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ORIGINAL ARTICLE

Outcomes of ultrasound guided renal mass biopsies

Edward L. Sutherland[1] · Agnieszka Choromanska[1] · Sayf Al-Katib[1] · Mary Coffey[2]

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Abstract

Purpose The purpose of this study was to evaluate the rate of nondiagnostic ultrasound-guided renal mass biopsies (RMBs) at our institution and to determine what patient, procedural, and focal renal mass (FRM) factors were associated with non-diagnostic ultrasound-guided RMBs.

Methods Eighty-two ultrasound-guided renal mass biopsies performed between January 2014 and October 2016 were included in our study. Biopsy outcomes (diagnostic vs. nondiagnostic) and patient, procedural, and FRM characteristics were retrospectively reviewed and recorded. Univariate statistical analyses were performed to identify biopsy characteristics that were indicative of nondiagnostic biopsy.

Results Ultrasound-guided RMBs were diagnostic in 70 out of 82 cases (85%) and non-diagnostic in 12 cases (15%). Among the diagnostic biopsies, 54 (77%) were malignant cases, 94% of which were renal cell carcinoma (RCC). Of the 12 nondiagnostic cases, the final diagnosis was RCC in 4 cases and angiomyolipoma in one case; seven of the nondiagnostic cases were lost to follow-up. A weak association ($p=0.04$) was found between the number of needle passes and the biopsy outcome. None of the remaining collected RMB characteristics showed a significant correlation with a diagnostic or nondiagnostic RMB. Six patients (7%) experienced complications.

Conclusion Ultrasound-guided renal mass biopsy is a safe and effective method for the diagnosis of renal masses with a low rate of nondiagnostic outcomes. A nondiagnostic biopsy should not be treated as a surrogate for a diagnosis since a significant number of patients with nondiagnostic biopsies have subsequently been shown to have renal malignancies. Repeat biopsy should be considered in such cases.

Keywords Ultrasound · Kidney · Biopsy · Renal cell carcinoma · Renal mass

Sommario

Obiettivi Lo scopo di questo studio era di valutare il tasso di biopsie di masse renali ecoguidate con risultato non diagnostico nel nostro istituto e di determinare quali fattori inerenti i pazienti, la procedura e le masse fossero associate con tali esiti.

Metodi Sono state incluse nello studio ottantadue biopsie ecoguidate di masse renali eseguite tra Gennaio 2014 ed Ottobre 2016. Sono stati revisionati e registrati i risultati della biopsia (diagnostico vs. non diagnostico) e le caratteristiche dei pazienti, procedurali e delle masse. Per identificare le caratteristiche indicative di esito non diagnostico, è stata eseguita un'analisi statistica univariata.

Risultati Le biopsie ecoguidate sono state diagnostiche in 70 casi su 82 (85%) e non diagnostiche in 12 casi (15%). Tra le biopsie diagnostiche, 54 (77%) erano casi maligni, con 94% di Carcinomi a Cellule Renali (RCC). Dei 12 casi non diagnostici, 4 erano carcinomi RCC; 1 era un angiomiolipoma; i restanti 7 casi sono andati persi al follow-up. È stata trovata una debole associazione ($p=0.04$) tra numero di campionamenti e l'esito bioptico. Nessun'altra delle restanti caratteristiche ha mostrato una correlazione significativa con un esito diagnostico o non-diagnostico. Ci sono stati sei pazienti con complicanze (7%).

Conclusioni La biopsia ecoguidata delle lesioni renali è un metodo sicuro ed efficace con un basso tasso di esiti non-diagnostici. Una biopsia non diagnostica non dovrebbe essere considerata un surrogato di una diagnosi in quanto un numero

✉ Edward L. Sutherland
Edward.Sutherland@beaumont.org

Extended author information available on the last page of the article

significativo di tali casi si è dimostrato essere una neoformazione maligna. In tali casi, la ripetizione della biopsia dovrebbe essere considerata.

Introduction

The development of advanced cross-sectional imaging techniques has led to the increased detection of incidental focal renal masses (FRMs). Despite these advances, in most circumstances, the exact pathology of the FRM cannot be diagnosed with imaging alone. Over the last decade, dynamic image-guided renal mass biopsy (RMB) has been increasingly employed to obtain tissue for histological evaluation. Improved interventional techniques facilitate safe biopsies and reliable and accurate diagnoses [1–4]. RMB has become an important diagnostic tool that precedes final, sometimes radical, treatment [3, 4]. However, it sometimes has nondiagnostic results, which may lead to clinical confusion, increased patient morbidity, delayed treatment, and frustration on the parts of the physician and patients. The purpose of this study was to evaluate the rate of nondiagnostic ultrasound-guided RMBs at our institution and to determine what patient and FRM factors were associated with nondiagnostic ultrasound-guided RMBs.

