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ORIGINAL PAPER

The use of renal biopsy in the kidney tumor management: A retrospective analysis of consecutive cases in a referral center

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Summary ***Introduction: Ultrasound-guided renal masses biopsy (RMB) is a useful and underestimated tool to evaluate suspected renal tumors. This study aimed to assess the safety and feasibility of this technique.***
Materials and Methods: Data of 80 patients with suspected primary or secondary kidney tumors who underwent RMB between January 2012 and December 2020 were included in this retrospective study. Twelve patients were excluded due to incomplete data. Biopsy outcomes were collected through our electronic medical records system and then compared with definitive pathology.
Results: RMB was performed in 68 cases. Pathological examination reported 43 (63%) malignant cases, while RMB was negative in 15 (22%) samples. On the other hand, a benign lesion was present in 8 (12%) cases, and 2 (3%) biopsies were non diagnostic. One major and one minor post-procedure complication were reported among the patients. A total of 31 patients underwent renal surgery including 19 partial and 12 radical nephrectomies. Out of them, 4 patients had a negative biopsy, but radiological imaging strongly suggested malignancy.
The concordance between biopsy and definitive pathology occurred in 22 out of 31 (71%) cases, with a higher rate among the masses greater than 4 cm, 9/11 (82%) compared to smaller ones 13/20 (65%). Pathologic examination of the 4 cases with negative biopsy showed 3 renal cell and a translocation renal cell carcinoma.
Conclusions: Ultrasound-guided biopsy for renal masses is a safe and effective procedure. Its ability to identify malignancy is evident, especially for primary renal tumors. However, low concordance between biopsy and definitive pathology in cases with negative biopsies, especially for tumors < 4 cm, does not reliably guarantee the absence of tumor and, therefore, strict follow-up or repeat biopsy may be indicated.

KEY WORDS: Kidney tumors; Renal masses biopsy; Ultrasound; Small renal mass; Nephron-sparing surgery; Active surveillance.

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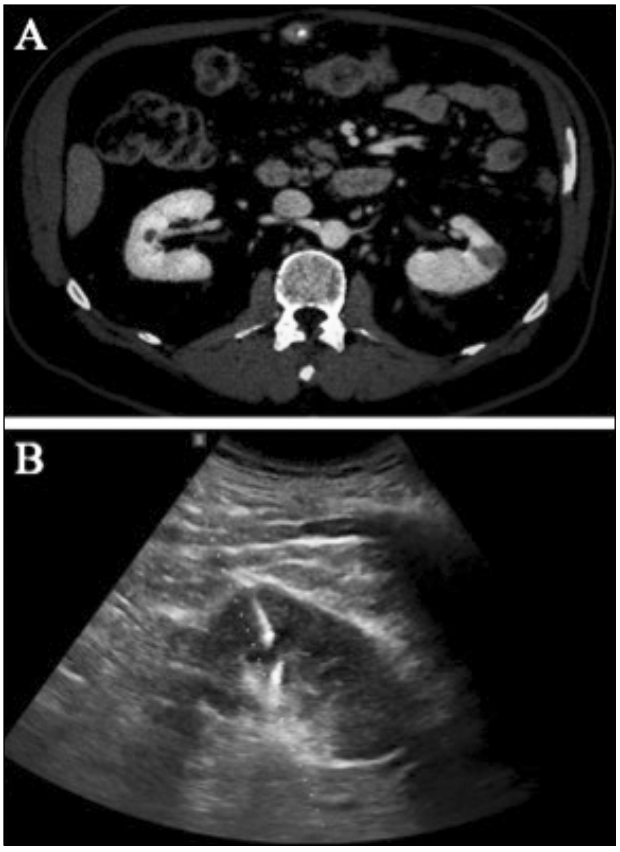
INTRODUCTION

