Renal tumour size measured radiologically before surgery is an unreliable variable for predicting histopathological features: benign tumours are not necessarily small

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OBJECTIVE

To compare histopathological findings as a function of radiological tumour size, as published data suggest that small renal tumours are often benign and large tumours are renal cell cancer (RCC).

RESULTS

In all, 80 lesions (14.7%) were benign on final histology; tumour size did not correlate with benign histology ($P = 0.660$). Histopathological tumour size was not statistically significantly different ($P = 0.521$) from measured tumour size on CT, and there was no statistical significance between CT and histopathological tumour size ($P = 0.528$). Only 13 (17%) of lesions were correctly defined as benign on CT before surgery, whereas 67 (83%) were considered to be suspicious for malignant disease. Only one patient with a tumour correctly defined as benign had a radical nephrectomy; by contrast, 28 of 67 (42%) had a radical nephrectomy for benign lesions not correctly identified as benign on CT before surgery ($P < 0.001$).

CONCLUSION

Substantially many renal masses are benign, independent of tumour size. Radical nephrectomy could potentially have been avoided in 42% of patients with benign renal tumours. These data provide a good argument for the use of a more refined preoperative diagnostic evaluation, in particular needle biopsy.

KEYWORDS

angiomyolipoma, Fuhrman classification, oncocytomas, renal cell cancer, small renal masses

INTRODUCTION

In large series of solid renal masses, the incidence of benign lesions was 12.8% [1] to 16.9% [2]. There has been a greater incidence of all stages of RCC, with the greatest increase in patients with localized tumours, probably caused by stage migration as a result of earlier detection [3]. However, significantly many of these lesions are actually benign tumours, especially oncocytomas and angiomyolipomas with low fat content, which remain difficult to differentiate from RCC, even when the most advanced cross-sectional imaging techniques are used [4]. The increase in incidentally detected small renal tumours has led to an increase in the incidence of benign renal masses and probably to an associated increase in the number of unnecessary surgical interventions for benign renal tumours.

Tumour size was therefore retrospectively correlated with histopathological features in renal tumours removed surgically over a 10-year period. The relationship between tumour diameter, as measured before surgery by helical CT on two-dimensional imaging, was correlated with histopathological features of the tumours.

PATIENTS AND METHODS

Data of all patients who had solid renal tumours at diagnosis, and that were removed surgically between September 1994 and December 2004 at our institution, were analysed retrospectively. Only patients with complete pathological and radiological documentation were included in the study. Patients with known hereditary disease like Von Hippel-Lindau and tuberous sclerosis were excluded. All histopathological specimens were reviewed by the same pathology team (supervised by M.S.) and were classified using the Heidelberg system [5].

Papillary adenoma was defined as a low-grade papillary tumour of <5 mm in greatest diameter, and larger lesions were defined as papillary RCC [6]. Oncocytoma was defined as a benign renal epithelial neoplasm, consisting of oncocytes with a granular eosinophilic cytoplasm and round and regular nuclei. Classic angiomyolipomas were defined as composed of mature fat cells, abnormal vascular tissue and smooth muscle.

The following clinical, CT and histopathological data were collected from the case files: surgery date and type of operation; age of patient; site, location and size of the tumour as determined by preoperative CT; histological type and


PREOPERATIVE HELICAL CT.

The mean tumour size was 61.2 (15.0) years; 46% were male and in 48% of left kidneys. Overall, RCC was found in 463 tumours (85.3%); the rate of RCC was significantly higher in tumours of ≤4 cm (254, 88.2%) than those ≤4 cm (209, 81.9%; P = 0.028). With larger tumours, advanced stages (pT3a) and higher grade (G3/G4) were significantly more common (P < 0.001). RCCs were detected in 62.9% of men and in 48% of left kidneys. In all, 80 tumours were confirmed as benign (Table 1); the distribution of RCC and benign lesions according to tumour size is shown in Fig. 1a. The mean patient age in this group was 61.2 (15.0) years; 46% were male and in 46% the lesions were on the left side.

