Radiofrequency ablation for T1a tumors in a solitary kidney: promising intermediate oncologic and renal function outcomes

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Objective: *The experience with radiofrequency ablation (RFA) in solitary kidneys is limited in numbers and follow-up. Therefore, we report our oncologic and renal function outcomes of RFA for T1a tumors in patients with a solitary kidney.*

Methods: *From April 2000 to August 2007, 242 patients were treated with RFA for renal cortical masses. Sixteen patients with localized tumors ≤ 4 cm in a solitary kidney were identified. Clinical and radiographic data were reviewed to assess indications, complications, disease recurrence, and renal function.*

Results: *Twenty-one renal masses were ablated in 16 patients with a solitary kidney. The mean patient age was 66.1 years, and the mean tumor size was 2.6 cm (range, 1.1-4.0). Preoperative biopsy was diagnostic of renal cell carcinoma (RCC) in 75% of cases. At a mean follow-up of 30.7 months (range, 1.5-66.0), 14/16 (88%) patients had no radiographic evidence of disease recurrence. One patient with three masses in a solitary kidney had a local recurrence managed by salvage RFA. The other patient with a local failure also had severe baseline renal insufficiency with progression to end stage renal disease 2.5 years following RFA and underwent a radical nephrectomy. Mean glomerular filtration rate (GFR) decreased from 54.2 ml/min/1.73m^2 preoperatively to 47.5 ml/min/1.73m^2 at last follow-up ($p = 0.015$). There were no major complications, and four patients had minor complications which resolved without intervention.*

Conclusion: *Radiofrequency ablation is an attractive alternative for the management of patients with T1a renal cortical tumors in a solitary kidney. Renal function appears to be adequately maintained with promising oncologic outcomes at 2.5 years.*

Key Words: glomerular filtration rate (GFR), kidney mass, renal cell carcinoma (RCC), RFA, thermal ablation

Introduction

Radiofrequency ablation (RFA) is an emerging nephron-sparing treatment option for select patients with small renal tumors. Several groups have reported favorable RFA outcomes for renal masses with 2 to 5 years follow-up.[1-3] While surgical extirpation remains the gold standard therapy for small renal masses,[4-6] the promising oncologic outcomes, improved convalescence and minimal parenchymal loss make ablative therapy an option for high-risk patients.

Renal tumors in a solitary kidney present a challenging therapeutic dilemma. Renal preservation

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is essential, and current surgical therapies include open and laparoscopic partial nephrectomy.[7,8] However, the associated morbidity for extirpative surgery in a solitary kidney may be high due to the need for vascular clamping with resultant global renal ischemia.[9-11] As such, ablative technology which obviates ischemic insults may be an attractive alternative for managing small tumors in solitary renal units.[12]

Prior to routine implementation of RFA practice for managing tumors in a solitary kidney, it is incumbent to demonstrate sound oncologic outcomes, adequate preservation of renal function, and a low complication rate. The literature, thus far, is limited on this front. While some early series are promising,[13-16] the presence of concurrent metastatic disease and a relatively short follow-up interval make interpretation of oncologic and renal function outcomes difficult. Clearly, additional experience and longer follow-up is essential before this therapy can be adopted into mainstream practice. Here then, we present our experience of RFA for T1a renal cortical tumors in solitary kidneys at a mean follow-up of 2.5 years.

Methods

Patient selection

The Institutional Review Board (IRB) approved the prospective collection of data from patients managed by either laparoscopic or percutaneous RFA. Of the 242 patients treated between April 2000 and August 2007, 16 had clinically localized tumors $\leq$ 4 cm in a solitary kidney. Prior to treatment, all patients were counseled regarding the full complement of available surgical options including radical nephrectomy, partial nephrectomy (open or laparoscopic), and ablative techniques. RFA therapy was based upon both patient selection as well as surgeon recommendation based on comorbid conditions.

RFA technique

RFA was performed by either laparoscopic (n = 4) or percutaneous (n = 12) approaches. The surgical modality was dependant upon tumor size, configuration, and proximity to adjacent structures. All percutaneous procedures were performed under general anesthesia with CT guidance. We have previously described our technique for radiofrequency ablation of renal tumors.[17] Briefly, RF energy was applied using a RITA model 1500 RF generator (RITA Medical Systems, Mountain View, CA). A 14-gauge Starburst XL probe consisting of nine active tines with real-time temperature feedback from five independent thermocouples was utilized. An ablation zone diameter 0.5 cm-1.0 cm beyond the maximum CT-measured tumor diameter was created. The generator modulated power up to 150W in order to achieve an average ablative temperature of 105ºC. Once the target temperature was achieved, tumors < 2 cm in diameter were treated with two cycles of 5 minutes duration each, tumors 2 cm-3 cm were treated for two cycles of 7 minutes duration each, and tumors > 3 cm were treated for two cycles of 8 minutes duration each.

