Enhancing Renal Tumors in Patients with Prior Normal Abdominal Imaging: Further Insight into the Natural History of Renal Cell Carcinoma

Paul L. Crispen,*,† Aldiana Soljic,† Gregory Stewart,† Alexander Kutikov,‡ Daniel Davenport† and Robert G. Uzzo§

From the University of Kentucky, Lexington, Kentucky (PLC, GS, DD), University of Massachusetts, Worcester, Massachusetts (AS), and Fox Chase Cancer Center, Philadelphia, Pennsylvania (AK, RGU)

Purpose: Patients undergoing serial cross-sectional abdominal imaging to evaluate abdominal symptomatology may have a renal tumor develop during followup of an unrelated disease process. Evaluation of such patients provides an opportunity to further define the radiographic inception, natural history and growth patterns of renal tumors.

Materials and Methods: Renal tumor databases from 2 institutions were reviewed for patients in whom an enhancing renal tumor developed despite a prior normal cross-sectional radiographic examination of the kidneys. Variables evaluated included age, gender, tumor size at presentation, calculated tumor growth rate from negative scan to radiographic presentation and pathology in patients undergoing definitive treatment.

Results: We identified 36 patients with an average age of 65 years (range 44 to 82). Mean tumor size on presentation was 2.3 cm (range 1.0 to 5.0). The presumed absolute growth rate based on the timing of the initial negative imaging study and tumor diameter at presentation was significantly greater than the observed absolute growth rate after tumor detection (0.71 vs 0.039 cm per year, p = 0.028). No difference was noted between presumed and observed tumor growth based on absolute change in tumor volume (1.44 vs 5.37 cm^3 per year, p = 0.203). Presumed relative growth rates based on tumor diameter (665% vs 23% per year) and volume (1,397% vs 169% per year) were significantly greater than observed relative growth rates (p = 0.005 and p = 0.013, respectively).

Conclusions: The presumed growth rate of the tumors was significantly greater than the observed growth rate, suggesting that tumor growth rates do not follow a linear pattern throughout their development and progression.

Key Words: kidney neoplasms, watchful waiting, disease progression

Editor's Note: This article is the second of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1402 and 1403.

THE routine use of cross-sectional abdominal imaging has led to a significant increase in the detection of incidental renal tumors. The majority of these renal tumors are small, less than 4 cm in diameter, and undergo definitive therapy.[1] However, a small number of these tumors are not managed with definitive therapy and instead undergo active surveillance. The reasons patients undergo active surveillance are commonly based on other medical conditions rendering them suboptimal surgical candidates.[2]

Published series evaluating the active surveillance of renal tumors have provided valuable insight into their natural history. Based on available

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data, the majority of small renal tumors grow slowly with an average growth rate of approximately 3 mm per year.[3] In addition, a significant proportion of renal tumors undergoing active surveillance will not demonstrate interval growth.[4] These findings suggest a rather indolent course for many small renal tumors, which is supported by the observed low rate of stage progression. Local tumor progression during active surveillance rarely influences future treatment options and is associated with pathological up staging in only 6% of cases.[5] Furthermore, the rate of progression to metastatic disease appears to be low at approximately 2% over a median of approximately 3 years and is typically associated with rapid primary tumor growth during active surveillance.[6]

To further our understanding of the natural history of renal tumors, we evaluated a group of patients with prior normal renal imaging in whom enhancing renal tumors subsequently developed. Based on the timing of prior normal imaging, we calculated the presumed growth rate of renal tumors and made comparisons to the observed growth rates of tumors following their clinical detection.

METHODS

After institutional review board approval a retrospective review of 2 institutional renal mass databases was performed from 2005 to 2010 for patients in whom an enhancing renal mass developed after a prior normal contrast enhanced CT of the kidneys. During the study period the Fox Chase Cancer Center renal tumor database included 1,242 patients and the University of Kentucky renal tumor database included 590 patients. All lesions were locally confined to the kidney based on standard radiographic staging protocols. Patients with hereditary renal cancer were excluded from study.

Variables examined included patient age, gender, indication for imaging, radiographic tumor features (cystic vs solid), tumor size (maximal diameter and volume), tumor growth (assumed and observed) and surgical pathology. Tumor size was measured as the maximal cross-sectional diameter. Tumor volume was calculated using the maximal cross-sectional tumor diameter, with the equation, $V = 0.523x^3$. Tumor growth was calculated as absolute and relative growth rates. Absolute tumor growth rates, based on tumor diameter (ATD) and volume (ATV), represent the change in tumor size per year. Relative tumor growth rates, based on tumor diameter (PTD) and volume (PTV), represent percentage change in tumor size per year. All growth rates were calculated as previously described.[2] Doubling time could not be used to evaluate changes in tumor volume because not all tumors demonstrated interval growth. Tumor diameter and volume for all lesions at the time of the normal CT were considered 0 cm. Presumed growth was defined as the change in tumor size from the date of normal CT to the date of the CT demonstrating the renal tumor. Two presumed growth rates were calculated to establish a probable range of presumed growth rates, 1 based on tumor growth starting at the

time of normal renal imaging, and 1 based on tumor growth starting halfway between normal renal imaging and renal tumor detection. Presumed growth rate based on tumor growth starting at the time of normal renal imaging was used for all comparisons to observed growth rates. Observed growth was defined as the change in tumor size from the date of the first CT demonstrating a renal tumor to the date of the most recent CT. Observed tumor growth rates were calculated only in patients whose followup after tumor detection was at least 12 months. In these patients serial cross-sectional imaging was performed at 3 to 6-month intervals and tumor size was measured at consistent levels in the kidney by direct comparison to prior studies. All CT including the time zero scan in which the tumor was not identified were reviewed by the treating urologist. Presumed vs observed growth rates were compared in individual patients using matched pairs nonparametric analyses (Wilcoxon signed rank tests). SPSS® version 19 was used to perform the analyses.

RESULTS

We identified 36 patients who met the study inclusion criteria. Table 1 presents patient demographics and radiographic tumor features at the time of the first CT demonstrating renal tumor. The average time between the normal CT and the first CT demonstrating a renal tumor was 40.3 months (median 35, range 14 to 105). Figure 1 provides 2 examples of patients in whom a renal tumor developed following a prior normal radiographic examination. The indications for the initial CT demonstrating the renal tumor are presented in table 1. The majority of patients, 89% (32 of 36), did not have a history of

Table 1. *Patient demographics and radiographic tumor features at presentation*

No. gender (%):	
M	20 (56)
F	16 (44)
Age:	
Av	65
Median	68
Range	44–82
No. indication for CT (%):	
RCC followup	4 (11)
Abdominal pain	11 (31)
Hematuria	4 (11)
Other abdominal disease	17 (47)
Tumor diameter (cm):	
Av	2.3
Median	1.9
Range	1–5
Tumor vol (cm³):	
Av	11.8
Median	3.6
Range	0.52–65
No. radiographic appearance (%):	
Solid	30 (83)
Cystic	6 (17)