Overall, benign lesions, at 4.7 (3.4) cm, were significantly smaller than RCC lesions, at 5.2 (2.7) cm (P = 0.011). The median (range) tumour diameter was 3.8 (1.4–16) cm.

The distribution of benign lesions stratified by radiological tumour size is shown in Fig. 1b. In tumours of ≤4 cm the incidence of benign lesions was 30%, 22% and 19.9% in tumours of 0–2, 2–3 and 3–4 cm (P = 0.660). In tumours of >4 cm the incidence of benign lesions was 18.3%, 6.5%, 11.4% and 14.3% for tumours of 4–5, 5–6, 6–7 and >7 cm (P = 0.125), respectively. In larger tumours (>4 cm) the incidence (10%) of benign lesions was significantly lower than in smaller renal tumours (≤4 cm; 20%; P = 0.005).

Although there was a trend towards histopathological tumour size being less than tumour size measured before surgery by CT, the differences were not statistically significant (P = 0.521; Table 2).

According to the preoperative helical CT report, only 13 (17%) of the benign tumours were correctly defined as benign lesions, with the remainder identified as suspected malignant tumours. The mean tumour diameter of tumours correctly defined as benign was 5.65 (2.1) cm. The histology of the correctly identified benign lesions was angiomylipoma in 10, leiomyoma in one and oncocytoma in two.

Benign lesions incorrectly defined as RCC (83%) on preoperative CT had a mean size of 3.9 (2.0) cm, which was not significantly different from those correctly defined as benign (P = 0.235). Histologically these were oncocytoma in 34, angiomylipoma in 18, leiomyoma in four and adenoma in four.

Only one patient with a correctly identified benign lesion (central oncocytoma of 5.2 cm) had a radical nephrectomy. By contrast, 28 of 67 patients (42%) with benign lesions incorrectly identified as malignant by CT had a radical nephrectomy.

According to CT diameter, 34 benign lesions were ≥4 cm; the remaining 46 were ≤4 cm. The mean tumour size for small benign lesions (≤4 cm) and larger benign lesions (>4 cm) was 2.8 (0.82) and 6.6 (2.4) cm, respectively. The benign lesions had no correlation with lesion diameter (P = 0.660).
DISCUSSION

There are recent reports on the expectant, conservative management of small renal masses in high-risk surgical candidates. This might reflect the large proportion of small renal masses that are found to be benign or low-grade RCCs [9,10], as a histopathological diagnosis is usually not available. There is a general view that small renal masses might be benign and larger renal masses are RCC. Frank et al. [1] reported retrospectively that 30%, 22% and 19.9% of renal lesions of <2, <3 and <4 cm were benign. However, even with large renal masses, a substantial proportion has been shown to be of benign histology [1,10]. If benign lesions could be accurately identified before surgery this could alter the surgical approach to these lesions, as NSS is the goal even for larger tumours.

Based on the present findings, tumour size alone does not provide adequate information for deciding the optimum surgical treatment. Although the percentage of benign renal tumours was significantly less in tumours of >4 cm than ≤4 cm, the proportion of benign lesions was significant in both groups (10% and 20%, respectively). We found that 17.5% of the benign lesions were >7 cm. The distribution of benign lesion had the same percentage in tumours of ≤4 cm and >7 cm (Fig. 1b), although the percentage of RCC increased with tumour size (Fig. 1a).

As well documented elsewhere [11], and underlined by this contemporary series, helical CT is not able to differentiate RCC from benign lesions with adequate accuracy. In the present series, only 17% of all benign lesions were correctly identified as benign on preoperative CT; most of these were angiomyolipomas (77%). Most angiomyolipomas contain sufficient fat [11] to be diagnosed as such, but ≈5% of angiomyolipomas have minimal or no fat and are therefore misdiagnosed on CT [12]. Tuncali et al. [13] reported that 30% of benign lesions referred for percutaneous ablative treatment were low fat angiomyolipomas.

