MINIMALLY INVASIVE AND ROBOTIC SURGERY

Thermal ablation of small renal masses: intermediate outcomes from a Canadian center

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Introduction: Cryoablation (CA) and radio frequency ablation (RFA) are nephron sparing procedures that destroy renal tissue in situ rather than by surgical removal. Both thermal ablative techniques are advocated in select patient population with a small renal mass and multiple comorbidities which may preclude major surgery. Unfortunately long term oncologic outcomes of these procedures are unknown.

Materials and methods: We report oncologic outcomes following CA and RFA in patients with small renal masses, from a single center, during a 48 month follow up period. Thirty patients underwent thermal ablation of a small renal mass, 7 with RFA and 23 with CA.

Introduction

Small renal mass can be defined as a contrast enhancing mass equal to or less than 4 cm in the greatest dimension, on abdominal imaging.¹ Small renal masses constitute 48%-68% of all renal tumors and approximately 38% of all surgically removed renal tumors.^{2,3} Up to 80% of small renal masses are found to be malignant and 20% benign.⁴

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Results: Median tumor size on preoperative CT was 2.6 cm \pm 0.87 cm. Four patients experienced a locoregional treatment failure and underwent subsequent radical nephrectomy. Two patients were diagnosed with metastatic renal cell cancer in the follow up period. Six patients died during the follow up period, five from unrelated cause and one from metastatic RCC (overall survival 80%, RCC-specific survival 96%).

Conclusions: This study demonstrates low RCC recurrence rates and in combination with previously published reports supports the effectiveness of thermal ablation therapy as primary therapeutic option in a very specific patient population.

Key Words: nephron sparing procedures, renal cell cancer, cryoablation, radiofrequency ablation

Cryoablation (CA) and radio frequency ablation (RFA) are nephron sparing procedures that destroy renal tissue in situ rather than by surgical removal. Both techniques are advocated in select patient population with a small renal mass and multiple comorbidities which may preclude major surgery.

Both techniques offer decreased morbidity, shorter period of hospitalization, convalescence and renal function preservation.⁵ In contrast to laparoscopic or open partial nephrectomy, neither of the techniques requires clamping of the renal vessels nor advanced laparoscopic skills required for suturing and renal reconstruction.⁶ Both techniques are associated with low morbidity. This is an additional advantage when considering the treatment of patients with small renal mass who are older, and may have coexisting medical morbidities. Unfortunately long term oncologic outcomes for these procedures are unknown. We report oncologic outcomes following cryoablation and radiofrequency ablation in patients with small renal masses, from a single center, during a 4 year follow up period.

Materials and methods

We performed a retrospective chart review of patients who had CA and RFA at our institution, during the 2003-2009 year period. Institutional ethics approval was obtained (UWO HSREB 1150E). The indication for CA or RFA was a stage T1 renal cancer less or equal to 4 cm in the greatest diameter that enhanced on preoperative abdominal CT scan. Biopsy was performed prior to ablation in all cases except for patients who were on anticoagulant medications, in which case the biopsy was performed immediately pretreatment, when the anticoagulation was reversed.

Twenty-three renal masses were found to be posterior on the renal surface and accessible with percutaneous approach. Of the 23 masses all were smaller than 4 cm. Fourteen masses were found to be $\geq 50\%$ exophytic, 6 masses $\leq 50\%$ exophytic and 3 masses were found to be completely endophytic. Of the 23 masses 16 were found to be ≥ 7 mm away from the renal hilum/sinus, 7 were found to be within 4 mm-7 mm from the renal hilum/sinus. Of the 23 masses, eight were found to be located completely within upper or lower pole of the kidney, in relation to the polar line. Eleven tumors were found to cross the polar line and four were found to be $\geq 50\%$ across the polar line or to cross the axillary line of the kidney.

Laparoscopic CA was performed in seven patients by a single surgeon, as previously described in the literature (Galil Medical, 4.8 mm cryoprobe).⁷ All seven patients had anterior tumors, judged to be inaccessible by percutaneous approach. All other CA and RFA cases were performed percutaneously, by a single interventional radiologist, with the urologist's input. Two freeze-thaw cycles were performed in each CA case, with 3-5 probes. The RFA was performed with two heating cycles using the RITA250 generator (RITA Medical Systems, Inc., Mountain View, CA), with final RFA ablation of the needle tract.