Outcome variables

Clinical and radiographic data were reviewed to obtain surgical indication, demographic data, preoperative renal function, tumor pathology, acute and chronic complications, follow-up of renal function, and disease recurrence status based on computed tomography (CT) or magnetic resonance imaging (MRI). GFR was calculated by the simplified Modification of Diet in Renal Disease (MDRD) equation: [GFR (ml/min/1.73m^2) = 175 x (SCr)$^{-1.154}$ x (Age)$^{-0.203}$ x (0.742 if female) x (1.212 if black), where GFR = glomerular filtration rate and SCr = serum creatinine].[18] Measurements were made preoperatively and at 6 weeks, 3 months, 6 months, 12 months, and semiannually thereafter. Axial cross-sectional imaging (CT with non-ionic contrast, CT with gadolinium, or MRI with gadolinium) was performed at our institution and reviewed by both a urologist and radiologist at these same time intervals. Contrast enhancement or lesion growth in the zone of ablation was considered evidence of radiographic local treatment failure.

Statistical analysis

Excel 2003 (Microsoft, Redmond, Washington) software and SPSS version 13.0 (SPSS Inc., Chicago, IL) were used to perform statistical calculations with $p < 0.05$ considered statistically significant. Mean GFR over time were compared using paired, non-parametric tests (Wilcoxon).

Results

Clinical characteristics

Table 1. Twenty-one renal masses $\leq$ 4 cm were ablated in 16 patients with a solitary kidney. Fourteen patients had a single tumor, two had two tumors, and one patient had three masses. ASA scores ranges from 2 to 4 with 13/16 patients having an ASA score of 3 or higher. Mean tumor size was 2.6 cm (range, 1.1-4.0). Fifty percent of the tumors were exophytic, and over 60% were located on the lateral surface of the kidney. Seventy-five percent (12/16) of the patients had a history of a contralateral nephrectomy due to metachronous RCC at a mean interval of 9.4 years (range, 3.8 to 16.7) prior to the

TABLE 1. **Clinical characteristics**

No. patients	16
No. tumors	21
Gender (male/female)	12/4
Age, years	66.1
(range)	(52.3-81.4)
Comorbid conditions (%)*	
CAD	4 (25)
DM	7 (44)
HTN	6 (38)
Hyperlipidemia	9 (56)
Radiographic tumor size, cm	2.6
(range)	(1.1-4.0)
Tumor location** (%)	
Exophytic	10 (48)
Mesophytic	4 (19)
Endophytic	7 (33)
Medial	8 (38)
Lateral	13 (62)
Approach (%)	
Percutaneous	12 (75)
Laparoscopic	4 (25)
Length of stay (days)	
Mean (range)	0.75 (0-3)

*Several patients had multiple comorbidities
**Exophytic > 60% extension off the natural surface of the kidney, endophytic tumors were defined < 40% of the lesion extending off the surface of the kidney, and mesophytic were defined as those lesions extending 40% to 60% off the surface of the natural border of the kidney
CAD = coronary artery disease; DM = diabetes mellitus
HTN = hypertension

present diagnosis. Of the remaining four patients, two had a congenital solitary kidney and two had a contralateral nephrectomy for non-functional, chronically infected kidneys.

Oncologic outcomes

Table 2. Preoperative biopsy performed just prior to ablation was diagnostic of renal cell carcinoma (RCC) in 75% of the masses. Two biopsies were non-diagnostic, and one patient with multiple renal masses only had one of these tumors biopsied which was diagnostic of RCC. At a mean follow-up of 30.7 months (range, 1.5-66.0), 14/16 (88%) of patients had no radiographic evidence of disease recurrence (defined by lesion growth or enhancement). One patient with three masses in a solitary kidney had radiographic enhancement suggestive of a local recurrence at the deep margin of one ablation zone 14 months following RFA therapy. This presumptive failure was managed by salvage RFA without a subsequent biopsy. The other patient with a local failure had severe baseline renal insufficiency (preoperative CrCl of 22.1 ml/min/1.73m^2) attributed to longstanding hypertension and diabetes with progression to end stage renal disease 2.5 years following RFA. This radiographic local recurrence was identified 36 months following RFA and was addressed by an open radical nephrectomy. The final pathology was a 3.6 cm Fuhrman grade III pT3aN0Mx clear cell RCC. No other patients developed a local recurrence or metastatic disease.

