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Original article

Evaluation of anatomic and morphologic nomogram to predict malignant and high-grade disease in a cohort of patients with small renal masses

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Abstract

Objective: To evaluate a nomogram using the RENAL Nephrometry Score (RENAL-NS) that was developed to characterize masses as benign vs. malignant and high vs. low grade in our patients with small renal masses treated with partial nephrectomy (PN). The nomogram was previously developed and validated in patients with widely variable tumor sizes.

Materials and methods: Retrospective review of PN performed between 1/2003 and 7/2011. Imaging was reviewed by a urologic surgeon for RENAL-NS. Final pathology was used to classify tumors as benign or malignant and low (I/II) or high (III/IV) Fuhrman grade. Patient age, gender, and RENAL score were entered into the nomogram described by Kutikov et al. to determine probabilities of cancer and high-grade disease. Area under the curve was determined to assess agreement between observed and expected outcomes for prediction of benign vs. malignant disease and for prediction of high- vs. low-grade or benign disease.

Results: A total of 250 patients with 252 masses underwent PN during the study period; 179/250 (71.6%) had preoperative imaging available. RENAL-NS was assigned to 181 masses. Twenty-two percent of tumors were benign. Eighteen percent of tumors were high grade. Area under the curve was 0.648 for predicting benign vs. malignant disease and 0.955 for predicting low-grade or benign vs. high-grade disease.

Conclusions: The RENAL-NS score nomogram by Kutikov does not discriminate well between benign and malignant disease for small renal masses. The nomogram may potentially be useful in identifying high-grade tumors. Further validation is required where the nomogram probability and final pathologic specimen are available.

Keywords: Kidney cancer; Nephrometry; Nomogram; Prediction; Prognostics; RENAL; Renal cell cancer; Validation

1. Introduction

The clinical behavior of the stage T1a small renal mass (SRM) is variable, ranging from benign masses to indolent tumors that do not grow over time to aggressive lesions harboring high metastatic potential. There is a finite, yet potentially very useful, information set that can be acquired at initial presentation without relying on invasive renal biopsy or time dependence (growth kinetics) to predict clinical and pathologic outcomes [1]. Age and gender are 2 such preoperative patient characteristics that predict likelihood of benign vs. malignant histology. Lane et al. identified that younger women were much more likely to have benign disease (36%) than men were (8%); conversely, older women were more prone to malignant disease than older men were [2]. Eggener et al. reported similar rates of malignant disease, with 36% of SRMs in women who were 18 to 45 years old being benign compared with 9.5% of SRMs in young men [3].

Efforts to include radiographic characteristics into counseling algorithms for SRMs are also underway [4–6]. Kutikov et al. described patient characteristics and RENAL nephrometry score (RENAL-NS) to determine if radiographic features correlated with high-grade disease and histology (Appendix 1) [7]. The acronym RENAL stands for [R]adius maximal diameter in cm, [E]xophytic or endophytic nature, [N]earness to the collecting system or sinus in mm, [A]nterior or posterior, and [L]ocation relative to the polar lines [8]. The authors reported that the

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nephrometry score correlated with both histology ($P < 0.0001$) and tumor grade ($P < 0.0001$). They constructed a nomogram with age, gender, and RENAL score with an area under the curve (AUC) of 0.73 for grade and 0.76 for histology [7]. Wang et al. validated the grade component of the nomogram in a series of patients treated with surgical resection for renal cell carcinoma [9].

Both nomogram creation and validation were done in patients with variable tumor size and clinical stage. The greatest value of the nomogram, however, would lie in discriminating benign vs. malignant disease and high vs. low grade in patients with SRMs. Such knowledge would help patients weigh active surveillance, ablation, or extirpative management for their small renal tumor. Certainly, in the short and intermediate term, benign and low-grade cT1a tumors behave similarly, and differentiating them from high-grade lesions is of foremost concern. Herein, we describe application and evaluation of the RENAL-NS nomogram in a cohort of patients treated with minimally invasive partial nephrectomy (MIPN) for SRMs at our institution.