Materials and methods

The study was approved by and conducted in accordance with our institution's Human Investigation Committee. Two hundred twenty-eight image-guided core needle kidney biopsies performed between January 2014 and October 2016 were retrospectively reviewed. Cases without a contrast-enhanced CT prior to biopsy, CT-guided biopsies, and random renal biopsies were excluded. Each biopsy was performed on a unique patient. Eighty-two cases met our inclusion and exclusion criteria. The data were collected through an electronic medical records system, and the evaluation of the US and CT exams took place on commercial PACS software.

A board-certified radiologist performed or supervised all procedures and conducted them with ultrasound (US) guidance. Biopsies were obtained using a side-cutting automated biopsy gun with an 18-gauge or 20-gauge needle. The needle was directed into the FRM with direct US guidance. One to nine cores were collected per biopsy, giving an average of four. The cores were sent to the laboratory for evaluation.

The independent variables included the following: core biopsy needle gauge, number of passes, patient BMI, skin-to-tumor distance, thickness of subcutaneous fat, involvement of a trainee during RMB, kidney laterality, location of the FRM within the kidney, FRM size, FRM enhancement on CT, presence of cystic component within the FRM, and final histological subtype. Skin-to-tumor distance was measured as the shortest distance from the skin to the tumor in the axial plane on CT. Lesion size was taken as the average of the anterior–posterior and lateral dimensions of the lesion in the axial plane. Lesion location was separated into the lower pole, mid-pole, and upper pole. In some cases, large lesions were considered to be both lower and mid-pole or upper and mid-pole. Lesions were also divided among the anterior cortex, posterior cortex, and neither in the axial plane. The complete independent variables are listed in Tables 1, 2.

The dependent variable was the biopsy outcome: diagnostic or nondiagnostic. The outcome of a nondiagnostic study was defined as normal renal or non-renal tissue. Complications were rare and not included as a dependent variable.

All formal significance testing looked at the outcome variable of biopsy result (diagnostic vs. nondiagnostic). All variables were examined to determine whether there was any association between the independent variables in the data set and the biopsy result. Tests of association for categorical variables were conducted using Pearson's Chi square tests, Fisher's exact tests, and exact Cochran–Armitage trend tests. Exact tests were used when there were contingency tables with expected values of under five in at least one cell of the table. During the comparison of the values of continuous variables for diagnostic vs. nondiagnostic subjects, Wilcoxon two-sample rank-sum tests were conducted since, in all cases, at least one group was found to be non-normal in distribution. All

Table 1 Sample characteristics

	No. (%)	Median (range)	Mean (SD)
Core needle passes per patient		4 (1–9)	4
18-gauge needle (cases)	76 (95)		
20-gauge needle	4 (5)		
Patient BMI		28.6 (19.7–58.2)	29.6 (6.1)
<30	52 (65)		
≥30	28 (35)		
Skin-to-tumor distance		6.7 (1.7–14.5)	6.7 (2.5)
<7 cm	50 (61)		
≥7 cm	32 (39)		
Thickness of subcutaneous fat		2 (0.7–11.5)	2.5 (1.9)
<3 cm	62 (76)		
≥3 cm	20 (24)		
Involvement of a trainee	54 (66)		

Table 2 Kidney lesion characteristics

	No. (%)
Right kidney	34 (41)
Left kidney	48 (59)
Mass location	
Upper pole	22 (27)
Lower pole	30 (37)
Mid-pole	32 (39)
Cortical location	
Anterior cortex	33 (40)
Posterior cortex	35 (43)
Neither	14 (17)
Endophytic vs. exophytic	
Completely endophytic	14 (17)
<50% exophytic	33 (40)
>50% exophytic	35 (43)
Mass size (cm)	
<4cm	65 (79)
>4cm	17 (21)
Enhancement (>20HU)	81 (99)
Cystic vs. solid	
Cystic component ≥50%	11 (13)
Cystic component <50%	18 (22)
No cystic component	53 (65)