Patients records were reviewed for patient age, existing comorbidities, type of thermoablative therapy used, pre and operative hemoglobin, pre and postoperative serum creatinine. All patients had a negative metastatic work up. Tumor specific information was obtained including tumor size on the initial CT scan, initial tumor enhancement, results of pre CT-guided tumor biopsy, tumor size, enhancement on the follow up CT scans and results of post treatment renal mass biopsy. At our institution the patient follow up was CT contrast study of the abdomen and pelvis at 3, 6, 12, 24, 36 and 48 months post treatment. All patients received renal function adjusted contrast and had renal function protective measures implemented, such as adequate hydration. Post treatment renal biopsy was performed at 6 months following the treatment, in all patients available for follow up. Treatment outcome was recorded as no recurrence if there was no mass enhancement on post treatment imaging or if the mass involuted or disappeared and a negative post treatment biopsy. Recurrence post treatment was defined as contrast enhancement of the mass, increase in size or a positive post treatment biopsy.

Data was analyzed using GraphPad Prism 4 software (GraphPad, San Diego, CA, USA). Data were analyzed using Analysis of Variance (ANOVA) with Dunnett's Multiple Comparison post test (> 2 groups). Significance was assessed at p < 0.05.

TABLE 1. Patient characteristics

Patient age (range, mean)	49-82 (67.6 ± 11.8)	
ECOG status	-, (,	
0	4	
1	8	
2	9	
3	8	
4	1	
Mean tumor size (largest diameter)	2.71 ± 0.9	
Mean preoperative creatinine (μmol/L)	115.6 ± 49.4 (75-315)	
Mean postoperative creatinine (µmol/L)	114.9 ± 49.9 (67-301)	
Mean preoperative Hb (mmol/L)	138.3 ± 21.4 (81-182)	
Mean postoperative Hb (mmol/L)	127.1 ± 20.2 (80-173)	
Treatment modality		
RFA	7	
Cryoablation		
Laparoscopic	7	
Percutaneous	23	
Number of cryotherapy probes used		
1	7	
2	8	
3	9	
4	5	
0	1	



Figure 1. Kaplan-Meier survival curves after thermal ablation of small renal mass in 30 patients.

Results

Thirty patients underwent thermal ablation of the small renal mass, Figure 1. Choice of treatment modality (RFA versus CA) was non-randomized and based on availability of resources at our center. We performed 7 RFAs and 23 CA in the specified time period. The patient age range was 49-84 years. Median ECOG score was 2. Mean tumor size on preoperative CT was 2.6 cm \pm 0.87 cm. The average length of follow up was 48 months. Patient's demographic information and tumor characteristics on imaging are in Table1.

Seven patients were treated laparoscopically, as the tumors were found to be on the anterior renal surface and inaccessible percutaneously. Four had a nephrometry score of 4a (1+1+1+a+1) and three had a score of 5a (1+2+1+a+1).

Twenty-four out of 30 patients had a pretreatment biopsy diagnosed as RCC. Results of image guided renal mass biopsies can be seen in Table 2.

Twenty patients were available for postoperative renal mass biopsy. Two patients were diagnosed with post treatment persistent malignancy on post treatment renal mass biopsy, four had a final pathology report as

TABLE 2. Pretreatment renal mass biopsy results		
Non diagnostic	4	
Neoplasia, not specified	6	
Clear cell RCC	7	
Papillary RCC	5	
Chromophobe RCC	7	
Angiomyolipoma	1	
Oncocytoma	1	
Not performed	4	

TABLE 3. Post	t treatment renal	mass biop	sy results
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Negative for malignancy	12	
Non-diagnostic	10	
Suspicious for malignancy	4	
RCC	2	

"suspicious for malignacy". Post treatment renal mass biopsy results are presented in Table 3.

Four patients experienced a loco-regional treatment failure and underwent subsequent radical nephrectomy. Three patients had clear cell RCC on final surgical pathology, one papillary RCC. The RCC recurrence occurred 6-23 months post thermal ablative therapy. Two patients were diagnosed with metastatic renal cell cancer in the follow up period. One patient developed metastatic disease to the brain and had undergone radiation therapy. This patient is alive with the disease. Overall outcomes of CA and RFA are represented in Table 4.

We examined the pre-treatment imaging of the four patients who recurred to further describe their lesion using the nephrometric system. The first patient had a nephrometry score of 7p (1+2+2+p+2) and was found to have a persistent tumor enhancement at 6 months post CA. He had a negative post cryoablation biopsy, final post nephrectomy pathology report demonstrating pT3aN0Mo clear cell RCC. The second patient had a nephrometry score of 7p (2+1+1+p+3) and was diagnosed with a recurrence at 6 months post RFA. He recurred along the RFA tract in addition to kidney. His final post nephrectomy pathology report demonstrated pT4NxM1 clear cell RCC, with brain and lung metastases. The third patient had a score of 7p (1+2+1+p+3) and was found to recur at 6

TABLE 4. Outcomes of renal mass ablation treatment

	Biopsy + RCC/ neoplasia
Number of patients	20
Number of recurrences (%) Loco-regional Metastatic	6 (20%) 4 (13%) 2 (6.7%)
Number of cancer deaths (%)	1 (3.3%)
% 5 year survival Overall Disease specific Disease free	24/30 (80%) 24/25 (96%) 20/25 (80%)

months post CA. His post nephrectomy pathology report demonstrated pT3b clear cell RCC. The fourth patient had a nephrometry score of 5p (1+2+1+p+1) and experienced a recurrence at 23 months post CA. His post nephrectomy pathology report demonstrated pT1aN0M0 papillary RCC.

