Original Article

Pathological nature of renal tumors - does size matter?

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Abstract

Introduction: We examined the relationship between the size and nature of renal masses in term of malignant potential, histological grading, pathological staging and presence of necrosis and sarcomatoid changes.

Materials and Methods: Retrospectively, we reviewed 323 consecutive nephrectomies between 2000 and 2010. Final pathology was correlated with tumour size. The renal tumours were stratified into three groups according to the largest diameter, defined as 4 cm or smaller, greater than 4 cm to 7 cm, and greater than 7 cm. We recorded the proportion of benign tumours, tumour grade and stage, presence of necrosis and sarcomatoid change.

Results: Small renal masses ≤4 cm (SRMs) were more likely to be localised to the kidney (90%) and of lower histological grade (75%). The proportion of benign tumours in SRMs (15%) was higher than other two groups with the majority of benign tumours being oncocytomas. There was a statistically significant trend with greater necrosis and sarcomatoid change for the large size group.

Conclusions: SRMs are likely to be low grade and organ confined with little or no adverse pathological features. There is increased likelihood of benignity in SRTs with the majority of benign tumours being oncocytomas.

Keywords: Carcinoma, histology, kidney, neoplasm staging, nephrectomy, prognosis, renal cell, risk

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INTRODUCTION

Modern imaging techniques have resulted in a dramatic change in the clinical landscape of renal tumors, with a significantly higher number of small lesions being detected in asymptomatic patients.[1]

Treatment decision-making for small renal masses (≤4 cm) (SRMs) is an increasingly frequent and challenging clinical problem, especially in elderly and unfit patients. There are wider options of treatment now available, which includes minimally invasive ablation therapies, nephrectomy, and potentially active surveillance where nonmalignant mortality outweighs the risk of SRM, and this should be critically assessed.

The decision of the best treatment modality is usually based on clinical judgment of comorbidities and tumor

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characteristics. Currently, tumor stage, nuclear grade, and histological subtype are thought to be the most important prognostic factors in renal tumors.[2] Recently, percutaneous biopsies have been increasingly used to clarify the histology of renal tumors to aid with treatment decisions for SRMs.[3,4] However, biopsies of SRMs are nondiagnostic in up to 20% of cases, and they underestimate tumor grades in about 55% of cases.[5]

Radiological size is an essential element for clinical staging and has been shown to have prognostic implications independent from other histopathological features.[6] Although previous studies have demonstrated that risk of high-grade tumors increased with tumor size, Hsu *et al.* reported that smaller tumors (<3 cm) showed high prevalence of high nuclear grade and tumor extension beyond the renal capsule, with no difference in comparison with larger tumors (3–5 cm).[7]

To clarify these issues and provide more evidence for preoperative prediction and decision-making, we conducted this study by examining a consecutive series of renal masses resected in our institution. The aim of our study was to examine the relationship between the radiological size and the pathological nature of solid renal tumors in terms of malignant potential, histological grading, pathological staging, and the presence of necrosis and sarcomatoid changes.

MATERIALS AND METHODS

The records of 323 consecutive patients who underwent radical nephrectomy or partial nephrectomy for primary solid renal tumors in our institution between 2000 and 2010, were retrospectively reviewed. All patients had preoperative contrast-enhanced computed tomography (CT) examination of their kidneys for diagnostic and staging purposes.

The pathology and radiology reports were reviewed from our pathology database and radiology information system, respectively. To ensure completeness of data collection and minimize attrition bias, additional data sources were utilized and compared with available data from the pathology and radiology databases, including operating theater log books and multidisciplinary meeting records. We recorded the patient's demographics, radiological tumor size, and histological subtype (2004 WHO classification system).[8] For malignant tumors, we recorded the histological grade using Fuhrman classification system,[9] tumor stage, presence of necrosis and sarcomatoid change. The tumor stage was reassessed according to the 2009 updated TNM classification system,[10] and grade was assessed according to the classification of Thoenes *et al.*[11]

The radiological size of tumor was taken as the largest axial dimension on CT examination on abdominal windows. For patients with multiple tumors on radiological imaging, only the largest tumor was evaluated. For those who had solitary tumors on radiological imaging but multiple satellite lesions at the pathological examination, only the tumor seen on CT was evaluated. Histological tumor size is generally smaller than radiological tumor size due to the absence of perfusion and some shrinkage of the kidney. For the treatment decision, only radiological and not pathological tumor size was available, and therefore, we selected this parameter for stratification.

The renal tumors were stratified into three groups according to the largest diameter as measured by preoperative contrast-enhanced CT, defined as ≤4 cm (small size group [SRMs]); 4–7 cm (medium size group); and >7 cm (large size group). The final pathology results of the nephrectomies were collected and correlated with the radiological size of the tumor. The three groups were compared with regard to the proportion of benign tumors to malignant tumors. The malignant tumors in the three groups were compared regarding histological grade, pathological stage, and the presence of necrosis or sarcomatoid changes.

