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Ultrasound-Guided Biopsy of Homogenous Solid Renal Masses

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Abstract

Objectives: We evaluated the reliability of sonographic criteria in selecting solid renal masses for percutaneous fine-needle biopsy.
Methods: In study 1 (intraoperative ultrasound study), we prospectively examined 100 consecutive patients scheduled for partial/radical nephrectomy by using two different high-resolution probes (Philips HDI 5000, CT8-4, L12-5; 4–12 MHz). The main tumor was intraoperatively evaluated by B-mode and power Doppler sonography. Morphologic characteristics seen on ultrasound were categorized in (non-)homogenous and (non-)cystic renal masses and were related to findings of pathological examination. Study 1 provided the selection criteria for study 2.

In study 2 (percutaneous biopsy study), under local anesthesia and with the use of an 18-G needle, we prospectively performed two to three sonographically guided percutaneous biopsies in 30 consecutive patients whose tumors appeared to be homogenous and noncystic according to the sonograph (convex array 3.5 MHz, HDI 5000, C5-2 and Falcon 2101 EXL, B+K Medical).
Results: In the ultrasound study, only 16 (22.9%) of the 76 clear-cell carcinomas but all 9 (100%) oncocytoma appeared homogenous and noncystic on high-resolution intraoperative ultrasound.

By applying these results to 30 patients of study 2 (18 men, 12 women; aged 63 ± 7.7 yr, tumor size 29 ± 11.3 mm) who met these sonographic criteria on preoperative transabdominal ultrasound, we bioptically diagnosed 8 (26.7%) benign tumors; 25 of 30 (83.3%) patients were accurately diagnosed. Small tumors (<3 cm), decreased breathing compliance, and medially located renal lesions seem to negatively influence biopsy results.
Conclusions: Kidney tumors that appear noncystic and homogenous on preoperative ultrasound are more likely to be of benign origin.

Ultrasound-guided percutaneous biopsy of these solid renal masses could determine renal tumor patients for whom surveillance might be an option. However, experienced and dedicated histopathologic evaluation remains crucial to observe patients with clearly benign biopsy results. All even slightly questionable biopsy findings require surgical exploration.

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1. Introduction

As urologists we are aware of a rather contradictory development of tumor biopsies. Because of the lack or availability of reliable imaging modalities, prostate biopsies are extensively performed, whereas renal tumor biopsies are fairly uncommon. However, ultrasound, computed tomography (CT), and magnetic resonance imaging provide only limited information on whether a renal mass is of benign or malignant origin, which rarely but regularly leads to unnecessary surgical procedures.

Recently, renal tumor biopsy was reported to result in high accuracy rates for histopathologic evaluation of renal masses [1–4]. However, the incidence of benign renal lesions is known to be low. Consequently, many biopsies will find only a few benign tumors. To address this problem, we studied the sonographic appearances of renal tumors: From gross pathology it has been known for years that necrosis, hemorrhage, and cysts are common in renal cell carcinoma but almost always absent in oncocytoma [5]. Particularly on B-mode ultrasound, these characteristics are likely to produce distinctive differences in the form of (non-)cystic or (non-)homogenous tumor regions, possibly leading to patient selection for biopsy according to ultrasound criteria.

In this study we evaluated the application of sonomorphologic criteria of renal masses for tumor biopsy.

2. Methods

For ultrasound studies, detail resolution can be improved by increasing the frequency and using linear instead of convex arrays but at the expense of imaging depth. Consequently, we performed all ultrasound scans intraoperatively.

In study 1 (intraoperative ultrasound study), we prospectively examined 100 consecutive patients scheduled for partial/radical nephrectomy by using two different intraoperative high-resolution probes (Philips HDI 5000, CT8-4, L12-5; 4–12 MHz, compound imaging). The main tumor was intraoperatively evaluated by B-mode and power Doppler sonography (hypo-, iso-, or hypervascularized). Morphologic characteristics seen on ultrasound were categorized in (non-)homogenous and (non-)cystic renal masses, and were related to findings of pathologic examination. Study 1 provided the selection criteria for study 2.

In study 2 (percutaneous biopsy study), under local anesthesia and with the use of an 18-G needle, we prospectively performed two to three ultrasound-guided percutaneous biopsies in 30 consecutive patients whose tumors appeared to be homogenous and noncystic according to the sonograph (convex array 3.5 MHz, HDI 5000, C5-2 and Falcon 2101 EXL; B+K Medical; biopty gun PRO-MAG ULTRA; MiroMed).

