Evaluation of Diagnostic Accuracy of Percutaneous Biopsy for Small Renal Masses and First Report of Post-Biopsy Adhesions: A Prospective Study

Tunkut Doganca*, Can Obek

Purpose: In the present study, we evaluate the biopsy results, complications due to biopsy, and the correlation with the final pathology specimen of 19 patients who had surgery for their small renal masses.

Materials and Methods: A total of 19 patients (11 male, 8 female) underwent percutaneous biopsy of their renal mass under ultrasound guidance. All patients subsequently underwent extirpative surgery. Preoperative biopsy results were compared with postoperative specimens in terms of tru-cut and fine needle aspiration biopsies' histopathological accuracy and the complications noted.

Results: Average age was 56±10.5 years and tumor size was 37±10.6 mm. Six patients had only fine needle, 4 patients had only tru-cut, and 9 patients had both fine needle and tru-cut biopsies. Malignancy was reported in 14, and benign results in 5 patients. Sensitivity, specificity, PPV and NPV's were 64%, 100%, 100%, 33% respectively for FNAB. Sensitivity, specificity, PPV and NPV's were all 100% for tru-cut core biopsy. Two perirenal hematoma was detected which resolved spontaneously under conservative therapy. In 11 patients there were adhesions due to biopsy, which caused difficulty of dissection during the operation.

Conclusion: In this relatively small series, percutaneous ultrasound guided biopsy to determine the histology of small renal masses achieved a high diagnostic accuracy. FNAB alone has a low diagnostic accuracy with false negative results when compared. However, tru-cut core biopsy has a diagnostic accuracy of %100. Therefore we recommend tru-cut biopsy when histopathological diagnosis is required for small renal masses. Adhesions due to biopsy may cause difficulties during dissection.

Keywords: biopsy adhesions; biopsy complications; renal biopsy; renal cancer; small renal masses

INTRODUCTION

Incidence of small renal masses (< 4cm) (SRM) is increasing due to widely use of cross-sectional imaging techniques and management of these clinical issue is getting more important and complicated depending on which patients will need therapy and which therapy option is feasible and effective. Biopsy of a renal mass is not the standard of care and is suggested in specific circumstances only. There has been a stage shift within the recent years with renal masses presenting at lower stages and smaller sizes at diagnosis. SRM show heterogeneous histological properties with both malign and benign characteristics. Smaller lesions tend to be more benign.[1,2] These patients may potentially be offered a variety of management options changing from observation only to radical surgery. The information which gained by the tissue sampling with accurate biopsies, can be decisive at choosing treatment method. In addition to the change in clinical presentation and management, advances in biopsy and immunohistochemical analysis techniques, along with successful outcomes of renal biopsies have caused an increased interest in the potential role of biopsy in renal masses.[3,4]

In the present study, we evaluate diagnostic accuracy of two different biopsy techniques (tru-cut and FNAB) and the correlation with the final pathology specimen of 19 patients who had surgery for their small renal masses. Also biopsy related complications such as post biopsy adhesions were noted and discussed.

MATERIALS AND METHODS

Study Population

A total of 20 patients with a renal mass (<5 cm.) who are candidates for extirpative surgery has been offered biopsy. Size of the tumors measured with coaxial imaging techniques such as CT and MRI. Nineteen patients accepted the procedure and after consultation with radiology department, biopsies were performed.

Study Design

Cysts with heterogeneity and masses suspected for collecting system malignancies were excluded. All patients underwent surgery after the biopsy and final pathological results were compared with the biopsy results. Inefficient tissue samples, normal renal parenchyma, extrarenal tissue, blood cells and necrosis were accepted as inadequate biopsy result. Biopsy related early and late complications were also noted and a post-op questionnaire for the surgeons was used to determine if the biopsy procedure affected and challenged the surgi-

Department of Urology, Acibadem Taksim Hospital, Istanbul 34300, Turkey.
*Correspondence: Acibadem Taksim Hospital, Department of Urology, Istanbul, Turkey.
Mailing Adress: Inonu Mah., Nizamiye Cad. No:1, 34373 Sisli/Istanbul/Turkey.
GSM: +905327042325 Fax: +902122190987. tunkutdoganca@gmail.com.
Received October 2017 & Accepted July 2018

Table 1. Demographic data of patients and histological diagnosis for each biopsy type and final pathology.

