Original Study

Small Renal Masses in Close Proximity to the Collecting System and Renal Sinus Are Enriched for Malignancy and High Fuhrman Grade and Should Be Considered for Early Intervention

Andres F. Correa,[1] Amir Toussi,[2] Milon Amin,[3] Ronald L. Hrebinko,[4] Bishoy A. Gayed,[5] Anil V. Parwani,[6] Jodi K. Maranchie[4]

Abstract

The small renal mass is a heterogeneous entity that needs careful consideration before treatment selection. Merging radiographic and clinical-pathological data from 334 patients we aimed to assess if renal mass anatomical characteristics were associated with malignancy and high-grade histology. Nearness to the collecting system was the only variable found to be associated with the diagnosis of cancer and high-grade disease.

Introduction: Recent reports show a correlation between renal tumor radiographic characteristics and pathologic features. We hypothesize that a more central location within the relatively hypoxic renal medulla might confer a more aggressive tumor phenotype. To test this, radiographic tumor characteristics were compared with tumor grade and histology. **Materials and Methods:** We retrospectively reviewed renal masses <4 cm in diameter that underwent resection between 2008 and 2013. Tumor location was recorded using standard R.E.N.A.L. Nephrometry Score. Multivariate logistic regression was performed to compare independent anatomic features with incidence of malignancy and high nuclear grade. **Results:** A total of 334 renal tumors had information available for analysis. Univariate analysis showed that increasing endophycity and proximity to the collecting system (<4 mm) were predictors of malignancy and high-grade features. In multivariate analysis, proximity to the collecting system <4 mm remained the as the only anatomical variable predictive of malignancy (odds ratio [OR], 3.58; 95% confidence interval [CI], 1.06-12.05; $P = .04$) and high nuclear grade (OR, 2.81; 95% CI, 1.44-5.51; $P = .003$). **Conclusion:** Malignancy and high tumor grade occur with much greater frequency when tumors are located deep in the kidney, in close proximity to the collecting system and renal sinus. Ninety-six percent of small renal masses in this region were cancers and nearly half were Fuhrman Grade 3 or 4, suggesting that these small centrally located tumors should be targeted for early intervention.

Clinical Genitourinary Cancer, Vol. ■, No. ■, ■-■
Keywords: High Grade, Histology, Location, Renal cell carcinoma, Small renal mass

Introduction

The incidence of renal cell carcinoma has increased over the past 20 years in large part because of the widespread use of cross-sectional imaging, leading to the overdetection of small asymptomatic tumors.[1] Despite the increase in diagnosis and stage migration toward localized disease, improvement in disease-specific mortality has not followed, likely because of the benign and indolent nature of the small renal masses being diagnosed.[2]

Numerous clinical-pathological studies of small renal masses (cT1a) have shown that a significant percentage of these masses are

[1]Department of Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA
[2]Department of Urology, Mayo Clinic, Rochester, MN
[3]Affiliated Pathologists Medical Group, Torrance, CA
[4]Department of Urology, University of Pittsburgh Medical Center, Pittsburgh, PA
[5]Department of Urology, University of Pittsburgh Medical Center, Pittsburgh, PA
[6]Department of Pathology, Ohio State University, Wexner Medical Center, Columbus, OH

Submitted: Oct 4, 2017; Revised: Jan 16, 2018; Accepted: Jan 27, 2018

Address for correspondence: Andres F. Correa, MD, Department of Surgical Oncology, Division of Urologic Oncology, Fox Chase Cancer Center, Temple University Health System, 333 Cottman Ave, Philadelphia, PA 19111
Tel: 412-414-1862;
e-mail contact: Andres.correa@fccc.edu

1558-7673/$ - see frontmatter
https://doi.org/10.1016/j.clgc.2018.01.017

benign (20%-30%), and in the case of malignancy they tend to be of low grade histology.[3,4] All together, these findings have led to a shift in the treatment of small renal masses in which risk stratification with percutaneous biopsy or a period of active surveillance has been favored[5-8] to help identify clinically relevant cancers and avoid overtreatment of benign or indolent disease.

Because of the potential risk associated with percutaneous biopsy[9] and uncertainty associated with surveillance,[10] renal mass characteristics on preoperative imaging have been used to predict renal mass pathology and aggressiveness.[11,12] Kutikov and colleagues were the first to introduce the concept of renal mass complexity as a predictor of malignancy and high grade features.[11] In their original publication masses of various sizes were included in the analysis, limiting the use of the nomogram for small renal tumors. Others have attempted to apply a similar analysis to small renal masses with conflicting results.[13,14]

Although the association tumor location with histology remains controversial, the kidney remains a heterogeneous organ with highly specialized zones characterized by unique microenvironments. We hypothesized that tumor growth in proximity to the relative hypoxia of the renal medulla might promote high-risk features. To test our hypothesis we assessed the association between renal mass anatomic features on preoperative imaging and aggressive pathology using a large cohort of cT1a renal masses.