Bleeding risks identified by clinical and laboratory tests were contraindications for this study. The percutaneous biopsy was targeted within the peripheral tumor area allowing a 1.7×0.1 cm specimen to be obtained (Biopty-Gun Pro-Mag Ultra). Renal ultrasound was repeated to exclude hematoma 2 h and 3 d after the procedure, respectively.

Histopathologic evaluation of the biopsy cores was performed after hematoxylin-eosin staining by one pathologist. Subclassification of renal epithelial neoplasm was based on the 2004 World Health Organization consensus classification guidelines. We routinely used standard hematoxylin-eosin stain for basic histopatholgy. Histochemical techniques included Hale and PAS staining. In difficult or inconclusive cases immunohistochemistry was applied. These included vimentin, cytokeratin 7 (CK7), and Ki-67 antigen tests.

Parameters studied were patient age, gender, tumor size and location, and histopathology. All patients showing malignant or inconclusive findings after biopsy underwent partial/radical nephrectomy. Nephron-sparing procedures were performed depending on tumor size, location, and intraoperative evaluation. Final histopathologic analysis was compared with biopsy results.

Informed consent was obtained from all patients included in both studies, which had been approved by the local ethics committee.

3. Results

In study 1, of the 100 patients examined, 54% were male and mean patient age was 62.3 ± 9.8 yr (range: 37.5–84.1). Of the tumors, 53% were localized in the left side of the kidney.

Mean tumor size was 4.9 ± 2.7 cm (range: 0.11–13.2). Intraoperatively, in two cases no tumor could be detected (CT false positive). Histopathologic examination of the remaining 98 patients revealed 76 clear-cell RCCs, 9 oncocytoma, 4 chromophobic RCCs, 4 papillary RCCs and 7 other lesions (3 renal cysts, 1 liposarcoma, 1 spindle cell carcinoma, and 1 granular cell carcinoma).

Interestingly, only 16 (22.9%) of the 76 clear-cell carcinoma but all 9 (100%) oncocytoma appeared homogenous and noncystic on high-resolution intraoperative ultrasound (Table 1).

Encouraged by these results, we focused on B-mode preoperative transabdominal ultrasound and scanned for renal tumors that appeared homogenous and noncystic. Thirty consecutive patients were selected who met these criteria (18 men, 12 women; aged 63 ± 7.7 yr; tumor size: 29 ± 11.3 mm). We bioptically diagnosed eight (26.7%) benign tumors (six oncocytoma, one adenoma, one leiomyoma); 25 of 30 (83.3%) patients were accurately diagnosed. The biopsy results are summarized in Fig. 1. Mean follow-up was 10 mo.

Table 1 – Comparative study of intraoperative sonographic and histopathologic finding: clear-cell RCC versus oncocytoma

	Homogenous and noncystic				Homogenous and cystic				Nonhomogenous and noncystic				Nonhomogenous and cystic			
	n	%	Ø mm	± mm	*n*	%	Ø mm	± mm	*n*	%	Ø mm	± mm	*n*	%	Ø mm	± mm
Clear-cell RCC *n* = 70	16	22.9	36.0	10.4	6	8.6	44.2	10.9	25	35.7	54.9	28.9	23	32.8	54.3	30.1
Oncocytoma *n* = 9	9	100	34.4	22.2	0	0			0	0			0	0		

Other tumors with low rate of occurrence: 4 papillary RCCs: (4 nonhomogenous and noncystic; 4 chromophobic RCCs (2 nonhomogenous and noncystic, 1 nonhomogenous and cystic, and 1 homogenous and noncystic); 7 tumors excluded: 3 pure cystic RCCs, 2 tumors that could not be evaluated because of intraoperative bleeding, 1 tumor that remained undetected on intraoperative ultrasound.

Of the 5 failed biopsies, four patients underwent surgery. Histopathology revealed 4 RCCs in all cases (clear-cell RCC in three patients, chromophobic RCC in one patient). Thirteen of 16 bioptically diagnosed RCCs were operated on (12 clear-cell RCCs, 1 papillary RCC). Although 5 of the 8 bioptically diagnosed benign tumors were observed, one patient underwent nephrectomy because of increasing tumor size after 1 yr of surveillance. The remaining three patients were diagnosed as ''most likely'' oncocytoma. All underwent partial nephrectomy. Histopathologic examination confirmed biopsy findings in all three cases. The only complication we observed was one case of bleeding accompanied by persistent flank pain followed by the development of renal hematoma.