The outcome variables were binary for the following parameters: benign versus malignant, <pT3a versus ≥pT3a for pathological staging, and yes versus no for sarcomatoid change. For necrosis, three outcome categories were used, namely, no necrosis, some necrosis, or extensive necrosis. For histological grading, patients were stratified according to the conventional four-tiered Fuhrman grading system. Tumors with Grade 1 or 2 were regarded as low-grade tumors, and tumors with Grade 3 or 4 were classified as high-grade tumors. The cases where Fuhrman grading was not applicable or not reported were excluded from the analysis. Statistical analysis was performed using the Chi-squared test for trend with $P < 0.05$ considered statistically significant.

RESULTS

A total of 323 renal masses were identified in 323 patients. The mean patient age was 62.2 years (range: 29–88) with a male to female ratio of 3:2. Of the 323 renal masses, 23 (7%) were benign, including 12 oncocytomas, 4 angiomyolipomas (AML), 2 xanthogranulomatous pyelonephritis, 1 carcinoid, and 4 classified as "others." This group of "others" includes renal lesions with nonspecific pathological changes of inflammation and/or scarring. There were 300 malignancies, the vast majority of

which were clear cell carcinoma (88%). Details regarding demographics and pathological subtypes of benign and malignant tumors are shown in Table 1.

Table 2 provides the distribution of benign and malignant tumors by tumor size group.

The small size group (≤4 cm) consisted of 91 lesions, 14 of which were benign (15%). About 71% of these benign tumors were oncocytomas. Nearly, 75% (58/77) of the malignant lesions were low grade (Fuhrman grade 1 or 2) and 90% (69/77) were confined to the kidney (pT1a). Only 10% (8/77) of the malignant lesions showed evidence of necrosis, and none showed sarcomatoid change.

There were 121 lesions in the medium size group (4–7 cm) with only 4 lesions being benign (3%). Nearly, 68% (80/117) of the malignant lesions were Grade 1 or 2, and 67% (79/117) were confined to the kidney. About 23% (27/117) of lesions showed evidence of necrosis, and 4% (5/117) showed sarcomatoid change.

The large size group (>7 cm) had 111 lesions that were larger than 7 cm, of which only 4% (5/111) were benign. About 51% (54/106) of the malignant lesions were high grade (Fuhrman Grade III or IV), and 67% (71/106) were extracapsular (≥pT3a). Nearly, 48% (51/106) of lesions in this group showed evidence of necrosis, and 16% (17/106) showed sarcomatoid change. The relationship between radiological size with Fuhrman grade, pathological stage, and the presence of necrosis and sarcomatoid change is summarized in Tables 3 and 4.

Statistical analyses using the Chi-squared test for trend showed statistically significant trends between the three groups regarding the proportion of benign lesions ($P = 0.004$), histological grade, pathological stage, presence of necrosis and sarcomatoid change (all $P < 0.001$).

Table 1: Demographic information of all patients and tumors

	Number of patients/tumors (%)
Total number of patients	323
Male	195 (60)
Female	128 (40)
Age of patients, range (mean)	29-88 (62.2)
Benign	
Oncocytoma	12 (52.1)
Angiomyolipoma	4 (17.4)
Xanthogranulomatous pyelonephritis	2 (4.4)
Carcinoid	1 (8.7)
Others	4 (17.4)
Malignant	
Clear cell carcinoma	264 (88)
Papillary	24 (8)
Chromophobe	9 (3)
Others/unclassified	3 (1)

Table 2: Summary of the proportion of benign to malignant tumors according to size for the three groups

Groups	Benign (%)	Malignant (%)	Total (%)
≤4 cm	14 (15.4)	77 (84.6)	91 (28)
4-7 cm	4 (3.3)	117 (96.7)	121 (38)
>7 cm	5 (4.5)	106 (95.5)	111 (34)
Total	23 (7.1)	300 (92.9)	323 (100)

$P=0.004$ (Chi-squared test for trend)

Table 3: The distribution of Fuhrman tumor grading and tumor node metastasis staging

Groups	Tumor grade		Tumor stage		Total (%)
	1-2 (%)	3-4 (%)	<T3a (%)	≥T3a (%)	
≤4 cm	58 (75)	19 (25)	69 (90)	8 (10)	77 (100)
4-7 cm	80 (68)	37 (32)	79 (67)	38 (33)	117 (100)
>7 cm	52 (49)	54 (51)	35 (32)	71 (67)	106 (100)

$P<0.001$ (Chi-squared test for trend)

