Growth characteristics of renal cortical tumors in patients managed by watchful waiting

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Objective: *To characterize tumor growth of patients managed conservatively for renal cell carcinoma.*
Methods: *Patients electing conservative management of radiographically determined renal cell carcinomas were referred to a surveillance database. Exclusion criteria consisted of locally advanced disease (>T2) and those with metastatic disease. Clinical follow-up included renal imaging with ultrasound or computed tomography at least every 6 months.*
Results: *Twenty-two patients were originally managed conservatively, two of whom subsequently underwent nephrectomy because of rapid tumor growth. Mean follow-up was 26 months. Mean tumor volume and diameter at presentation was 62.4 cc and 4.08 cm respectively. Overall tumor growth was 24 cc/year by volume or .86 cm/year diameter.*
Conclusions: *Given the stage migration of incidentally detected renal masses, the natural history of these tumors remains incomplete. Overall tumor growth in selected populations appear to be slow even in those diagnosed with larger masses. These data may be useful in counseling patients and directing further trials on conservative therapy for renal cell carcinoma.*

Key Words: kidney, kidney neoplasms, carcinoma, renal cell, natural history, conservative management, watchful waiting, imaging

Introduction

The presentation of renal cell carcinoma (RCC) by incidental detection has increased from 10% to greater than 60% over the last 30 years, [1,2] resulting in a significant downward stage migration.[3] Autopsy series confirm this frequent occurrence of incidental RCC as well as other renal cortical solid masses.[4-7] The increasing incidence rate of RCC in North America may be significantly influenced by the detection of slow-growing, asymptomatic tumors from imaging for other indications.

Despite the increasing detection of lower stage, presumably highly curative renal masses, the mortality rate from RCC has remained relatively stable.[8] This could be partially explained by a length-time bias from the detection of more indolent tumors. In fact, the largest increase of incidence of RCC is seen with patients in the 7th to 9th decades[9] in which a slow-growing lesion may not affect mortality.

Since the standard management of most renal masses remains immediate surgical extirpation, the contemporary natural history of these lesions remains incomplete. A few recent reports do suggest that the rate of tumor growth of renal masses managed conservatively is minimal (0-1.3 cm per year).[10-13] These investigators report a low chance of metastatic disease in their surveillance period, however, these were mostly very small tumors with a median size at less than 2 cm - 3 cm at initial presentation. The purpose of this study is to report on the growth characteristics of renal masses entered into our surveillance program despite the size of the tumor at presentation.

Methods

Patients with radiologically detected renal masses consistent with renal cell carcinoma based on imaging

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characteristics who elected conservative management were referred to a surveillance database. Although there were no tumor size restrictions, patients were excluded if they were known to have locally invasive disease (renal vein/perinephric tissue) or had metastatic disease on presentation. Clinical follow-up consisted of history and physical examination as well as either abdominal sonography (US) or computerized tomography (CT) at least every 6 months.

A total of 22 patients (15 males, 7 females) were entered into the surveillance database. The median patient age at diagnosis was 77 years (range 60-92). The stated reasons for conservative follow-up were due to co-morbidities in 15 patients, and patient preference for seven patients. Two patients had a remote history of previous nephrectomy for metachronous RCC. The detection of the renal masses was due to incidental imaging in 16 patients, with the remaining six patients presenting with symptoms of hematuria and/or pain. Seven of the patients had some degree of cystic component to the renal mass consistent with Bosniak IV complex cyst. Mean follow-up was 26 months.

Tumor growth rate was based on diameter and tumor volume. Tumor volume was calculated as previously described[11] depending on the available dimensions reported on imaging data. We used the formula to calculate an ellipsoid volume for three dimensions (0.5326xyz), the formula 0.5326xy (x+y/2) when two dimensions were reported and the formula for volume of a sphere $0.5326x^3$, if only one dimension was reported by the radiologist.

The results were summarized by a 2-sided p value and 95% confidence interval. Student's 2-sample t test was used to test the hypothesis that growth rates differed among groups with different tumor characteristics and a Student's 1-sample t test was used to test the hypothesis that the average growth rate was 0.

Results

The mean volume of the 22 renal lesions at diagnosis was 62.4 cc (range 1.8-362.95 cc), and the mean diameter 4.08 cm (range 2-8.8 cm). Figures 1 and 2 illustrate the overall tumor size in diameter and volume for all of the patients in the study. The overall tumor growth in diameter was .86 cm/year (95% CI .2-1.52) and in volume was 24 cc/year (95% CI 4.03-43.97). There was no apparent difference between the growth rate of lesions with cystic components and those without. Patients who had symptoms on presentation appeared to have lesions that grew at a higher rate of 45.03 cc/year (95% CI .13-89.93) than those who were asymptomatic 16.12 cc/year (95% CI -5.26-37.5), although this was not statistically significant (p=0.11).

