Tumor Complexity Predicts Malignant Disease for Small Renal Masses

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Abbreviations and Acronyms

RAPN = robot-assisted partial nephrectomy

RCC = renal cell carcinoma

SRM = small renal mass

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Purpose: Approximately 20% to 30% of suspicious small renal tumors are benign. A significant proportion of malignant tumors are low grade and potentially indolent. We evaluated whether preoperative patient and tumor characteristics are associated with adverse pathological features.

Materials and Methods: A total of 886 patients underwent robot-assisted partial nephrectomy, as done by 1 of 5 high volume surgeons. Demographic and clinical data were compared between patients with benign/malignant disease, clear cell/nonclear cell renal cell carcinoma and high/low grade tumors. Tumor complexity was quantified by R.E.N.A.L. (radius, exophytic/endophytic, nearness of tumor to collecting system or sinus, anterior/posterior, hilar and location relative to polar lines) nephrometry score and described as low—4 to 6, intermediate—7 to 9 or high—10 or greater. Logistic regression analyses were performed to test the association between tumor and patient characteristics, and high grade renal cell carcinoma. Subanalyses were done for patients with renal tumors 4 cm or less.

Results: High grade renal cell carcinoma was larger and more likely to develop in men. Patients with malignant tumors and with clear cell histology were more likely to have intermediate or high complexity tumors. Increasing tumor complexity independently predicted malignancy, high grade malignancy and clear cell histology on multivariate regression analysis (each $p < 0.05$). Male gender was independently associated with malignancy and high grade renal cell carcinoma. When considering tumors 4 cm or less, tumor complexity predicted malignancy but not tumor grade.

Conclusions: High R.E.N.A.L nephrometry score and male gender are associated with an increased risk of malignancy and high grade malignancy in tumors treated with partial nephrectomy.

Key Words: kidney; carcinoma, renal cell; robotics; nephrectomy; risk

THE incidence of RCC has steadily increased in the last 2 decades, driven largely by the incidental detection of SRMs on cross-sectional imaging.[1,2] In fact, SRMs, defined as tumors 4 cm or less, currently account for 48% to 66% of newly diagnosed renal tumors.[3] While the gold standard for treatment of these lesions is partial nephrectomy, 20% to 30% are benign and treatment is unnecessary.[4,5] Conversely, a reported incidence of metastases in 5.2% of patients with an SRM clearly indicates that a subset of

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these lesions is highly malignant and should be aggressively treated.[6] Differentiating aggressive tumors from indolent lesions using cross-sectional imaging could potentially aid in counseling patients on available management options.

The imaging features and anatomical characteristics of renal masses have been evaluated as predictors of malignant histology after extirpative renal surgery. Except for noncalcified fat, which represents a diagnostic finding in angiomyolipoma, no other cross-sectional imaging feature has reliably distinguished benign from malignant renal masses.[7,8] However, anatomical characterization of solid renal masses has more promise. Solitary descriptions of renal masses, including size,[9] penetration depth[10] and the angular interface with adjacent renal parenchyma,[11] have promise for predicting malignant pathology after renal surgery. However, when considering small tumors, no single feature has reliably predicted malignant disease after partial nephrectomy.

Originally introduced to standardize the reporting of renal tumor anatomy, the R.E.N.A.L. nephrometry score is a quantitative measure of tumor complexity that is associated with high grade RCC after nephrectomy.[12–14] Whether these relationships exist in tumors amenable to nephron sparing surgery is not well established. We present what is to our knowledge the largest single study to analyze preoperative predictors of aggressive lesion pathology in a cohort of predominantly SRMs treated with RAPN.

MATERIALS AND METHODS

From 2007 to 2011 patients treated with RAPN for clinically localized renal tumors were prospectively recorded in 1 of 5 institutional review board approved institutional databases. Five high volume surgeons, each of whom had done 100 or more RAPNs, individually performed the operations at a total of 5 academic institutions. Postoperatively tumors were examined by a genitourinary pathologist. A centralized pathological review was not done. Tumors were assigned a pathological diagnosis based on gross and microscopic findings, and primary RCC was assigned a grade in accordance with the Fuhrman grading system.[15] The mentioned databases were retrospectively reviewed to determine the impact of preoperative tumor and patient characteristics on final tumor histology after RAPN.

Renal Tumor Characterization

Using preoperative cross-sectional imaging, tumors were classified by the R.E.N.A.L. nephrometry score as well as its individual components. Components include maximal tumor diameter, tumor exophytic/endophytic properties, nearness of the tumor to the collecting system or renal sinus, the anterior/posterior description of the tumor and tumor location relative to polar lines.[12] Hilar location was defined as a tumor that touches the main renal artery or vein. Renal tumors with a R.E.N.A.L. nephrometry score of 4 to 6, 7 to 10 and 10 or greater were classified as low, intermediate and high complexity, respectively. Preoperatively tumors were characterized by the attending urologist or a qualified trainee with appropriate supervision.

Malignant vs Benign Tumors

Malignant tumors were defined as any primary RCC or metastatic lesion. All other lesions, including but not limited to oncocytoma, angiomyolipoma and nonmalignant cystic lesions, were considered benign. Patient and preoperative tumor characteristics were compared between those with benign and malignant tumors. Univariate and multivariate regression analyses were performed to determine independent predictors of malignancy. Subanalysis was performed for tumors 4 cm or less in maximal diameter to determine independent predictors of malignancy when considering only SRMs.

Renal Cell Carcinoma

High vs low grade. Patients with RCC and an assigned grade were included in analysis. Tumors with Fuhrman grade 2 or less and greater than 2 were considered low and high grade, respectively. Patient and preoperative tumor characteristics were compared between high and low grade tumors. Univariate and multivariate regression analyses were done to determine individual predictors of high grade RCC. Subanalysis was performed for tumors 4 cm or less in maximal diameter to determine independent predictors of high grade RCC when considering only SRMs.

Clear cell vs nonclear cell. Tumor complexity was associated with clear cell histology when considering patients with pathologically confirmed RCC.[16] To verify this finding in a multi-institutional RAPN cohort, we compared patient and preoperative tumor characteristics among patients with and without clear cell RCC. Only patients with pathologically confirmed RCC were included in analysis. Univariate and multivariate regression analyses were done to determine independent predictors of clear cell histology. Subanalysis was performed for tumors 4 cm or less in maximal diameter to determine independent predictors of clear cell histology when considering only SRMs.

Statistical Analysis

Simple comparisons were made with the Student t and Wilcoxon rank sum tests, and chi-square analysis, as appropriate. Logistic regression analyses were performed to test the association between independent preoperative variables and the described binary outcomes. To further test the association between low complexity tumors and the described pathological outcomes, all analyses were repeated with nephrometry score considered a binary variable (low vs intermediate/high complexity tumors). Statistical calculations were performed with Stata®, version 11.0.

RESULTS

Benign vs Malignant Tumors

Of the 886 RAPNs performed 873 had a pathological diagnosis and were included in primary analysis. A total of 13 men without a pathological diagnosis were excluded from analysis. There were no other exclusion criteria. Upon pathological examination,