Table 3 Histological outcomes of diagnostic biopsies

Histological subtype	No. (%)
Clear cell renal cell carcinoma (RCC)	29 (41)
Oncocytoma	11 (16)
Papillary RCC	10 (14)
Unspecified RCC	4 (6)
Oncocytic RCC	3 (4)
Sarcomatoid RCC	3 (4)
Angiomyolipoma	2 (3)
Chromophobe RCC	2 (3)
Benign cyst	1 (1)
Metastatic breast cancer	1 (1)
Metastatic small cell lung cancer	1 (1)
Nodular adrenocortical hyperplasia	1 (1)
Tubulointerstitial nephritis	1 (1)
Urothelial carcinoma	1 (1)

Table 4. Final histological subtypes of non-diagnostic biopsies

Histological subtype	No. (%)
Clear cell renal cell carcinoma (RCC)	4 (33)
Angiomyolipoma	1 (8)
Unknown (lost to follow-up)	7 (58)

analysis for this study was conducted using SAS version 9.3 for Windows and R version 2.15.1 for Windows.

Results

The renal biopsy was diagnostic in 70 out of 82 cases (85%) and nondiagnostic in 12 cases (15%). Among the diagnostic biopsies, 54 (77%) were malignant cases, 94% of which were renal cell carcinoma (RCC). A second biopsy was performed in two of the 12 nondiagnostic cases, and a diagnosis of RCC was made in both cases. Five of the 12 nondiagnostic cases (including both cases with the repeat biopsy) went to surgery with a final diagnosis of RCC in four cases and angiomyolipoma in one case; seven cases were lost to follow-up. The histological outcomes of the diagnostic and nondiagnostic biopsies are listed in Tables 3, 4, respectively.

A weak association ($p = 0.04$) was found between the number of needle passes and the biopsy outcome. A median of 4 (SD = 1.66) passes was made in diagnostic studies, while a median of 3 (SD = 0.74) passes was made in nondiagnostic studies. No statistically significant association was found between any of the remaining independent variables and the dependent variable. The complete p values for the tests of association are listed in Table 5.

Table 5 Results

Independent variable	Odds Ratio (95% CI)	p
Core needle passes per patient	*	0.04
Core needle gauge	**	0.99
Patient BMI	*	0.69
Patient BMI ≥30	0.93 (0.21–4.80)	0.99
Skin-to-tumor distance	*	0.95
Skin-to-tumor distance ≥7 cm	0.59 (0.14–2.48)	0.52
Thickness of subcut. fat	*	0.98
Thickness of subcut. fat ≥3 cm	0.59 (0.14–3.07)	0.47
Involvement of a trainee	1.46 (0.33–6.00)	0.53
Kidney laterality	0.99 (0.24–4.37)	0.99
Cortical location	***	0.83
Endophytic vs. exophytic	***	0.99
Mass size (cm)	*	0.30
Mass size <4cm	1.36 (0.25–14.08)	0.99
Enhancement (<20HU)	**	0.99
Cystic	*	0.83

*Numeric variable, therefore Wilcoxon two-sample rank-sum test was used for significance testing and the odds ratio was not calculated for individual pairs

**Insufficient data to run formal significance testing on this variable

***Odds Ratio was not calculated for individual pairs

Although only a statistically significant association was found between the number of needle passes and the diagnostic outcome, several additional trends were noted. An increasing skin-to-tumor distance and greater thickness of subcutaneous fat trended with a higher incidence of nondiagnostic results: 12% of biopsies were nondiagnostic with a skin-to-tumor distance < 7 cm vs. 19% in cases with a distance ≥ 7 cm ($p = 0.52$); likewise, 13% were nondiagnostic with < 3 cm of subcutaneous fat vs. 20% in cases with a thickness of ≥ 3 cm ($p = 0.47$). Smaller tumor size also trended with a higher incidence of nondiagnostic results. Surprisingly, no significant relation was noted between the BMI value and biopsy results. The involvement of a trainee did not influence the biopsy results.

Six subjects (7.1%) experienced complications. Three subjects experienced hematuria following biopsy, three subjects experienced perinephric hematoma, one subject had an adrenal crisis, and one subject had a clot in the ureter. No subjects died or required a blood transfusion.

Discussion

Multiple imaging modalities, including computer tomography (CT), magnetic resonance imaging (MRI), US, and contrast enhanced ultrasound (CEUS), are useful for identifying, characterizing, and following up on FRMs after treatment. However, none of these modalities can reliably differentiate between benign and malignant solid renal masses [5–7]. Ultrasound elastography has shown some potential utility in distinguishing focal angiomyolipomas from RCC in early studies [8]. However the results of these studies are controversial, and more research is necessary before the modality can achieve wide acceptance. Therefore, although multiple imaging modalities are useful for evaluating FRMs, RMB is frequently required for definitive diagnosis.