2. Material and methods

All consecutive cases of laparoscopic partial nephrectomy and robotic-assisted laparoscopic partial nephrectomy performed by a single surgeon between January 2003 and July 2011 were retrospectively reviewed following Institutional Review Board approval. Patients for whom preoperative imaging was not available were excluded from the analysis. Demographic and pretreatment clinical variables including tobacco use were accessioned. The Surgical procedure was performed via the transperitoneal approach as previously described [10,11]. Available preoperative computed tomography (CT) scans were reviewed by a urologic surgeon; RENAL-NS was assigned as described by Kutikov et al. [8]. All specimens were reviewed by a pathologist with expertise in genitourinary pathology.

Analyses were performed with SPSS v.19.0 (SPSS Inc, Chicago, IL). Each patient with clear cell, papillary, or chromophobe renal cell carcinoma was coded as having an actual malignancy. There were no patients with sarcomatoid, medullary, or collecting duct subtypes in this cohort. Patients with oncocytoma, angiomyolipoma (AML), and other benign tumors were coded as benign. Resected AMLs were not recognized on preoperative imaging (fat-poor AML). The subgroup of patients with confirmed malignancy had Fuhrman grade categorized as low (Grade I/II) or high (Grade III/IV). The patient's gender, age, and RENAL-NS were entered into the nomogram described by Kutikov et al. (Appendix 1) to determine the probability of cancer and of probability of high-grade disease [7]. Subset analysis of patients with malignancy ($n = 141$) also had gender and RENAL-NS entered into the nuclear grade portion of the nomogram to determine probability of high-grade disease [7]. RENAL-NS components were compared between patients with benign vs. malignant disease and between patients with high- vs. low-grade disease using the chi-square statistics. Prognostic ability of the prediction models were assessed by creating receiver operating characteristic (ROC) curves. AUC was determined to assess the agreement between observed and expected outcomes with 50% essentially representing a coin toss and 100% indicating a perfect prediction model. This was done 3 times: (i) for the prediction of benign vs. malignant disease in the entire cohort; (ii) for prediction of high-grade vs. low-grade disease in the entire cohort, whereby patients with benign tumors were grouped with those with low-grade tumors (together classified as 'tumors of low metastatic potential'); and (iii) for prediction of high- vs. low-grade disease only in patients with confirmed malignancies.

3. Results

MIPN was performed in a total of 250 patients with 252 masses during the study period. Of these, 179 patients (71.6%) had preoperative imaging available. RENAL-NS was assigned to a total of 181 renal masses (2 patients had bilateral disease). Histologic characteristics are summarized in Table 1. Twenty-two percent of tumors were benign (23 oncocytoma, 9 AML, 6 benign multilocular cysts, cystic nephroma, or benign hemorrhagic cyst). On final pathologic studies, 1 patient had metastatic adenocarcinoma from an unidentified primary tumor. Table 2 outlines RENAL-NS scores for all patients as well as according to final pathology. All surgical margins in this series were negative.

Table 1
Clinicopathologic characteristics of 179 patients with 181 renal masses

Characteristics	All patients
Mean age at surgery, y (range)	57 (18–83)
Male gender, no. (%)	98 (54)
Mean BMI, kg/m^2 (range)	30 (17–50)
Smoking history (%)	24
Hypertension (%)	50
Diabetes (%)	16
Coronary artery disease (%)	8
Histology/*n* (%)	
Malignant	141 (78)
Clear cell	104 (57.4)
Papillary	31 (17.1)
Chromophobe	7 (3.9)
Oncocytoma	23 (12.7)
AML	9 (5)
Benign	6 (3.3)
Other malignant	1 (0.5)
Fuhrman grade, *n* (%)	
1–2	107 (73.8)
3–4	32 (22.8)
Not specified	5 (3.4)