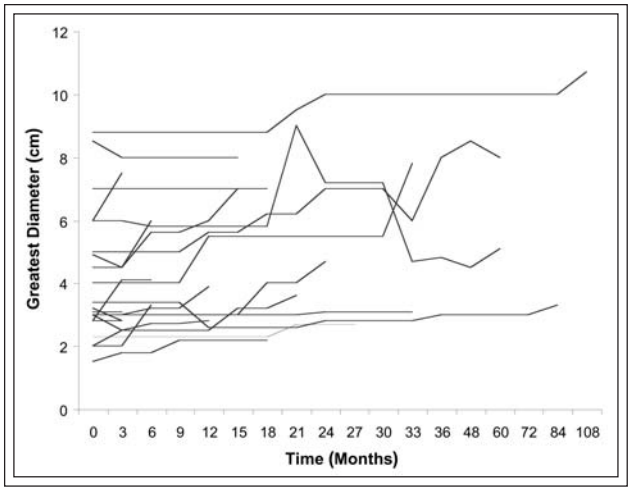

Figure 1. Renal mass growth rate measured by greatest diameter.

There were nine patients who presented with tumors greater than 4 cm in diameter. The overall tumor growth in diameter in this group was 1.43 cm/year and in volume was 57 cc/year. Table 1 illustrates the presenting size of these tumors and their mean growth rates in the study. Patients #1 and 8 appeared to have rapid growth rate but follow-up was only 6 and 1 month respectively. There was no statistically significant difference in growth rates of tumors in this group compared to those <4 cm.

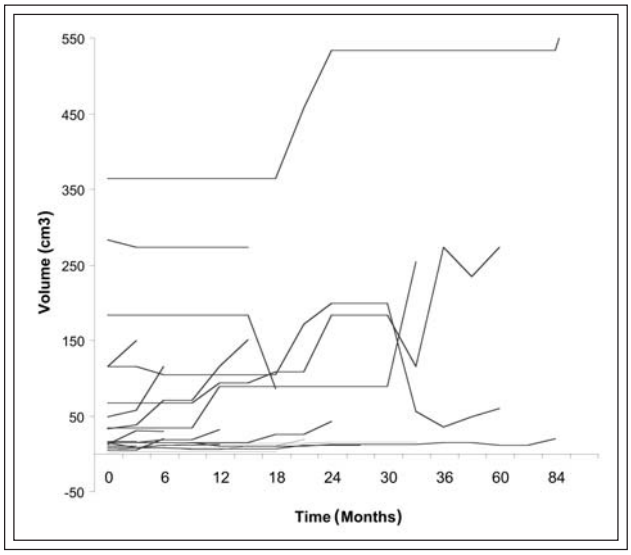

Figure 2. Renal mass growth rate measured by volume.

TABLE 1. **Characterization of renal masses greater than 4 cm in diameter at presentation**

Patient #	Size of renal tumor at diagnosis		Mean tumor growth rate		Follow-up (months)
	Volume (cc)	Diameter (cm)	Volume (cc/year)	Diameter (cm/year)	
1	48.5	4.5	113	3	6
2	66.6	5	41.2	0.6	64
3	34.1	4	79.5	1.4	32
4	282.1	8.5	0	0	14
5	363	8.8	32.2	.2	111
6	115	6	0	0	55
7	32.7	4.9	93.7	1.7	15
8	115	6	134.2	6	1
9	182.7	7	0	0	17

One patient with a tumor <4 cm and patient #8 had nephrectomy due to rapid tumor growth (two patients in total). Both were renal cell carcinoma at pathology. One patient death occurred on follow-up that was unrelated to RCC (patient #4) and one patient developed metastases on follow-up (patient #5). Patient #5 had embolization treatments twice during follow-up because of recurrent hematuria.

Discussion

The increasing incidence of incidentally detected renal masses with a significant downward stage migration raises the possibility of over-treatment of more indolent tumors with a modest natural history. Given the tendency towards early surgical therapy, especially with minimally invasive techniques, the available reports of the natural history of renal masses managed conservatively are limited to small, selected populations with very small tumors at presentation. The possibility that these series include benign masses in their cohort of patients with incidentally detected small renal masses also makes interpretation difficult.[14]

In the largest of the contemporary reports of RCC managed conservatively, Bosniak et al[10] reported on 68 patients with small renal masses and found minimal tumor growth of 0-1.1 cm/year over a mean follow-up of 3.3 years. No patients were reported to have metastatic disease in their surveillance period. However, the mean lesion diameter at presentation was 1.8 cm, and of those subsequently removed, 14% were oncocytomas. Rendon et al[11] prospectively followed 13 patients with solitary renal masses. Median lesion diameter at presentation was 2.95 cm, patients were followed for a median of 3.5 years. They found a growth rate of 0.22 cm/year and no patients developed metastasis. More recently, Kassouf and colleagues[13] reported on the conservative management of 24 patients with small renal masses (median 2.7 cm) and found that only five patients demonstrated any significant tumor growth over the surveillance period.