TABLE 2. **Oncologic, renal function outcomes and complications**

Pre-ablation pathology (%)	
Renal cell carcinoma	16 (76)
Oncocytoma	2 (10)
Non-diagnostic	2 (10)
No biopsy	1 (5)
Follow-up (months)	
Mean	30.7
Range	1.5-66.0
Pts. NED (%)	14 (88)
GFR (ml/min/1.73m^2)	
Pre-op	
Mean	54.2
Range	22.7-89.9
Last F/U	
Mean	47.5
Range	16.0-76.7
% change from baseline	11.8
Complications (%)	
Acute	4 (25)
Hematuria	1
Ileus	1
Subcapsular hematoma	1
Paresthesia	1
Chronic	2 (13)
Hydrocalyx	1
Hemodialysis	1

Renal function outcomes

Table 2. The mean preoperative GFR using the simplified MDRD equation was 54.2 ml/min/1.73m^2 consistent with stage 3 chronic kidney disease (CKD) (GFR 30-59 ml/min/1.73m^2). At last follow-up, mean GFR had declined by 11.8% to 47.5 ml/min/1.73m^2

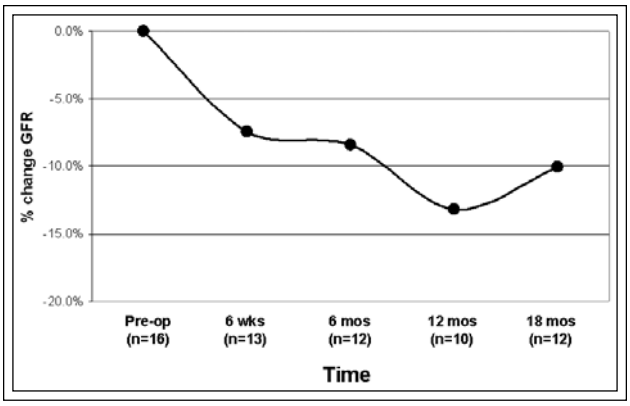

Figure 1. Mean percentage change from baseline creatinine clearance. Time points with 10 patients or greater were included in analysis.

(p = 0.015). Of the four patients with preoperative GFR consistent with stage 2 CKD (> 60 ml/min/1.73m^2), 100% maintained a GFR > 60 ml/min/1.73m^2 at last follow-up. Figure 1 graphically represents the mean percentage decline in GFR from baseline pre-operative values. Following an initial 7.5% decline 6 weeks following RFA, GFR remained relatively stable up to 18 months and later.

Complications

Table 2. In the acute setting, there were no major complications, and four patients developed minor complications. One patient developed hematuria that resolved spontaneously. Another reported flank numbness following percutaneous RFA that had improved by 3 months follow-up. A third patient was noted to have a subcapsular hematoma on follow-up imaging. The patient recovered without a transfusion requirement. Finally, following laparoscopic RFA, one patient developed a transient ileus requiring hospitalization until post-operative day 3.

Two patients developed chronic complications. One patient with severe baseline renal insufficiency (CrCl 22.1 ml/min/1.73m^2) and a 3.9 cm renal tumor became dialysis-dependant 2.5 years following RFA. Another patient was incidentally found to have a hydrocalyx on CT imaging 18 months postoperatively. The patient remains asymptomatic and has required no intervention to date.

Discussion

Partial nephrectomy is currently the standard of care for the management of renal masses in a solitary kidney.[7,8,19-22] Favorable oncologic outcomes have been reported by both open and laparoscopic techniques. However, the ischemic insult incurred during surgical therapy is of concern when considering longterm kidney function. Reports of renal function outcomes are difficult to interpret as most series include only serum creatinine changes or CrCl calculated by the Cockcroft-Gault formula. It is now well appreciated that the MDRD study equation is more accurate than serum creatinine levels, CrCl estimated from the Cockcroft-Gault equation, or measured CrCl in patients with reduced glomerular filtration.[18,23] Nonetheless, the bulk of contemporary literature does imply worsening renal function with some series noting an almost 10% progression to kidney failure requiring dialysis.[7,8,10,20-22]

