. Three patients suffered procedure-related ischemic episodes. One suffered an episode of cerebral ischemia the day after the procedure from which she completely recovered. Two additional patients complained of chest pain prior to the beginning of the procedure. Electrocardiograms showed ischemic changes and both patients were emergently treated with cardiac catheterization and coronary stenting. In both cases, there was a significant stenosis within a previously placed coronary stent, which was unmasked by the interruption of Plavix treatment. Both patients recovered promptly and were able to have their RCC treated. Finally, two cases of arrhythmias were documented, one ventricular tachycardia and one asystole, both recovering spontaneously. In both cases the target lesion was close to the adrenal gland in non-premedicated patients. Again, this experience prompted us to alter our protocol to include premedication with alpha and beta blockers for all patients with upper pole tumors in close proximity to the adrenal gland. There was no case of arrhythmia in patients who were premedicated irrespective of the extent of the adrenal coverage by the "ice-ball". There were no patients who progressed to renal failure after cryoablation. Median plasma creatinine was 1.4±0.5 mg/dl prior to ablation and 1.3±0.7 mg/dl one month post-ablation.
Fig. 2: Figure 2. Flow diagram of the patient population included in the study. From February 2006 to September 2012, 261 stage 1 RCC in 246 consecutive patients were treated with CT-guided, percutaneous cryoablation. Of the 229, which were biopsied, 189 biopsy specimens were of diagnostic quality, resulting in 146 positive specimens for RCC. Twelve patients were lost to follow-up with the remaining 134 RCC included in the study.

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Fig. 3: Figure 3. Histopathology findings of the RCC biopsy specimens. In 43 of the 189 (21%) diagnostic-quality biopsies, histopathology was benign (see figure 1). Of the 146 RCC, 69% were clear cell and 24% were papillary type, mirroring the reported rates in the literature.

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Table 1.

Table 1: Table 1. Oncologic outcomes of the 134 patients with stage 1 biopsy-proven RCC treated with CT-guided, percutaneous cryoablation. The 1-, 2-, 3-, 4- and 5-year cancer-free survival (efficacy) of our patient population was 99.2%, 99.2%, 98.9%, 98.5% and 97.0%, respectively. The 5-year cancer-specific survival was 100% and the overall survival was 97.8%.

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Fig. 4: Figure 4. An example of protective dissection. The pre-ablation CT (A) shows a postero-lateral exophytic mass from left kidney abutting the descending colon. The distance between the two (arrow) is inadequate for effective cryoablation. Immediate post-ablation CT (B) shows the descending colon at a safe distance from the still-frozen mass (arrowhead), having been pushed away by injection of air.

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Table 2: Complications of CT-guided, percutaneous cryoablation for renal masses according to the CTCAE 4.0. A total of 265 ablation sessions were performed (biopsy-proven and those with non-diagnostic biopsies) (261 tumors, 4 of which were staged). The significant complication rate (CTCAE >2) of percutaneous cryoablation for renal mass is 6%. The most common complication is hemorrhage requiring transfusion at 1.6%. There was no procedure-related mortality.

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Conclusion

The results of our prospective study show a 5-year, cancer-specific survival of 100% and a 5-year recurrence free survival of 97%, for image-guided percutaneous cryoablation for RCC. This rivals open or laparoscopic cryoablation, betters the results of all other ablative modalities and in these selected patients, rivals other surgical options. The safety profile of percutaneous cryoablation is excellent with an overall significant complication rate of 6%, similar to other ablative modalities and better than surgical options.

Provided that the expertise of the urology-interventional radiology collaborating group is substantial, image-guided, percutaneous cryoablation for stage 1 RCC can offer long-term oncologic outcomes that rival other options, and with an improved safety profile.
References