Patient no.	Gender	Age	FNAB	Tru-Cut	Final Pathology
1	M	55	RCC	-	RCC
2	F	46	BENIGN	-	RCC
3	F	50	INADEQUATE	BENIGN	BENIGN
4	F	68	BENIGN	-	RCC
5	F	52	BENIGN	RCC	RCC
6	F	33	RCC	RCC	RCC
7	F	62	-	RCC	RCC
8	F	56	BENIGN	RCC	RCC
9	M	64	RCC	RCC	RCC
10	M	44	RCC	-	RCC
11	F	63	RCC	RCC	RCC
12	M	60	-	RCC	RCC
13	M	68	BENIGN	-	BENIGN
14	M	65	-	RCC	RCC
15	M	50	BENIGN	BENIGN	BENIGN
16	M	66	RCC	-	RCC
17	M	40	INADEQUATE	RCC	RCC
18	M	52	RCC	RCC	RCC
19	F	69	-	RCC	RCC

Abbreviations: FNAB, Fine needle aspiration biopsy; F, female; M, male; RCC, renal cell carcinoma

cal procedure. Sensitivity, specificity, positive and negative predictive values were also calculated. Informed consent was obtained from all patients which had been approved by the local ethics committee (Istanbul University Ethics Committee, file no: 01.09.20/s11)

Biopsy Technique

All biopsies were performed under local anesthesia with the guidance of ultrasonography (USG). Patients were evaluated for hemorrhagic diathesis and routine biochemical tests were performed before the procedure. Fine needle biopsy (FNB) in 6, tru-cut biopsy in 4, and FNB+tru-cut biopsies were performed in 9 patients. Main concern about performing tru-cut biopsy was excessive vascularity of the tumor or nearness to the renal hilum. A cytopathologist evaluted FNAB samples in the procedure room simultaneously and FNA biopsies were repeated up to 3 times according to the information from the cytopathologist. Tru-cut biopsies were performed by 18gauge needle. Both center and peripheral zones of the tumors were tried to be sampled. Separate tru-cut sampling technique were chosen instead of co-axial technique. Necessity of using a trocar needle thicker than 18 gauge was the main concern in terms of higher possibility of bleeding. Patients were observed for two hours with ultrasonography in case of hematoma formation.

RESULTS

There were 11 male and 8 female patients with average age of 56 (± 10.5) years. Average tumor size was 36 mm (20-50) (± 10.6). Mean time between biopsy and operation was 26.4 (± 7.2) days. Nine of the tumors were right and 10 of them were left sided. Final pathological results were 16 renal cell carcinoma (RCC), 2 oncocytoma and 1 glomus tumor. Immunohistochemical techniques used in 4 specimens (%21. 2 of them were oncocytomas and 2 RCCs). (**Table 1**)

FNB results were inefficient in 2, benign in 6 and malign in 7 patients. Only 2 of 6 benign results were correlated with final pathology (4/6 false negative results). Tru-cut samples were always adequate for histological evaluation. Two benign and 11 malignant results were reported. All of these results show consistency with the final pathology. (FNAB and Tru-Cut needle biopsy results are presented in **Table 2**)

Sensitivity, specificity, positive and negative predictive values were %64, %100, %100 and %33 for FNAB respectively. There were no false negative or false positive results in tru-cut, so all of the above values were %100. (**Table 2**)

Complications

Two patients with post-biopsy hematomas (3 and 4 cm) managed conservatively and required no intervention. No clinical infection, pleural injury or pneumo/heamothorax were observed.

There were adhesions in 11 patients (%61) which made the surgical procedure difficult according the post-op surgeon questionnaires. These adhesions also compromised tumor margins to be properly determined during surgery. In absence of validated or generally accepted adhesion scores for retroperitoneal surgery, effect of adhesions were evaluated with a simple questionnaire after the operation by the operating surgeon who defined the effects of biopsy on increased difficulty of dissection as minimal, moderate or severe. In 11 procedures, surgeons' statements were as 2 moderate and 9

Table 2. Pathological diagnosis for FNAB and Tru-cut biopsy.

	Final Pathology, malignant	Final Pathology, benign	Total
FNAB, malignant pathology	7	0	7
FNAB, benign pathology	4	2	6
Total (FNAB)	11	2	13
Tru-cut, malignant pathology	11	0	11
Tru-cut, benign pathology	0	2	2
Total (Tru-cut)	11	2	13

Abbreviations: FNAB, Fine needle aspiration biopsy

Table 3. Classification of biopsy and surgery complications based on modified Clavien classification for patients who had developed severe adhesions after biopsy.

Pt. No.	Biopsy Complication (Clavien Grade)	Management	Surgery Complication (Clavien Grade)	Management
1	Fever (I)	Antipyretics	None	-
2	None	-	None	-
3	Hematoma formation (I)	Conservative	Prolonged ischemia time (I)	Conservative
4	None	-	Prolonged ischemia time (I)	Conservative
5	Hematoma formation (I)	Conservative	None	-
6	Hematuria (I)	Conservative	None	-
7	Hematuria (I)	Conservative	None	-
8	None	-	Fever (I)	Antibiotics
9	None	-	None	-

severe adhesions. Frozen section evaluation of tumors showed two positive surgical margin status and resulted in re-excision which also caused prolonged ischemia time. Adhesions were mainly detected in biopsy tracts but in some patients minor hemorrhagies and possible desmoplastic reactions caused severe adhesions also in perirenal fat tissues.

