Oncologic Efficacy of Radio Frequency Ablation for Small Renal Masses: Clear Cell vs Papillary Subtype

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Purpose: Current radio frequency ablation series do not distinguish renal cell carcinoma subtypes when reporting oncologic efficacy. Papillary neoplasms may be more amenable to radio frequency ablation than clear cell carcinoma because they are less vascular, which may limit heat energy loss. We report the long-term outcomes of patients treated with radio frequency ablation for small renal masses by renal cell carcinoma subtype.

Materials and Methods: The records of patients undergoing radio frequency ablation for small renal masses (cT1a) at 2 institutions from March 2007 to July 2012 were retrospectively reviewed. Patients were included in analysis if they had biopsy confirmed clear cell or papillary renal cell carcinoma histology. Patients had at least 1 contrast enhanced cross-sectional image following radio frequency ablation. Demographic data between tumor subtypes were compared using the paired t-test. Oncologic outcomes were determined by Kaplan-Meier survival analysis and survivor curves were compared with the log rank test.

Results: A total of 229 patients met study inclusion criteria. There were 181 clear cell tumors and 48 papillary tumors. Median followup was 33.2 months. There was no difference between tumor groups based on patient age, tumor size or grade, or months of followup. Five-year disease-free survival was 89.7% for clear cell tumors and 100% for papillary tumors ($p = 0.041$). There was no significant difference in overall survival (88.4% vs 89.6%, $p = 0.764$).

Conclusions: Radio frequency ablation outcomes seem to be determined in part by renal cell carcinoma subtype with clear cell renal tumors having less favorable outcomes. We hypothesize that this is due to differences in tumor vascularity. Our experience suggests that future tumor ablation studies should consider reporting outcomes based on tumor cell types.

Key Words: kidney; carcinoma, renal cell; catheter ablation; carcinoma, papillary; outcome and process assessment (health care)

Abbreviations and Acronyms

CT = computerized tomography
DFS = disease-free survival
MRI = magnetic resonance imaging
NSS = nephron sparing surgery
OS = overall survival
RCC = renal cell carcinoma
RFA = radio frequency ablation

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THE number of incidentally discovered renal masses continues to increase due to the widespread use of cross-sectional imaging. NSS remains the standard of care for small renal masses.[1] However, NSS can be technically challenging depending on tumor location and it may be associated with significant perioperative complications and morbidity.[2,3] Therefore, NSS may not be ideal in an older patient population with significant comorbidities. For these reasons focal ablative techniques such as

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cryoablation and RFA have been used in an effort to decrease morbidity and shorten the convalescence period. These modalities have been shown to be effective in terms of oncologic and renal functional outcomes.[4–7]

The success of surgical resection (ie negative margins) is independent of tumor subtype. However, there are differences in the biology of various renal tumors, which may affect ablation success. Of the 3 most prevalent RCC subtypes clear cell predominates (83% of cases) followed by papillary (11%) and chromophobe (4%).[8] Since RFA and cryoablation rely on large, sustained thermal energy changes for cell kill, they are susceptible to the heat sink effect of adjacent vasculature. It was hypothesized that increased intratumor and peritumor neovascularity also limits the effectiveness of these technologies as reflected by the higher recurrence rate of tumors greater than 3 cm treated with RFA.[6,9]

To our knowledge there are no studies to date that have analyzed oncologic outcomes of renal tumor ablation stratified by RCC subtype, although clear cell tumors are known to be more vascular than other tumors.[10] In the current study we retrospectively analyzed RFA outcomes based on RCC subtype with the hypothesis that for clinically localized RCC (cT1a) oncologic outcomes may differ between the more vascular clear cell carcinoma vs papillary renal carcinoma.

PATIENTS AND METHODS

Institutional review board approval was obtained to retrospectively review the records of patients at University of Texas Southwestern Medical Center and University of Miami who underwent RFA from March 2007 to July 2012. RCC subtype was specifically identified and only those with a pretreatment biopsy reporting clear cell RCC and papillary subtype were included in study. Patients had to have a minimum of 1 contrast enhanced cross-sectional image 3 months after RFA. Patients with an identified genetic disease predisposing to renal cancer were excluded from analysis, as were patients who had received a previous intervention to the ipsilateral kidney. There were only 3 patients with chromophobe RCC subtype in the identified cohort and they were excluded from study, although none experienced recurrence during followup. Papillary subtypes 1 and 2 were not routinely distinguished by pathologists.

RFA Technique

The technique of percutaneous and laparoscopic RFA depended on individual institutional practice patterns according to previously described methods.[11,12] Temperature targeted RFA was used in all cases with one of 2 systems, including a Model 1500 radio frequency generator (AngioDynamics®) with a tine array probe and a set target temperature[8] or an impedance based RFA generator (Covidien®) with multiple needle probes and real-time peripheral temperature monitoring using fiberoptic thermosensors (LumaSense® Technologies).[13] Percutaneous approaches were performed using CT guidance. Laparoscopic approaches were performed using ultrasound and tumor visualization to guide probe placement. At University of Texas Southwestern Medical Center biopsy was performed in most cases at the time of RFA if it had not been performed previously. During the laparoscopic approach biopsy was performed immediately after ablation using 5 mm toothed biopsy forceps. At University of Miami all biopsies were performed with a spring loaded 16 gauge needle (Terumo®) before ablation.

Followup after treatment included history, physical examination, chest radiograph and serum creatinine. Contrast enhanced CT or MRI studies were obtained at 6 weeks, 6 and 12 months, and at least annually thereafter. Incomplete ablation was defined as persistent enhancement (greater than 10 HU) in any portion of the treated lesion on the 6-week CT or MRI. Local recurrence was defined as any new enhancing portion within the ablation zone after the initial negative contrast enhanced CT or MRI. DFS was defined as freedom from recurrence at any site (local or metastatic). OS was defined as freedom from death from any cause.

Statistics

Descriptive statistics were calculated for all variables of interest. Differences between groups were analyzed with the Student t-test for continuous variables and the chi-square test for categorical variables. Two-tailed hypothesis tests were used for each comparison with $p \leq 0.05$ considered statistically significant. Survival analysis was calculated by the Kaplan-Meier method. Actuarial 5-year DFS and OS rates in each cohort were determined and compared using the log rank test. Statistical analysis was performed with IBM® SPSS®, version 19.

RESULTS

A total of 229 available patients from the 2 institutions met inclusion criteria for analysis. Median followup was 33.2 months. There were 181 clear cell tumors (79.0%) and 48 papillary tumors (21.0%). The table shows baseline patient and clinical characteristics. Compared to patients with clear cell neoplasms those with papillary neoplasms were more often male (79.2% vs 64.0%, $p = 0.03$). Patient age, tumor size, followup duration and treatment approach (percutaneous vs laparoscopic) did not differ significantly between the groups (see table). When comparing the 2 centers, tumor size was similar ($p = 0.886$). However, the rate of laparoscopic RFA at University of Miami was 47.2% compared to 28.2% at University of Texas Southwestern Medical Center ($p = 0.011$).

Five-year DFS was 89.7% for clear cell tumors and 100% for papillary tumors ($p = 0.041$, fig. 1).