In general, very small tumors (<3 cm), decreased breathing compliance, patient position, and medially located renal lesions seemed to negatively influence biopsy results (Table 2). Mean tumor infiltration of biopsy cores was 75% ± 22.6%.

Tumor vascularization seen on Doppler ultrasound did not show any significant differences between benign and malignant renal masses.

4. Discussion

Although some renal masses cannot be diagnosed confidently by imaging alone, percutaneous biopsy has not been routinely used in the past. In recent years, however, several advances in imaging, inter-

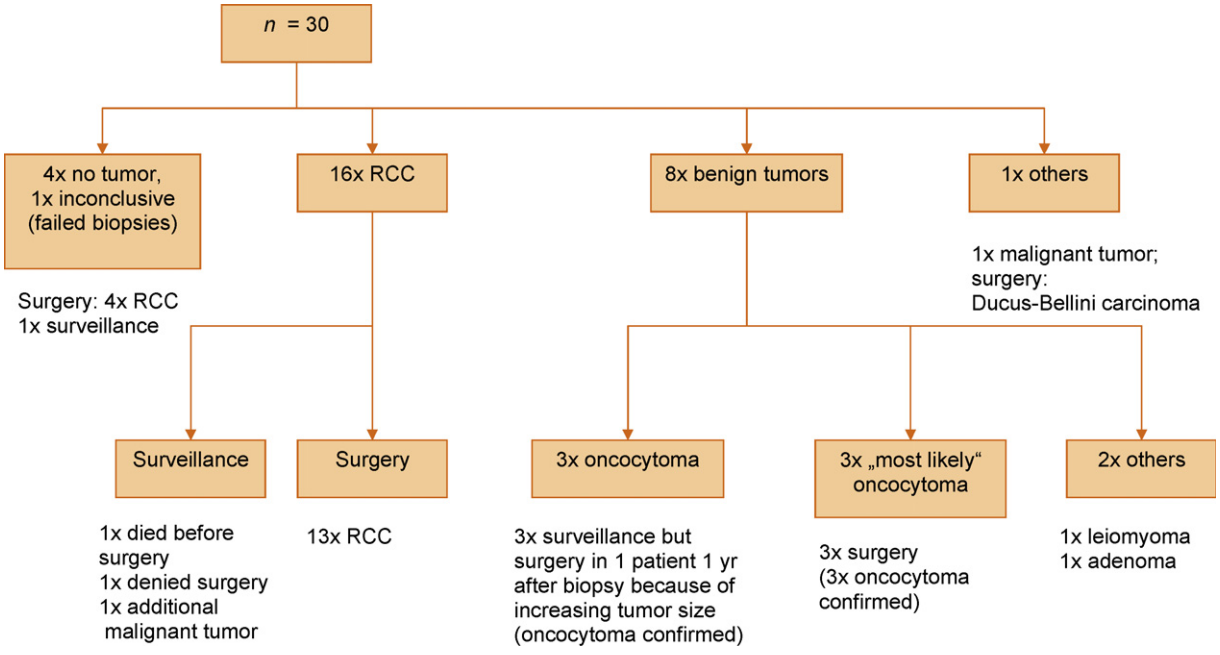

Fig. 1 – Results of percutaneous biopsy on 30 renal tumors that appeared homogenous and noncystic on transabdominal ultrasound.

Table 2 – Patients with failed biopsy

Age (yr)	Tumor size (cm)	Outcome	Specifications
51	1.5	Partial nephrectomy, clear-cell RCC	Very small tumor, more difficult to depict in prone vs. supine position
72	2.5	Partial nephrectomy, clear-cell RCC	Markedly decreased breathing compliance
62	2.2	Partial nephrectomy, chromophobic RCC	Small tumor, more difficult to depict in prone vs. supine position
81	4.4	Denied surgery	Medially located mass, isoechogenic on ultrasound, more difficult to depict in prone vs. supine position
41	4.5	Partial nephrectomy, clear-cell RCC	Isoechogenic intrarenal mass, difficult to depict on B mode ultrasound

ventional, cytogenetic, and cytologic techniques have allowed it to play a larger role in the evaluation of renal masses.