Table 4: Summary of the presence of tumor necrosis and sarcomatoid change

Groups	Tumor necrosis		Sarcomatoid change		Total (%)
	Yes (%)	No (%)	Yes (%)	No (%)	
≤4 cm	8 (10)	69 (90)	0 (0)	77 (100)	77 (100)
4-7 cm	27 (23)	90 (77)	5 (4)	112 (96)	117 (100)
>7 cm	51 (48)	55 (52)	17 (16)	89 (84)	106 (100)

$P<0.001$ (Chi-squared test for trend)

DISCUSSION

The clinical decision for treating renal cancer is best based on combination of patient condition, treatment availability, and tumor characteristics.[12] Currently, tumor stage, nuclear grade, and pathologic subtype are thought to be the most important prognostic factors.[13] There is currently no diagnostic test available that enables accurate prediction of biological behavior of renal tumors. In this series, we studied the relation of tumor size to its malignant potential. This may have an important implication in optimizing treatment decision-making.

There was a statistically significant trend that the SRMs were more likely to be localized to the kidney and lower grade compared with the medium and large size groups ($P < 0.001$). We found that 75% of the malignant SRMs were of low grade, and 90% were localized to the kidney (T1a). The proportion of patients with pT1a disease is comparable to previous studies.[14,15] However, Pahernik *et al.* and Rothman *et al.* reported a rate of 86% and 85% for low-grade disease in their cohort of SRMs, respectively, which is slightly higher than our figures.[16,17] However, of note is that Rothman *et al.* only included patients with localized renal cancer which could explain their higher rate of low-grade disease. Our results confirm previous

observations suggesting that the risks of malignancy and higher grade tumors increase as renal tumor size increases. The tables presented can be useful during the initial consultation with patients with a renal mass including patient counseling regarding surgical treatment options (partial versus radical nephrectomy).

In our study, there was a statistically significant trend with regard to the presence of necrosis and sarcomatoid change. Schlomer *et al.* similarly reported that sarcomatoid changes were seen more often in larger tumors.[18] Sarcomatoid change and tumor necrosis both have been shown to be independent prognostic factors for renal cancer.[19]

The proportion of benign tumors in SRMs was higher than the other groups at 15% ($P = 0.004$).

This figure is comparable to those previously reported in the literature which ranged from 17% to 23%.[14-16] Biopsy of SRMs is increasing particularly following recent reports of increased incidence of benign disease. However, we demonstrated that the vast majority of benign tumors were oncocytomas (71%) which is comparable to the large series by Frank *et al.*[14] Oncocytomas are generally regarded as benign tumors, and the standard treatment of oncocytomas is still surgery. There are several reasons for this policy. First, definitive preoperative histological diagnosis of oncocytoma is difficult. Second, oncocytomas and renal cancer may coexist within the same tumor (i.e., "hybrid tumors"), which may raise sampling issues even if benign oncocytoma is found on biopsy.[19] Finally, its natural history is unknown, and metastases from oncocytomas have been described in the literature.[20] Therefore, preoperative diagnosis of a renal oncocytoma in a fit patient usually does not change clinical decision as these tumors need to be surgically removed.

The other benign tumors that we found in our cohort were AML, adenoma, or inflammatory masses/scarring. AML usually contains macroscopic fat, and the diagnosis can usually be made radiologically. However, lipid-poor AML contains little or no fat and is therefore more difficult to diagnose radiologically. However, some lipid-poor AMLs demonstrate some imaging features that may suggest its diagnosis on CT, and in such circumstances, magnetic resonance imaging and/or biopsy may help to make a diagnosis.[21]

Biopsy of SRMs may be useful in selecting patients in whom avoidance of surgical management is being contemplated, such as those with high surgical risks. For instance, the finding of an oncocytoma or low-grade renal tumor on needle biopsy may help to make a clinical decision of active surveillance or minimally invasive ablation therapy in such patients. Biopsy is also indicated if imaging is suggestive of a benign entity. In this setting, if biopsy confirms the presence of benign lesion, surgery could be potentially avoided.

Several limitations of this study merit discussion. Our data represent a retrospective study from a single center. More importantly, we defined our study population as patients with renal tumors treated with resection. This criterion excludes most patients with metastatic disease and patients unwilling to undergo or unsuitable for surgery and those treated with percutaneous ablation. Furthermore, histological diagnosis and grading were not obtained from a single pathologist, which may be associated with different grading parameters, thereby introducing heterogeneity. However, our results are comparable to those surgical series in which a single pathologist was used.[22] Finally, our tumor size criteria were based on CT measurement, which may not be equivalent to pathological size.