Despite the larger size of tumors at presentation in this study, the overall renal mass growth rate of 0.86 cm/year was similar to those mentioned above. There was no statistically significant difference in the growth rate of tumors based on their imaging characteristics at presentation although it did appear that those patients that presented with symptomatic lesions grew at a faster rate than asymptomatic, incidentally detected renal masses. These results mirror previous reports suggesting that symptomatic lesions, may be at higher risk for growth and metastases despite the stage at presentation.[15-17] The nine patients in our study with presenting lesions greater than 4 cm did not have a significantly greater growth rate when compared with lesions smaller than 4 cm although one did develop metastatic disease.

Although morbidity from nephrectomy has improved with minimally-invasive techniques, it is still reported in 11% to 40% of cases.[18] The increasing detection of small and potentially indolent renal masses, particularly in the elderly population with other co-morbidities, raises the possibility of a change in the optimal management in selected populations. Our study and those other contemporary reports of the natural history of renal masses managed conservatively, confirm that the growth of small asymptomatic renal masses are minimal within 5 years

of presentation and that metastases appears unlikely without significant tumor growth. These studies may be important in directing further clinical inquiry into the conservative management of RCC. These data should also be considered in judging the efficacy of other minimally invasive ablative therapies, such as radio frequency ablation and cryotherapy, which utilize tumor growth as study endpoints. □

References

1. Konnak JW, Grossman HB. Renal cell carcinoma as an incidental finding. *J Urol* 1985;134:1094-1096.
2. Jayson M, Sanders H. Increased incidence of serendipitously discovered renal cell carcinoma. *Urology* 1998;51:203-205.
3. Luciani LG, Cestari R, Tallarigo C. Incidental renal cell carcinoma-Age and stage characterization and clinical implications: Study of 1092 patients (1982-1997). *Urology* 2000;56:58-62.
4. Hellsten S, Johnsen J, Berge T et al. Clinically unrecognized renal cell carcinoma. Diagnostic and pathological aspects. *Eur Urol, suppl* 1990;18:2-3.
5. Wunderlich H, Schumann S, Janititzky V et al. Increase of renal cell carcinoma incidence in central Europe. *Eur Urol* 1998;33:538-541.
6. Licht MR, Novick AC, Goormastic M. Renal adenoma and oncocytoma. *Semin Urol Oncol* 1995;13:262-266.
7. Bennington JL. Renal adenoma. *World J Urol* 1987;5:66-70.
8. Chow WH, Devesa SS, Warren JL et al. Rising incidence of renal cell cancer in the united states. *JAMA* 1999;281:1628-1631.
9. Katz DL, Zheng T, Holford TR et al. Time trends in the incidence of renal cell carcinoma: analysis of Connecticut tumor registry data, 1935-1989. *Int J Cancer* 1994;58:57-63.
10. Bosniak MA, Krinsky GA, Waisman J. Management of small incidental renal parenchymal tumors by watchful waiting in selected patients based on observations of tumor growth rates. *Proc Am Urol Assoc* 1996;155:584A.
11. Rendon RA, Stanietzky N, Panzarella T et al. The natural history of small renal masses. *J Urol* 2000;164:1143-1147.
12. Oda T, Miyao N, Takahashi A et al. Growth rates of primary and metastatic lesions of renal cell carcinoma. *Int J Urol* 2001;8:473-477.
13. Kassouf W, Aprikian AG, Laplante M et al. Natural history of renal masses followed expectantly. *J Urol* 2004;171:111-113.
14. Dechet CB, Sebo T, Farrow G et al. Prospective analysis of intraoperative frozen needle biopsy of solid renal masses in adults. *J Urol* 1999;162:1282.
15. Curry NS, Bissada NK. Radiologic evaluation of small and indeterminant renal masses. *UNCA* 1997;24:493-509.
16. Sweeney JP, Thornhill JA, Graiger R et al. Incidentally detected renal cell carcinoma: pathological features, survival trends and implications for treatment. *Br J Urol* 1996;78:351.
17. Pantuck AJ, Zisman A, Belldegrun AS. The changing natural history of renal cell carcinoma. *J Urol* 2001;166:1611-1623.
18. Lee CT, Katz J, Shi W et al. Surgical management of renal tumors 4 cm or less in a contemporary cohort. *J Urol* 2000;163:730-736.