During the early follow up after biopsies, there were no significant hypotension. Pain scores were mild (all < 6 via Visual Analog – Numeric Pain Scale) and didn't required any painkillers except paracetamol and non-steroids.

One patient developed high fever in first 24th hours. Ultrasonographic evaluation of biopsy site didn't show any abnormalities such as hematoma, collection or abscess formation. During follow-up, fever was responsive to oral hydration and paracetamol therapies and there was no need for prolonged antibiotic therapy.

Macroscopic hematuria were observed in two patients with endophytic renal masses but there were no need for urethral catheterization due to excessive bleeding or urinary clots. None of the patients required blood transfusion.

Postoperative period of 9 patients who had severe post-biopsy adhesions were not eventful. Prolonged ischemia time because of positive surgical margins at initial excision were not influential on postoperative creatinine levels. Two patients had high fever in first 48 hours with no positive bacterial growth in urine and blood cultures and were evaluated as possible atelectasis related fever which solved in first 48 hours of antibiotic therapy.

Complications are presented in **Table 3** with Clavien Classification.

DISCUSSION

Renal biopsy has not been routinely performed because of historical fear about hemorrhagic complications and tumor seeding. Low diagnostic results due to poor techniques and inefficient instruments also caused drawbacks about performing biopsy for SRMs.[1]

Biopsy can be performed with fine-needle or tru-cut biopsy needle under ultrasonography, computerize tomography or magnetic resonance imaging. Size, nature (necrotic areas or satellite lesions) and location of the lesion is important to determine sampling areas and numbers.[5]

According to EAU guidelines, biopsy is not recommended routinely for renal masses. Role of biopsy is currently limited to masses which are candidate for active surveillance or ablative therapies.[6]

Publications before 2001 on renal biopsy reported 88.9% accuracy and 0-25% false negative results.[7-9] However these discouraging results are primarily because of inadequate sampling.[10] Technical failure is also as high as 8.9%. In series published after 2001, accuracy was increased to 96% with better imaging techniques and better sampling with developments of biopsy needles.[1,5,11] Immunohistochemistry is also used around 50% for evaluation of biopsy samples.[3,4] Immunohistochemical techniques were also used in 4 patients in our study to determine histology.

Latest retrospective cohort study including 529 patients' data represented a diagnostic yield at 90%, reaching 94% when a repeat biopsy was performed after a failed one. Benign lesions were 20% likewise in other publications.[12]

There are limited studies in the literature that compares the biopsy results with the surgical specimens. SRM biopsy may not identify the whole mass because of partial sampling and heterogeneous nature of renal masses.[13,14] Appropriate biopsy technique is another important issue besides mass' characteristics. In recent studies, USG and CT imaging modalities were mostly used.[15-17] We preferred USG for guidance because of its accessibility and cost effectiveness. Also, biopsy needle types are important factors to achieve right diagnosis. There are some studies who stop using FNAB and continue with only with tru-cut needles because of high percentage of inadequate sampling and low specificity results with FNAB.[3] FNAB achieved the right diagnosis in only 9 of 15 patients in our study with a accuracy rate of 69%. However, final pathology correlation was 100% for tru-cut samples. Pathologist were not blind for the preoperative biopsy results when evaluating final specimens.

Correct subtyping of RCC's are up to 94% in literature with a 91% for clear cell, 91% for papillary type and 100% for chromophobe RCC.[1] Fuhrman grading is adequate only in 70% and 83%, with the reason of tumor heterogeneity.[1,7] In our study pathologists could report 9 biopsy samples' Fuhrman grades with a 100% correlation with final specimen.

Surgical challenge caused by post biopsy adhesions were never reported in literature. There were 11 moderate to severe adhesions in our study. Two of these patients had hematoma, which were detected after biopsy and it's uncertain that if these adhesions were related to hematoma formation or traumatic effect of biopsy needle at the tract. In one case, severe adhesion of perirenal fat tissue to the tumor, make difficult to determine safe surgical margins between tumor and parenchyma and resulted with conversion to open surgery from laparoscopy. Retroperitoneal adhesions are mainly considered about retroperitoneal laparoscopic surgical procedures and are often related with previous percutaneous stone