Although radical nephrectomy is still considered a standard procedure for treating RCC, recent studies show that in tumours of ≤4 cm in diameter, NSS yields oncologically comparable results, with low morbidity, excellent disease-free survival rates of 89–98%, and low local recurrence rates of 0–7.3% [14–17]. Thus, NSS has become the standard treatment for these lesions [14–17]. However, recent reports suggest that NSS is underused for even small (≤4 cm) renal masses, i.e. in the USA for <20% [18] and in England for <4% [19]. In the present series 57% of tumours of ≤4 cm were treated by NSS. Although there was no statistical difference in tumour size between those correctly and incorrectly defined as benign on CT, one of 13 and 28 of 67 (43%) of the present patients were treated by an unnecessary radical nephrectomy, respectively. In the series of Frank et al. [1] 65% (244/376) of benign lesions were treated by radical nephrectomy. If NSS is suggested for RCC up to 7 cm in diameter [20] the decision for it seems imperative for benign tumours, especially as radical nephrectomy is a significant risk factor for developing chronic kidney disease [21].

If about half of all patients harbouring a benign renal tumour lose otherwise oncologically beneficial renal parenchyma with no oncological benefit, it is strongly arguable that it is time to re-evaluate the treatment policy. Moreover, more reliable evaluation of lesions before therapy appears to be even
more important with the advent of less-invasive treatments for tumours of ≥3 cm, such as ablation with radiofrequency [22], high-intensity focused ultrasound [23] and cryotherapy [24]. Tuncali et al. [25] reported that a substantial number of tumours (10 of 27, 37%) referred for radiofrequency ablation (mean tumour size 2.2 cm) were benign. The ongoing discussion about expectant ‘watchful waiting’ management in comorbid patients assessed as poor candidates for surgery further underlines the need for better identification of low-risk tumours [26]. The most promising option is image-guided biopsy. Neuzillet et al. [27] showed that CT-guided fine-needle percutaneous biopsy had an accuracy of 92% and 70% for defining histological tumour type and Fuhrman grade, respectively, with no substantial morbidity. They showed that in nearly half of patients a radical nephrectomy could have been avoided in 42% of patients with benign tumours: an analysis of pathological findings at the time of nephrectomy for renal mass. Ann Surg Oncol 1997; 4: 570–4


Remzi M, Özyoz M, Klingler HC et al. Are small renal tumours harmless? Analysis of histopathological features according to tumour size in tumours 4 cm or less in diameter. J Urol 2006; 176: 896–9


Lee CT, Katz J, Shi W, Thaler HT, Reuter VE, Russo P. Surgical management of renal tumour 4 cm or less in a

TABLE 2 Comparison of tumour size measured on helical CT vs histopathological tumour size for benign lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No. of lesions</th>
<th>CT size, cm</th>
<th>Histological size, cm</th>
<th>Difference*, cm</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncocytoma</td>
<td>36</td>
<td>4.1 (2)</td>
<td>3.8 (2.2)</td>
<td>+0.1 (1.2)</td>
<td>0.547</td>
</tr>
<tr>
<td>Angiomyolipoma</td>
<td>28</td>
<td>3.7 (1.5–10)</td>
<td>3.1 (1.4–11.5)</td>
<td>+0.2 (5–5.5, +2.3)</td>
<td></td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>5</td>
<td>5.4 (4.9)</td>
<td>5.3 (5.3)</td>
<td>+0.12 (1.2)</td>
<td>0.944</td>
</tr>
<tr>
<td>Adenomatoid</td>
<td>4</td>
<td>2.2 (0.2)</td>
<td>2.1 (0.7)</td>
<td>−0.7 (0.98)</td>
<td>0.345</td>
</tr>
<tr>
<td>Others†</td>
<td>7</td>
<td>0.3 (0.2)</td>
<td>0.3 (0.1–0.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Defined as (CT tumour size – histological tumour size). †see Table 1.
20 Leibovich BC, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Nephron sparing surgery for appropriately selected renal cell carcinoma between 4 and 7 cm results in outcome similar to radical nephrectomy. J Urol 2004; 171: 1066–70
22 Klingler HC, Mauermann J, Remzi M, Susani M, Memarsadeghi M, Marberger M. ‘Skipping’ is still a common problem with radiofrequency ablation of small renal tumours. BJU Int 2007; in press

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Abbreviations: NSS, nephron-sparing surgery.