Since the past few decades, the incidence of clear cell renal cell carcinoma has dramatically increased, and currently counts approximately 431.000 new cases per year worldwide (1). Furthermore, it is the cause of death of over 179.000 people annually (1). This phenomenon reflects the development of advanced diagnostic imaging, which determines a greater detection rate. In a retrospective study involving 3001 consecutively registered asymptomatic adults, a renal mass of at least 1 cm occurred in nearly 15% of examinations (2).
Currently, there is an increased number of diagnoses of *small renal masses* (SRM), which consists of cystic or solid lesion measuring < 4 cm on cross-sectional imaging and with features suspicious of a cT1a RCC (3). Nowadays, several therapeutic options may be offered, in particular nephron-sparing surgery (NSS) is preferable to radical nephrectomy for tumors up to cT1b stage due to the preservation of renal function (4, 5). Furthermore, partial nephrectomy is associated with a decrease in cardiovascular events and overall mortality (6). Cryoablation is a valid option in patients with several comorbidities and low life expectancy, due to minimum effect on renal function and low post-procedure complication rate, despite the high treatment failure rates (7). Alternatively, active surveillance has demonstrated cancer-specific survival similar to primary intervention for patients with SRM (8).
The most appropriate treatment decision for the patient is based first on the patient's general condition (including comorbidities, renal function, and life expectancy) and the nature of the renal tumor. However, traditional diagnostic imaging provides data on mass characteristics, but it cannot determine whether the lesion is benign or malignant yet. There is evidence that dynamic magnetic resonance imaging may differentiate tumor subtypes (9), but tumor aggressiveness cannot be defined. For the latter, the details from ultrasound-guided *renal mass biopsy* (RMB) are crucial. This procedure plays a key role in approximately 60% of patients (10), guiding them toward the most appropriate therapy, whether medical or surgical.
This study aimed to describe our experience with RMB, evaluating its safety and feasibility.

MATERIALS AND METHODS

An institutional retrospective review was conducted with data analysis of 80 patients with suspected primary or secondary kidney tumors who underwent RMB between January 2012 and December 2020. Twelve cases were

Figure 1.
(A) An axial CT image of a left superior mesopolar renal mass. (B) An ultrasound image of the renal mass biopsy with the needle guide.



excluded due to the lack of complete data in the database. All patients had previously performed a contrast-enhanced *computed tomography* (CT) scan of the abdomen, which allowed for tumor characteristics evaluation (Figure 1A). Renal biopsy was indicated in the following cases: patients with various comorbidities in whom surgery is planned, patients with imaging findings suggestive of unresectable renal cancer, suspected metastasis in the kidney, and indeterminate cystic renal mass.
Two experienced radiologists performed all the RMB guided by ultrasound machine LOGIQ S8 XDclear (*GE Healthcare®, Chalfont St Giles, UK*) after the analysis of contrast-enhanced CT imaging. Specimens were obtained through an automated biopsy gun with an 18-Gauge needle (Figure 1B). One to four cores were collected per biopsy, giving an average of two. Patients' characteristics, including age, gender, *body mass index* (BMI), skin-to tumor distance and thickness of subcutaneous fat, were calculated through the radiology. Moreover, several radiological tumor characteristics were evaluated, such as size, location, endophyticity, cortical location and cystic component.
All data regarding post-procedure complications following primary intervention were reported and ranked according to *Clavien-Dindo* (CD) Classification (11) as collected through our electronic medical records system.
Qualitative variables were described using absolute frequencies and percentages. Quantitative variables were described using the median and interquartile ranges. IBM SPSS (V26) was used as statistical software.

Results

The median age of the patients was 71 years (36-85), and the median BMI was 27.5, as shown in Table 1. Median core needle samples per biopsy were 2. Tumor characteristics were reported in Table 2. Forty-four cases had an SRM (< 4 cm), and 24 had masses ≥ 4 cm. RMB in our series was performed in 68 cases. The histological outcomes of all the biopsies are listed in Table 3. The biopsy outcome was malignancy in 43 (63%) cases, and the *renal cell carcinoma* (RCC) was the most frequent tumor; 15 biopsies were negative, a benign lesion was present in 8 (12%) cases, and 2 (3%) biopsies were non diagnostic.
Two patients experienced complications after the biopsy procedure: 1 case of a subcapsular renal haematoma that

Table 1.
Patients and samples characteristics.

	No. (%)	Median (range)
Age, years		71 (36-85)
Gender		
Male	49 (72%)	
Female	19 (28%)	
Patient BMI		27.5 (18.6-44.2)
< 30	46 (68%)	
≥ 30	22 (32%)	
Core needle samples, n		2 (1-4)
Skin-to-tumor distance, cm		5.8 (15-120)
< 7 cm	43 (63%)	
≥ 7 cm	25 (37%)	
Thickness of subcutaneous fat, cm		1.9 (2 -54)
< 3 cm	50 (74%)	
≥ 3 cm	18 (26%)	

Table 2.
Tumor characteristics.