There are no absolute criteria for when a RMB is indicated. According to the American Urological Association, RMB should be considered whenever a renal mass "is suspected to be hematologic, metastatic, inflammatory, or infectious," except in cases when the patient is "unwilling to accept the uncertainties associated with RMB" or when it is unlikely to change clinical management regardless of the pathological diagnosis [9]. Additional standard contraindications such as uncontrolled hypertension, abnormal anticoagulation status, and/or local or systemic infection also apply [10].

RMB should be considered for FRMs with imaging features suggestive of lymphoma, for instance, multiple renal masses with or without perirenal involvement and lymphadenopathy. Additionally, RMB should be recommended when imaging findings suggest benign etiology for FRM such as in a mass with a central stellate scar suggestive of oncocytoma.

Percutaneous RMB can be conducted using CT, US, or MRI. US is favored for its real-time guidance and lack of ionizing radiation, while CT is often preferred for deeper lesions. MRI is rarely used. All modalities of percutaneous RMBs have been found to be effective and safe techniques for reaching a definitive diagnosis. A recent meta-analysis found an overall median diagnostic rate of 92% for all types of percutaneous RMB [1]. A review from 2012 found no significant difference in diagnostic yield between CT and US [11]. Studies evaluating the modalities independently have shown diagnostic rates of 79–94% [12–15] for CT and 81–92% for US [9, 16–18].

The diagnostic rate in our study (85%) for ultrasound-guided RMB is broadly consistent with prior studies and adds to the body of literature supporting the utility of RMB [2–6] Our study also lends support to the aggressive management of nondiagnostic RMBs as a significant number of the patients were subsequently shown to have renal malignancies. Repeat biopsy should be considered in such cases. In our study, an initially nondiagnostic biopsy was not predictive of a nondiagnostic repeat biopsy. The three repeat biopsies in our sample were all diagnostic.

Our study provides limited information regarding what characteristics predict a nondiagnostic biopsy. The weak association between the number of needle passes and biopsy outcome ($p = 0.04$) should be interpreted cautiously given the large number of variables in this study. However, this finding does agree with prior studies. A study by Park et al. found that three or fewer passes correlated with an increased nondiagnostic rate and recommended that at least four passes be performed to minimize nondiagnostic outcomes [18]. Park et al. noted that more than four passes might theoretically decrease the nondiagnostic rate; however, it might also increase the risk of bleeding and other complications [18]. Other guidelines suggest a minimum of two to three passes [9, 10].

Statistically significant predictors of a nondiagnostic outcome that were evident in prior higher-powered studies, for instance, tumor size [19–22] and presence of enhancement [20], were not observed in our study. However, the absence of a significant correlation between many of our variables, such as tumor location, and a nondiagnostic outcome is in broad agreement with the literature [3, 21]. The impact of such characteristics as BMI, skin-to-tumor distance, and thickness of subcutaneous fat is likely small since no impact was demonstrated in our sample of 84 patients. This may be due to the relative simplicity of the procedure. The high rate of biopsy success and minimal impact of patient habitus and tumor location may indicate that ultrasound-guided RMB is a viable option for smaller renal lesions and in patients with more challenging anatomy. However, prior studies have noted a significant correlation between smaller tumor size and nondiagnostic biopsy outcome [19–22].

Conclusions

Ultrasound-guided renal mass biopsy is a safe and effective method for diagnosing renal masses with a low rate of nondiagnostic outcomes and complications. A nondiagnostic biopsy should not be treated as a surrogate for a diagnosis because the majority of patients with such an outcome were subsequently shown to have renal malignancies. Repeat biopsy should be considered in such cases.

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Compliance with ethical standards

Conflict of interest The authors: Edward Sutherland, Sayf Al-Katib, Agnieszka Choromanska, and Mary Coffey have no conflicts of interest to report.

Research involving human/animal participants All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent The study was determined by the performing institution's Human Investigation Committee to be a retrospective case review with no patient identifiers and therefore exempt for the purposes of informed consent.

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Affiliations

Edward L. Sutherland[1] · Agnieszka Choromanska[1] · Sayf Al-Katib[1] · Mary Coffey[2]

[1] Department of Diagnostic Radiology, William Beaumont Hospital, 3601 W 13 Mile Rd, Royal Oak, MI 48073, USA

[2] Beaumont Health Research Institute, 3601 W 13 Mile Rd, Royal Oak, MI 48073, USA