Six patients died during our follow up, five from unrelated cause and one from metastatic RCC (overall survival 80%, RCC specific survival 96%). In the non-RCC group causes of mortality were: cardiac arrest in the recovery room immediately following the CA (one); complications following aortic valve replacement surgery (one); non-metastatic hip fracture and death from acute pneumonia while recovering following the orthopedic surgery (one); de novo pancreatic cancer (one); de novo squamous cell lung cancer (one).

Discussion

Thermal ablative therapy is currently considered as a legitimate treatment option for a patient with a small renal mass and medical comorbidities. Indications for use of thermal ablation are a renal tumor ≤4 cm occurring in the elderly patient, patient who is considered high risk for surgery due to medical comorbidities, patient with severe renal dysfunction, surgically scarred abdomen, a small renal mass in a post partial nephrectomy remnant or the request of an informed younger patient.⁵ Thermal ablative therapy relies on insertion of needle applicators within the renal mass and subsequent generation of temperatures which are cytocidal.⁸ The initial needle insertion can be performed either laparoscopically or percutaneously, with percutaneous approach associated with decreased morbidity.

Twenty patients in this series (67%) underwent postoperative needle biopsy at 6 months post treatment, four patients refused or were unable to undergo it. RCC was found in two patients and four had a final pathology report as "suspicious for malignancy". Two patients with a positive biopsy also had a persistent contrast enhancement on postoperative CT scan. Of the four patients who underwent a post thermal ablation nephrectomy, only two had a positive biopsy. The remaining two patients with suspicious biopsy had a complete involution of the renal mass and remain disease free at present. The indication for nephrectomy in the first patient was an enlarging renal mass. In the second patient the indication for surgery an enhancing mass along percutaneous tract. In 10 cases, the post thermal ablation biopsy was not diagnostic. Taken together, these data confirm that needle biopsy of the ablated tumor is not a fail-safe diagnostic modality and cannot be used for follow up alone. Furthermore, it

underscores the necessity of regimented and dedicated long term radiologic monitoring. A recent study⁷ argued that biopsy of the lesion must be performed and we have used this strategy in the cases discussed.

In this series, abdominal contrast-enhanced CT was used for follow up in all cases. In 20 patients, CT scan demonstrated an absence of contrast enhancement and gradual decrease in the renal mass. In four patients, persistent enhancement was demonstrated and subsequent nephrectomy performed. Two patients were followed with MRI or renal US due to pre-existing poor renal function.

In this series, we experienced a single peri-operative mortality (3%). This occurred in a 79-year-old female with a history of coronary artery disease and a previous 5 vessel coronary artery bypass. The indication for CA was a biopsy proven RCC that was initially observed but continued to enlarge radiographically. This patient underwent a successful CA and developed massive myocardial infarction in the recovery room. Additionally, we experienced one case of limited retroperitoneal bleed following RFA (3%). These results are similar to previously published reports, which demonstrated 1% cardiac complication rate, 1%-5% hemorrhage rate and 10% overall complication rate.⁷ We did not experience any ureteral injuries or strictures in this series.

Early comparisons of the two thermal modalities were in favor of CA.^{9,10} However, more contemporary series¹¹⁻¹⁵ suggest improved outcomes with RFA. In our series, we had four tumor recurrences, one of whom occurred in a patient treated with RFA, three in patients treated with CA. These results do not suggest a difference in recurrence between the two modalities and we cannot make definitive conclusions from this series due to the non-randomized nature of the study.

At present, there is a relative paucity of data on long term effectiveness of thermal ablation therapy. Reflecting this fact, our patient population was highly selected to include older patients with coexisting morbidities, who were found to be poor surgical candidates. We report 80% overall survival in our patient group and 96% disease specific survival during our follow up. These data are similar to recently published outcomes, demonstrating 84% overall and 92% disease specific 5 year survival.7,13,15 These data are inferior in comparison to contemporary series describing surgical management of T1 RCC, but still demonstrated low RCC recurrence rates. In combination with previously published reports, this report supports the effectiveness of thermal ablation therapy as primary therapeutic option in a very specific patient population.

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