Obviously, the low incidence of benign renal masses in nonselected patients is considered to be one of the points against renal tumor biopsy. Hence, many biopsies will detect only few benign tumors. From a large study it is known that smaller renal masses are more likely to be benign [6]. Thus, for tumor biopsy some authors recommend focusing on masses not larger than 3–4 cm [1]. Given a single renal mass, however, other more specific parameters indicating benignity are desirable.

Renal cell carcinoma and oncocytoma are the most common malignant and benign epithelial tumors, respectively. On macroscopic pathologic examination, both tumors show striking differences: necrosis, hemorrhage and cysts are common in renal cell carcinoma but are almost always absent in oncocytoma. As shown in Table 1, these characteristics did indeed produce distinctive differences on high-resolution intraoperative ultrasound. Cystic and nonhomogenous masses seem to virtually exclude oncocytoma, although approximately one fourth of all clear-cell carcinoma appeared undistinguishable from oncocytoma. Interestingly, these ''oncocytoma-like'' clear-cell RCCs were significantly smaller than all other clear-cell RCCs (36 vs. 44.2–54.9 mm). One may conclude that, with increasing tumor size, clear-cell RCCs are more likely to show their typical morphology of cysts and necrosis, leading to nonhomogenous and/or cystic appearance on ultrasound. In other words, sonographically noncystic and homogenous renal masses larger than 5 cm in size are even more likely to be benign than are tumors less than 4 cm.

We could not expect to achieve similar results with preoperative transabdominal ultrasound compared with intraoperative ultrasound since obviously the imaging depth needed to be increased for study 2, thereby sacrificing resolution. By strictly applying these ultrasound criteria to 30 patients whose tumors appeared noncystic and homogenous (or basically excluding masses that appeared cystic

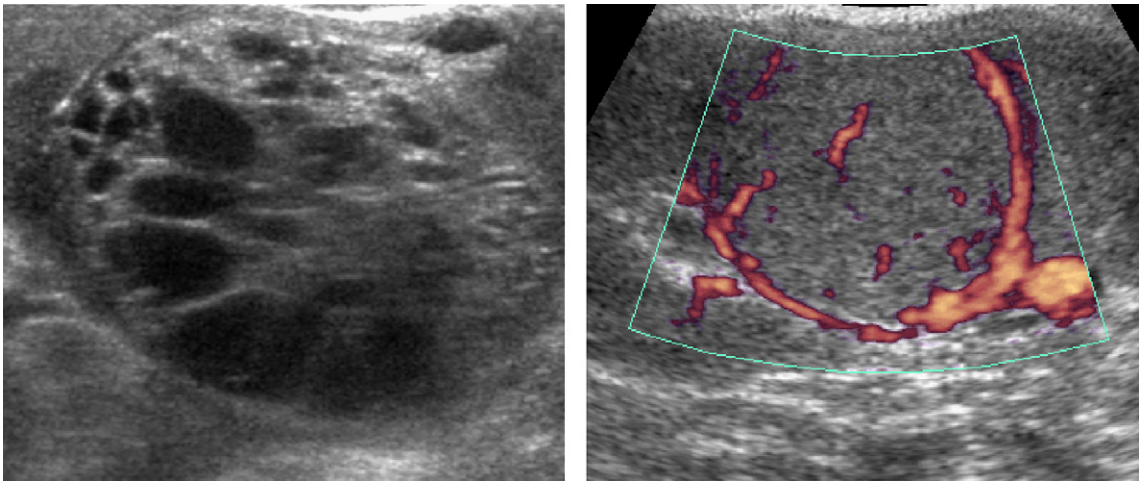

Fig. 2 – Renal tumor morphology on intraoperative ultrasound: left – non-homogenous and cystic, right – homogenous and non-cystic.

and/or nonhomogenous on transperitoneal ultrasound), we bioptically diagnosed eight (26.7%) benign tumors. leading to the desired better selection of patients with benign renal masses (Fig. 2). However, these results do depend on two essential conditions.

First, ultrasound settings should be adapted individually, and technical innovations such as compound [7,8] and harmonic [9] imaging that improve B-mode ultrasound, which are now widely available, should be applied. Second, only experienced histopathologic evaluation of renal biopsy specimens guarantees a reliable diagnosis. Immunohistochemistry and additional markers are useful and necessary to confirm initial and sometimes uncertain findings of basic histopathology. We used vimentin, CK7, and Ki-67, which are often positive in RCC but normally negative in oncocytoma. Regressive forms of oncocytoma may, however rarely stain positive. There has been ongoing research for new markers that especially differentiate between chromophobic RCC and oncocytoma, which still remains diagnostically challenging. Recently, Caveolin-1, if compared with CK7, was found to be useful as an additional immunohistochemical staining marker.