	No. (%)
Side	
Left	25 (37)
Right	43 (63)
Tumor size	
< 4 cm	44 (65)
≥ 4 cm	24 (35)
Mass location	
Mesorenal	22 (32)
Upper pole	26 (38)
Lower pole	18 (27)
Renal pedicle	2 (3)
Cortical location	
Anterior cortex	18 (27)
Posterior cortex	32 (47)
Neither	18 (27)
Endophytic vs. exophytic	
Completely endophytic	10 (15)
< 50% exophytic	29 (43)
≥ 50% exophytic	29 (43)
Cystic vs. solid	
Cystic component ≥ 50%	5 (7)
Cystic component < 50%	10 (15)
No cystic component	53 (78)

Table 3.
Histological outcomes of diagnostic biopsies.

Histological subtype at RMB	No. (%)
Clear cell RCC	21 (29)
Papillary RCC	9 (13)
Oncocytoma	8 (12)
Unspecified carcinoma	3 (4)
Oncocytic RCC	2 (3)
Lymphoma	3 (4)
Urothelial carcinoma	1 (1)
Skeletal muscle cancer (metastasis)	1 (1)
Collecting (Bellini) duct carcinoma	1 (1)
Translocation Renal Cell Carcinoma	1 (1)
Lung cancer (metastasis)	1 (1)
Non diagnostic	2 (3)
Negative	15 (22)

RMB: renal mass biopsy; RCC: renal cell carcinoma.

not required treatment (CD 1), and 1 case of renal bleeding, who required Super-Selective Embolization (CD 3), occurred.
Table 4 reported the treatment offered to the patients.

Table 4.
Therapeutic management.

	No. (%)	< 4 cm	≥ 4 cm
Nephron sparing surgery (NSS)			
RCC	9 (13)	8	1
Others	10 (15)	7	3
Radical Nephrectomy			
RCC	8 (12)	2	6
Others	4 (6)	3	1
Active Surveillance			
RCC	1 (1)	1	0
Oncocytoma	8 (12)	6	2
Others	2 (3)	2	0
Oncologic treatment (chemo or immunoterapy)			
RCC	2 (3)	0	2
Others	5 (7)	2	3
Watchful waiting			
RCC	1 (1)	0	1
Others	2 (3)	1	1
Patients lost during follow-up	16 (24)	12	4
RCC	2 (3)	1	1
Others	14 (21)	11	3

RCC: renal cell carcinoma.

Table 5.
Concordance between biopsy and definitive pathology.

	Concordance with definitive pathology in all masses	Concordance with definitive pathology in masses < 4 cm	Concordance with definitive pathology in masses ≥ 4 cm
Overall, n (%)	22/31 (71)	13/20 (65)	9/11 (82)
RCC, n (%)	22/23 (96)	13/14 (93)	9/9 (100)
Unspecified carcinoma, n (%)	0/3 (0)	0/2 (0)	0/1 (0)
Others, n (%)	0/1 (0)	0/1 (0)	0/0 (0)
Negative, n (%)	0/4 (0)	0/3 (0)	0/1 (0)

RCC: renal cell carcinoma.

Chemo- or immunotherapy was proposed to the seven patients with locally advanced disease or primary tumor in another location. Active surveillance was offered to the 8 cases of oncocytoma, while 3 cases of watchful waiting occurred.
As shown in Table 5, the overall concordance between RMB and definitive pathology was 22/31, with a higher rate for masses greater than 4 cm. Ultrasound-guided biopsy demonstrated its reliability in diagnosing RCC, both for small and large masses. Tumor subtype was confirmed by definitive pathology in 82% of cases (22/27). However, in two cases of unspecified carcinoma, after excision, one had a histological outcome of skeletal muscle metastases and the other urothelial cell carcinoma. Four patients with negative biopsies underwent surgery because of highly suspicious lesions for tumor on radiological imaging. Biopsies reported only necrosis in two of them and solid component of a cystic lesion in the other two. The final diagnosis was RCC in three patients and translocation renal cell carcinoma in one.
In summary, the overall sensibility was 71%, with a higher value for masses greater than 4 cm than the smaller ones (82% *vs* 65%, respectively). Furthermore, the positive predictive value was 96%.