Ablative techniques, such as RFA, obviate the need for hilar clamping and renal ischemia. As such, it may present a particularly attractive alternative for patients with an anatomic or functional solitary kidney and baseline renal insufficiency. In 2006, Salagierski et al published on percutaneous RFA for 42 high risk surgical patients, 14 of whom had a solitary kidney.[14] In this series, 93% of tumors were successfully treated by a single ablation, while three patients required a second ablation due to incomplete tumor destruction. The complication rate was low except for one patient who required hemodialysis due to acute renal insufficiency. Interpretation of outcomes, however was limited by a relatively short follow-up interval (14 months), lack of renal function monitoring, and the grouping of solitary kidney patients with all other high-risk patients. Syvanthong and colleagues specifically addressed renal function outcomes in 12 patients with a solitary kidney undergoing percutaneous RFA.[15] Patients in this study had baseline stage 3 CKD with a mean preoperative creatinine clearance of 40.8 ml/min. The authors noted successful tumor ablation in all cases with a 16% increase in serum creatinine and a 13% decrease in creatinine clearance post-RFA. The study, however, is limited by its very short mean follow-up of 2.9 months. The most comprehensive assessment to date is by Jacobsohn and colleagues reporting on 16 patients with renal tumors in a solitary kidney.[16] This series included patients with metastatic disease who had RFA performed for local, palliative control. Renal function was well preserved with a 13.3% decline within the first week and a 9.1% decline at a mean follow-up of 15.3 months following RFA. Four of 16 patients did have major acute complications (3 clot obstruction, 1 perinephric bleed), and 1 patient developed renal failure 4 months after the procedure. While the reported renal function outcomes at 1-year are promising, the inclusion of patients with

metastatic disease confounds interpretation of oncologic outcomes. Further, the relatively high complication rate raises concerns regarding the role of RFA in these clinical scenarios.

In this study, we report on outcomes from 16 patients with 21 lesions ≤ 4 cm in a solitary kidney treated by RFA. No patients had radiographic evidence of metastatic disease prior to ablation. Three-fourths of patients had a history of a contralateral nephrectomy for RCC underscoring the predilection for metachronous multifocality. At a mean follow-up of 2.5 years, 14 of 16 (88%) patients had no evidence of disease recurrence. One patient who had three masses ablated had radiographic enhancement at the periphery of one of the ablation zones 14 months following initial therapy. This presumed local recurrence was salvaged by RFA. The other patient with a local failure had developed end stage renal disease, and the recurrence was managed by a radical nephrectomy. There was no other evidence of local recurrence or metastatic disease. Our oncologic outcomes provide more substantiative follow-up to previously reported observations, and also mirror results for ablation of masses in patients with a normal contralateral kidney.[1-3] Of course, we acknowledge that there are some series that question the adequacy of tumor destruction and long-term oncologic outcomes of RFA.[24,25] Clearly, longer follow-up will better delineate the therapeutic efficacy of this ablative technique.

Regarding renal function, 75% of our patients had baseline stage 3 CKD with a mean preablation GFR of 54.2 ml/min/1.73m^2. This is lower than most open series and reflects the natural selection bias of ablative therapy for patients who are more "ill". However, it further underscores the importance of renal preservation in this patient population as chronic kidney disease is an independent risk factor for substantial comorbidity and death.[26] We found that following an initial 7.5% decline 6 weeks following RFA, GFR remained relatively stable with an overall decrease of 11% at a mean follow-up of 2.5 years. These observations are consistent with the natural history of medical renal disease noted in patients with stage 3 to 5 chronic kidney disease.[27] In contrast, extirpative surgery may have a more deleterious effect on global renal function in a solitary kidney system. When considering partial nephrectomy with cold ischemia, Yossepovitch et al reported a median GFR decrease of 30% during the early postoperative period and 32% 12 months afterwards.[28] Clearly, definitive comparisons are impossible given potential variability in lesion size and location as well as baseline renal function. However, these observations do suggest the potential for future prospective studies comparing outcomes of ablative therapy with partial nephrectomy for patients with small renal tumors in a solitary kidney.

Finally, our series emphasizes that RFA for tumors in a solitary kidney can be performed with a minimal complication profile. This endpoint is imperative particularly when weighing this therapy against excisional surgery. It is likely that patient and appropriate lesion selection is crucial, and the success of RFA will directly reflect such considerations. We acknowledge that this study is limited by a small sample size. Further, as ablative therapy is still in its infancy, our follow-up interval is still not sufficient to provide longterm oncologic outcomes. However, our current data are promising and we anticipate that the patient volume and follow-up will mature over time.

Conclusion

Radiofrequency ablation is an attractive alternative for the management of patients with small localized tumors in a solitary kidney. The complication rate is low, renal function appears to be adequately maintained, and oncologic outcomes are promising at 2.5 years. □

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