Moreover, molecular genetics can add important information in those difficult cases by determining RCC subtype-specific chromosomal alterations [10,11]. Current research focuses on oncocytoma-specific gene expression studies [12].

Finally, all even slightly questionable biopsy findings require surgical exploration.

Surveillance can be recommended to patients whose tumor biopsy revealed oncocytoma. However, counseling about diagnostic confidence as well as follow-up ultrasound are necessary since oncocytoma seems to grow with variable velocity [13]. To prevent radical nephrectomy, nephron-sparing surgery is indicated during follow-up, especially in quickly growing tumors and in younger patients as long as imaging suggests its feasibility.

Practical limitations are obviously small tumor size and breathing compliance. Before considering biopsy, renal masses should be sonographically visualized not only in the supine but also in the prone position, the latter of which is sometimes more difficult. The sensitivity of biopsy for diagnosing masses that are 3 cm or less in size is known to be lower than that for larger masses, clearly because smaller masses are more difficult to target [14]. Being able to hold one's breath is essential for biopsy.

Renal tumor biopsy is considered to be a safe procedure. Although some extent of perinephric hemorrhage almost always occurs [15], major bleeding is uncommon [16]. Further, pneumothorax and needle tract seeding are extremely rare [17]. Therefore, the diagnostic benefit of percutaneous renal tumor biopsy by far outweighs the risks of these two possible adverse effects. We recommend renal tumor biopsy (1) in renal masses, especially if they appear homogenous and noncystic on ultrasound; (2) if percutaneous radio/cryoablation is considered; (3) for patients whose renal masses may have been caused by infection; (4) for patients with suspected/known additional extrarenal malignancy; (5) in older patients or patients with considerable comorbidity; (6) for patients with a renal mass in a solitary kidney; and (7) in cases of complex renal cysts.

5. Conclusions

We have shown that for percutaneous renal tumor biopsy, transabdominal ultrasound is not only useful for needle guidance but also helpful if used for studying ultrasound B-mode tumor morphology. By selecting patients whose renal masses appear homogenous and noncystic, the probability of detecting benign renal masses rises above 20%. For these reasons, renal tumor biopsy should be performed under ultrasound guidance. Making use of modern ultrasound technology and dedicated histopathologic examination is crucial before observation may be recommended to those patients with clearly benign biopsy results.

However, for all patients with even slightly questionable biopsy findings, surgery remains mandatory.

Conflicts of interest

We have no disclosures to report.

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Editorial Comment on: Ultrasound-Guided Biopsy of Homogenous Solid Renal Masses

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Currently, most solid kidney tumours are still managed without preoperative diagnosis because it is supposed that most of them are uniformly malignant. But nowadays it is admitted that there are different histologic types of malignant renal tumours and that benign tumours are not exceptional [1]. Preoperative diagnosis of solid renal masses allows clinicians to tailor the treatment to the histologic type.

Renal masses can be characterised either by imaging modalities or by percutaneous biopsy [2]. In this study, Reichelt et al [3] evaluated the role of ultrasonography, B-mode and power Doppler, to select renal masses prone to biopsy. This is a very pertinent study and the first one to correlate the ultrasound findings of a renal mass with the biopsy findings. They found that 27% of solid renal masses that were homogenous were benign lesions with an accuracy of 83%. Reichelt et al confirm that some renal masses could be characterised and selected by ultrasonography. Moreover, recently, Raj reported that renal cell carcinomas could be characterised by ultrasonography [4].

Another key point of this study is that renal biopsy could be accurately performed under ultrasonography guidance with good results, whereas most of the reported series on tumour biopsies were performed under computed tomography guidance [2,5].

All renal tumours do not need preoperative biopsy. The indications for solid renal mass biopsy are becoming clearer and better defined. In a recent series a radiologic ''indeterminate mass'' had a 24% risk of being benign and, therefore, might justify a preoperative biopsy [6]. Reichelt showed that a homogenous noncystic renal mass is an indication for biopsy.

The diagnosis of an oncocytic tumour on biopsy indicates the need for ablation or active surveillance [7].

This series adds some new strong arguments for biopsy of renal masses and reinforces the role of ultrasonography in the management of renal masses.

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