CONCLUSIONS

The size of renal tumors remains the only noninvasive preoperative prognostic parameter available. In our cohort, we demonstrated that SRMs are likely to be low grade and organ confined. Although oncocytomas are generally regarded as "benign", they have unknown natural history and normally treated surgically. Recently, there has been a new trend of biopsing most SRMs due to previous similar reports of increased incidence of benign disease. However, based on our data, biopsy may have a role in selected patients in whom the results may change the therapeutic approach such as in patients with comorbidities or when a benign etiology is suspected on imaging.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. 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.
2. Sun M, Shariat SF, Cheng C, Ficarra V, Murai M, Oudard S, *et al.* Prognostic factors and predictive models in renal cell carcinoma: A contemporary review. European Urology 2011;60:644-61.
3. Wang R, Li AY, Wood DP Jr. The role of percutaneous renal biopsy in the management of small renal masses. Curr Urol Rep 2011;12:18-23.
4. Somani BK, Nabi G. Incidental renal tumours: the frequency of benign lesions and the role of pre-opertative core biopsy. BJU internaltional 2006;97:946-9.

5. Blumenfeld AJ, Guru K, Fuchs GJ, Kim HL. Percutaneous biopsy of renal cell carcinoma underestimates nuclear grade. Urology 2010;76:610-3.
6. Remzi M, Katzenbeisser D, Waldert M, Klingler HC, Susani M, Memarsadeghi M, *et al*. Renal tumor size measured radiologically before surgery is an unreliable variable for predicting histopathological features: Benign tumours are not necessarily small. BJU Int 2007;99:1002.
7. Hsu RM, Chan DY, Siegelman SS. Small renal cell carcinomas: correlation of size with tumor stage, nuclear grade, and histologic subtype. AJR Am J Roentgenol 2004;182:551-7.
8. Lopez-Beltran A, Scarpelli M, Montironi R, Kirkali Z. 2004 WHO classification of the renal tumours of adults. Eur Urol 2006;49:798.
9. Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. Am J Surg Pathol 1982;6:655-63.
10. Sobin LH, Gospodarowicz MK, Wittekind C, editors. TNM Classification of Malignant Tumours. 7th ed. Chichester, UK: Wiley-Blackwell; 2009.
11. Thoenes W, Storkel S and Rumpelt HJ. Histopathology and classification of renal cell tumours (adenomas, oncocytomas and carcinomas). The basic cytological and histopathological elements and their use for diagnostics. Pathol Res Pract 1986;181:125.
12. Levinson AW, Su LM, Agarwal D, Sroka M, Jarrett TW, Kavoussi LR, *et al*. Long-term oncological and overall outcomes of percutaneous radio frequency ablation in high risk surgical patients with a solitary small renal mass. J Urol 2008 ;180:499-504.
13. Moch H, Gasser T, Amin MB, Torhorst J, Sauter G, Mihatsch MJ. Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma: A Swiss experience with 588 tumours. Cancer 2000; 89:604-14.
14. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumours: an analysis of pathological features related to tumor size. J Urol 2003;170:2217-20.
15. Zhang C, Li X, Hao H, Yu W, He Z, Zhou L. The correlation between size of renal cell carcinoma and its histopathological characteristics: A single center study of 1867 renal cell carcinoma cases. BJU Int 2012;110:E481-5.
16. Pahernik S, Ziegler S, Roos F, Melchior SW, Thüroff JW. Small renal tumours: correlation of clinical and pathological features with tumor size. J Urol. 2007;178:414-7.
17. Rothman J, Egleston B, Wong YN, Iffrig K, Lebovitch S, Uzzo RG. Histopathological characteristics of localized renal cell carcinoma correlate with tumor size: A SEER analysis. J Urol 2009;181:29-33.
18. Schlomer B, Figenshau RS, Yan Y, Venkatesh R, Bhayani SB. Pathological features of renal neoplasms classified by size and symptomatology. J Urol. 2006;176(4 Pt 1):1317-20.
19. Petersson F, Gatalica Z, Grossmann P, Perez Montiel MD, Alvarado Cabrero I, Bulimbasic S, *et al*. Sporadic hybrid oncocytic/chromophobe tumor of the kidney: A clinicopathologic, histomorphologic, immunohistochemical, ultrastructural, and molecular cytogenetic study of 14 cases. Virchows Arch 2010;456:355-65.
20. Amin R, Anthony P. Metastatic renal oncocytoma: A case report and review of the literature. Clin Oncol (R Coll Radiol) 1999;11:277-9.
21. Silverman SG, Israel GM, Herts BR, Richie JP. Management of the incidental renal mass. Radiology 2008;249:16-31.
22. Yaycioglu O, Rutman MP, Balasubramaniam M, Peters KM, Gonzalez JA. Clinical and pathologic tumor size in renal cell carcinoma; difference, correlation, and analysis of the influencing factors. Urology 2002;60:33-8.