surgery or nephrostomy tube placement in case of hydronephrosis. These adhesions are generally firm and allow blunt dissection during laparoscopic intervention. Patients with SRM are candidates for nephron sparing surgery and determining safe surgical margin between tumor and renal tissue is essential during partial nephrectomy. Post-biopsy adhesions in case of hardening the clear surgical dissection and obtaining a clear cleavage may cause a rational drawback to perform biopsy. Small sample size is a major limitation for our study. Biopsy related complications such as hematoma formation was low, but within this small patient group, it's not suitable to discuss on percentages. However, there was a significant adhesion rate which needs to be mentioned. Retroperitoneal adhesions wre not studied and classified as intraperitoneal adhesions so far in the literature. Adhesions may be grouped as filmy/strong, needs blunt/sharp dissection, or vascularized. In our study, adhesion levels were examined by surgeons' feedback which is a highly subjective method. Biopsy technique may effect the development of post-biopsy adhesions. We chose separate tru-cut sampling from tumors, which means more than one access was needed. Using a trocar needle, which is thicker than 18 gauge as a co-axial technique may reduce access numbers but also increase bleeding possibility. Histopathological nature of adhesions were not determinable in our study, with lack of histologic sampling from adhesions. Fibrotic processes after biopsy related to tissue trauma or post bleeding formation are the main possible causes for these. But small size of groups did not allow us to compare these two techniques in terms of adhesion formation rate. However, high incidence of adhesions encouraged us on reporting.

In the present study sensitivity, specificity results were accordant with the literature. There were no major complications. This may be related to limited number of patients. Biopsy related adhesions which causes difficulties during surgical dissection is an issue which was not reported before and need to be evaluated with large series.

CONFLICT OF INTEREST

The authors report no conflict of interest.

REFERENCES

1. Dechet CB, Zincke H, Sebo TJ, et al. Prospective analysis of computerized tomography and needle biopsy with permanent sectioning to determine the nature of solid renal masses in adults. J Urol. 2003;169:71-4.
2. Campbell SC, Novick AC, Herts B, et al. Prospective evaluation of fine needle aspiration of small, solid renal masses: accuracy and morbidity. Urology. 1997;50:25-9.
3. Schmidbauer J, Remzi M, Memarsadeghi M, et al. Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. Eur Urol. 2008;53:1003-11.
4. Volpe A, Mattar K, Finelli A, et al. Contemporary results of percutaneous biopsy of 100 small renal masses: a single center experience. J Urol. 2008;180:2333-7.
5. Marcelin C, Ambrosetti D, Bernhard JC, Roy C, Grenier N, Cornelis FH. Percutaneous image-guided biopsies of small renal tumors: Current practice and perspectives. Diagn Interv Imaging. 2017;98:589-99.
6. Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol. 2015;67:913-24.
7. Murphy WM, Zambroni BR, Emerson LD, Moinuddin S, Lee LH. Aspiration biopsy of the kidney. Simultaneous collection of cytologic and histologic specimens. Cancer. 1985;56:200-5.
8. Truong LD, Todd TD, Dhurandhar B, Ramzy I. Fine-needle aspiration of renal masses in adults: analysis of results and diagnostic problems in 108 cases. Diagn Cytopathol. 1999;20:339-49.
9. Wood BJ, Khan MA, McGovern F, Harisinghani M, Hahn PF, Mueller PR. Imaging guided biopsy of renal masses: indications, accuracy and impact on clinical management. J Urol. 1999;161:1470-4.
10. Laguna MP, Kummerlin I, Rioja J, de la Rosette JJ. Biopsy of a renal mass: where are we now? Curr Opin Urol. 2009;19:447-53.
11. Lane BR, Samplaski MK, Herts BR, Zhou M, Novick AC, Campbell SC. Renal mass biopsy--a renaissance? J Urol. 2008;179:20-7.
12. Richard PO, Jewett MA, Bhatt JR, et al. Renal Tumor Biopsy for Small Renal Masses: A Single-center 13-year Experience. Eur Urol. 2015;68:1007-13.
13. Ball MW, Bezerra SM, Gorin MA, et al. Grade heterogeneity in small renal masses: potential implications for renal mass biopsy. J Urol. 2015;193:36-40.
14. Blute ML, Jr., Drewry A, Abel EJ. Percutaneous biopsy for risk stratification of renal masses. Ther Adv Urol. 2015;7:265-74.
15. Marconi L, Dabestani S, Lam TB, et al. Systematic Review and Meta-analysis of Diagnostic Accuracy of Percutaneous Renal Tumour Biopsy. Eur Urol. 2016;69:660-73.
16. Dave CN, Seifman B, Chennamsetty A, et al. Office-based Ultrasound-guided Renal Core Biopsy Is Safe and Efficacious in the Management of Small Renal Masses. Urology. 2017;102:26-30.
17. Jeon HG, Seo SI, Jeong BC, et al. Percutaneous Kidney Biopsy for a Small Renal Mass: A Critical Appraisal of Results. J Urol. 2016;195:568-73.