Materials and Methods

After institutional review board approval, a pathological database was used to search for patients who had surgical resection of renal masses measuring ≤4 cm in diameter between January 1 of 2008 and December 31 of 2013 at a single institution. All patients with radiological studies available for analysis were included in the study. Retrospective chart review was used to determine patient age at diagnosis, sex, and tumor size at time of diagnosis. All preoperative images were reviewed by A.F.C. and A.T., and a consensus score of 1 to 3 was assigned to each of 3 key radiographic characteristics included in the R.E.N.A.L. Nephrometry Score (RENAL-NS).[15] Radiographic review was blinded from pathological review to decrease confirmation bias.

All tumor specimens were reviewed by a single urological pathologist (A.V.P.) for diagnosis and, in case of malignancy for histological subtype, tumor, node, metastases stage, Fuhrman nuclear grade,[16] angiolymphatic invasion, or extracapsular extension per the seventh edition of the American Joint Commission on Cancer cancer staging manual.[17] For cases performed before January 2010, the staging for each tumor was updated for standardization of pathological reporting. Tumors with nuclear Fuhrman Grade 3 or 4 were classified as high grade. A sample of 50 specimens was sent for independent pathological review by 2 outside genitourinary pathologists (Jyoti P. Balani, MD, and Robert Allan, MD) for confirmation of histological and grade designations.

Associations with malignancy and high tumor grade were tested using the Pearson χ^2 test. Univariate logistic regression was performed for each of the nephrometry components and with age, male sex, and tumor size as a continuous variable. We then built a multivariate logistic regression to assess the effect of individual anatomic features on the incidence of malignancy or high tumor grade. Analyses were performed using SigmaXL software (SigmaXL, Toronto, Ontario, Canada) with P values $< .05$ being considered statistically significant.

Results

After retrospective chart review, 334 patients had complete radiographic and pathological information for analysis. Clinical-pathologic features for this cohort are presented in Table 1. The cohort consisted mostly of older (median age, 61 years) men (78%) with a median tumor diameter of 2.7 cm. Most of the masses were removed via a nephron-sparing surgery (78%). Benign histology was reported in 48 (14.4%) patients, with oncocytoma being the most common benign finding, accounting for 8.7% of the entire cohort. Two hundred eighty-six (85.6%) were renal cell carcinoma with 67% of those showing predominantly clear-cell histology. Among the renal cancers, 95 (28.4%) had high Fuhrman Grade and 13 (3.9%) were upstaged to pathologic stage pT3a.

After renal mass characterization using the RENAL-NS, the incidence of malignancy was significantly higher for completely endophytic masses ($P < .01$) and those <4 mm from the collecting system ($P = .01$), as shown in Table 2. The incidence of high nuclear Grade also increased with increasing endophycity and nearness to the collecting system with 32.2% completely endophytic masses and 44.8% of masses <4 mm from the collecting system harboring Fuhrman Grade 3 or 4 tumors ($P = .03$; $P < .01$).

In univariate analysis, increasing size, endophycity, and nearness to the collecting system were all predictive of malignancy and high-Grade histology (Tables 3 and 4). In multivariate analysis only size (odds ratio [OR], 1.58; 95% confidence interval [CI], 1.07-

Table 1 Demographic, Histological, and Pathological Characteristics of the Entire Cohort

Characteristic	Value
n	334
Female Sex, n (%)	148 (44.3%)
Male Sex, n (%)	186 (55.7%)
Mean Age at Diagnosis (Range), Years	61 (22-88)
Mean Tumor Size (Range), cm	2.7 (1-4)
Radical Nephrectomy, n (%)	72 (21.6%)
Histology, n (%)	
Malignant	286 (85.6)
Clear-cell RCC	222 (66.5)
Papillary RCC	44 (13.2)
Chromophobe RCC	16 (4.8)
Unclassified RCC	4 (1.2)
Benign	48 (14.4)
Oncocytoma	29 (8.7)
AML	12 (3.6)
Cystic lesion	5 (1.5)
Papillary adenoma	2 (0.6)
Tumor grade	
Low (Fuhrman 1 and 2)	191 (57.2)
High (Fuhrman 3 and 4)	95 (28.4)
TNM Stage	
T1a	273 (81.7)
T3a	13 (3.9)

Abbreviations: AML = angiomyolipoma; RCC = renal cell carcinoma; TNM = tumor, node, metastases.