Discussion

According to EAU guidelines, surgery is the first-line choice therapy for patients with a localized renal mass, preferring, whenever feasible, the NSS to radical nephrectomy (12).
Nowadays, there is a trend toward a conservative approach for renal surgery also for increasingly challenging cases. In a multicenter study involving 410 patients with high complexity masses, partial nephrectomy showed satisfactory long-term oncological and functional outcomes despite an acceptable rate of perioperative complications (13, 14). However, 20-50% of the definitive pathologies of this surgery find benign tumors, which might be managed by active surveillance (15). On the other hand, a multidisciplinary strategy is necessary for metastatic diseases or locally advanced renal cancer, which provides a palliative cytoreductive nephrectomy and systemic treatments (12). Moreover, microRNAs were proposed as a non-invasive biomarker for various roles in RCC management, although no definitive conclusions emerged from the literature (16). Therefore, a histological diagnosis is essential to guide the best therapeutic management.
Although ultrasound-guided biopsy may have other hints, as in glomerulonephritis, its more frequent use is in the field of oncology. RMB indication occurs in several cases, such as the diagnosis of tumor metastasis, unresectable renal cancer, indeterminate cystic or multiple renal mass, and in patients not fit for surgery (17).
The biopsy was proposed for SRM, although an inverse relationship was reported between tumor size and its risk of malignancy (18).
Ultrasound-guided biopsy showed good accuracy in defining the nature of the renal tumor. In our series, a concordance of tumor malignancy between biopsy and definitive pathology always

occurred. Moreover, the concordance of RCC between RMB and definitive pathology was 96%. In a large meta-analysis involving 5228 patients, its sensitivity and specificity were 99.1% and 99.7%, respectively (19).
Furthermore, the authors showed a concordance rate between tumor histotype on biopsy and surgical specimen of 90.3%, while concordance rates of tumor grade ranged from 43% to 93%. The last data raises several doubts about biopsies, especially for SMR. Similarly, *Pierorazio et al.* reported high percentages in terms of sensitivity and specificity, while the negative predictive value was 68.5% and non-diagnostic rates ranged from 0% to 22.6% for masses less than 4 cm (20). In the same way, in the present study, the concordance rate between biopsy and definitive pathology of all SRM dropped up to 65%.
The most critical aspect that emerged from our analysis is the specificity of RMB. Indeed, there was low concordance between biopsy and definitive pathology for negative or unspecified carcinoma diagnoses in our results. Abel et al. reported that when carrying out a biopsy of a metastatic lesion or primary tumor, as opposed to nephrectomy specimen examination, it is likely that only one subpopulation of cells is sampled, and prognostic information is based on only one subpopulation of cells (21). Therefore, high false-negative rates raise concerns about the reliability of the procedure. However, RMB may be repeated on all patients with unspecified masses or non-diagnostic cases to increase the diagnostic rate (22).
Furthermore, renal biopsy is not without complications, due to the procedure invasiveness, especially bleeding, although they are considered rare events. According to *Lane et al.*, minor and major complications after RMB are, respectively, less than 5% and 1% (23). Of these, the most common is undoubtedly bleeding, which often tends to present subclinically and requires transfusion in about 1.5% of cases (24). Indeed, both post-procedure complications were related to haemorrhage in the present study. Another frequent complication is the intrarenal arteriovenous fistulae occurred. According to *Rollino et al.*, the development of this clinical condition has an incidence of up to 5% when colour-coded Doppler sonography is used (25). However, no case was reported in our analysis.
The limitations of the present study are evident. First, it is a retrospective study and biases linked to its nature are predictable. Second, the pathological specimens were not reviewed independently for the current study. Moreover, a considerable number of subjects dropped out from our analysis: in fact our radiology department also accepts patients referred from other hospitals and, therefore, a loss of some of them in the follow-up is inevitable. At last, a relatively small sample size is involved in this analysis, not allowing to obtain definitive data.

Conclusions

Ultrasound-guided biopsy for renal masses demonstrated satisfactory ability to distinguish benign and malignant tumors. Concordance between biopsy and definitive pathology was high for RCC, particularly for masses greater than 4 cm. However, the low concordance in the negative biopsies, especially for tumors < 4 cm, may require a second biopsy. In any case, the procedure proved to be safe and effective in referring patients to the most appropriate therapeutic management. Considering the low prevalence of this procedure in routine clinical practice, its use is recommended whenever an indication occurs.

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