Percutaneous US-guided needle biopsies of solid renal masses

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Received October 5, 2010

Our objective was to examine the variables affecting diagnostic yield and complications in percutaneous ultrasonographyguided needle biopsies of solid renal masses. Percutaneous ultrasonography-guided needle biopsy of solid renal masses was performed in 172 patients with either large size (18G) cutting needles or small size (20G) aspiration needles. Retrospectively, 120 patients with diagnosis by percutaneous biopsy and follow-up data were included in this series. Age, gender, side, locations in kidneys, necrosis, calcification, maximum size, needle groups due to needle size and type (either 18G cutting needles or 20G aspiration needles), and needle pass were selected as variables. Their role was investigated in diagnostic yield. Two needle groups were divided and compared for diagnostic yield and safety. Also, change in treatment was evaluated. The mean maximum size of the masses was 8.8 ± 4.9 cm. The only predictor affecting accuracy was side of kidney (p=0.002). Among patients, 15 (12.5%) and 105 (87.5%) had benign and malignant solid masses, respectively. Small and large needle groups did not differ in accuracy, 80.3% vs. 87.1% (p=1.000). Technical success was detected as 100%. No major complications neither tumor seeding was seen. Percutaneous ultrasonography-guided needle biopsy of solid renal masses is effective and safe method with large size cutting needles and small aspiration needles. Change in clinical management was significant at 63.3% rate. Diagnostic yield was low in left kidney relating to right kidney, 69.4 vs. 93.1, while upper lobe location did not lead to significant false result. Repeat biopsies can be taken under CT guidance after nondiagnostic diagnosis in solid tumors of left kidney. All the needles including large cutting type were found safe.

Keywords: Ultrasound, urogenital interventions, biopsy, kidney/renal, cancer, hemorrhage

Percutaneous needle biopsy has been performed in most organ systems with excellent results and few complications. On the other hand, it has played a limited role as a diagnostic tool in evaluating renal masses [1].

Reported diagnostic sensitivities of fine-needle aspiration of renal masses vary from 75% to 90%, however, the diagnostic yield of fine-needle aspiration is controversial [2]. Researchers in several studies have reported that 18G core needle biopsy achieved 89-100% sensitivity for the detection of malignancy [3]. Even so, there are some raised questions on the complications such as renal hemorrhage relating to percutaneous biopsy. Additionally, it can result in seeding of the tumor along the needle track [4].

Some series have analyzed variables affecting accuracy of renal biopsy in the literature [3, 5], which are however limited and not conclusive [1-11]. As a result, we aimed to study the variables affecting accuracy in a series of 120 renal biopsies, which were patient age, gender, side, locations in kidneys, necrosis, calcification, maximum size of tumor, needle groups due to size and type, and number of needle pass. We examined also safety of renal biopsy and impact of renal biopsy on change in clinical management.

Patients and methods

Between 1993 and 2010, 172 patients underwent percutaneous ultrasonography (US)-guided liver biopsy of a solid kidney mass. Among them, 120 patients whose follow-up results were available (36 women and 84 men; age range, 23-80 years; mean age, 57.1±11.8 years) were included in this study. All the patients had a pathological diagnosis of the biopsy in this retrospective study. In 36 patients (30.0%) were biopsied with large size cutting needle (18G) whereas in 84 (70.0%) were performed with small size aspiration needle (20G). Large 18G needles were semi-automated cutting needles. Groups according to needle size and type were divided as large needle group and small needle group.

Technique. Procedures were mostly performed on an outpatient basis. Coagulation parameters were studied prior to the biopsy. All biopsies were performed under US guidance. All patients and 57 patients had US and computed tomography (CT) examinations before the percutaneous biopsy, respectively (Figures 1 and 2). Biopsies were performed under US guidance if they were obviously seen on US, even in difficult areas such as upper pole of left kidney. Patients fasted since the

previous overnight. No sedative or analgesic agent was used. Procedures were performed by staff radiologists or a radiology resident under staff supervision. On-site pathologist was not found in the biopsy-room at any intervention.

The biopsies were frequently applied to the patients in lateral decubitus position; however, sometimes performed in the other positions. After the puncture site and the path were chosen by US, overlying skin was cleaned. Local anesthetic (lidocaine-HCl) was given subcutaneously. Needle was advanced to lesion margin with free-hand technique under suspended respiration. Two types of needles were chosen for biopsies. Aspiration needles were preferred in large necrotic masses. In aspiration needle, stylet was withheld after seeing needle tip in the lesion. A 20-ml syringe was attached to the needle-hub, and the needle was advanced and withdrawn multiple times over a distance of 1 cm with rotating motion while maintaining continuous suction to the syringe. Cores were put into formalin if found in the material. Remaining material was injected and smeared onto slides, dividing them either air-dried or alcohol-fixated. Air-dried slides were stained with both May-Grünwald-Giemsa stain and Papanicolaou method, whereas alcohol-fixed slides were stained with Haematoxylin-Eosin. In cutting biopsies, core material was obtained and put into formalin fixation of 10%. Multiple passes with the needle were made until obtaining an adequate core. Any procoagulant agent was not injected along the needle track.

All inpatients were directly sent to their rooms whereas all outpatients were sent to home after at least 3 hours following the biopsy procedure in condition of no problem on observation. They were given a telephone number to call in case of any problem. Biopsy was repeated later if pathology report was insufficient material, and all of them were accepted as false negative.

Ethics considerations, follow-up, and analysis of results. Informed consent was obtained from each patient. All the data were obtained from our files and hospital electronic database system after taking permission of the institutional review board. We investigated the clinical, radiological, and laboratory examinations, follow-up records, complications, and pathological data. Diagnostic accuracy was evaluated with surgical diagnosis, if not, assessing clinical, radiological (US and CT), and laboratory findings with at least 6-month follow-up. Malignant and benign cytology which had the same diagnosis on surgery or on follow-up were accepted true positive and true negative; malignant and benign cytology which had different diagnosis on surgery or follow-up were accepted false positive and false negative, respectively. Successes were evaluated only after definitive diagnoses were determined. Successes of large and small needle groups were compared. Change in treatment was evaluated by dividing the patients avoiding nephrectomy with a true diagnosis to all the patients. This was applied to all patients in malignancy and only patients without any primary malignancy in benign lesions. Fuhrman nuclear grade has been recently be performed, for this reason, this could not be calculated in the study.

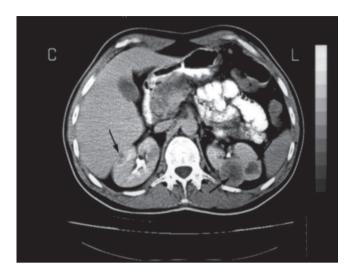


Figure 1. A contrasted CT shows small, diffuse pancreatic cystic lesions and bilateral hypodense solid renal masses with necrosis (arrows). Biopsy with 20G aspiration needle was obtained from the right kidney mass of maximum size 4 cm; renal cell carcinoma was diagnosed. This was confirmed with bilateral renal biopsies on operation. Diagnosis is von Hippel-Lindau syndrome.

Minor complications were hematuria and hematoma, if resolving spontaneously. Major complications were conditions requiring blood transfusion for bleeding, surgery, radiological intervention, also leading to sepsis, renal failure, and death, as in the literature [6]. Follow-up CT was performed every 6 months for control and seeding along the needle tract.

Statistics. Lesions were examined for any serious hemorrhagic complication. We evaluated the variables in affecting diagnostic yield, which were patient age, gender, right or left side, locations in kidneys (upper pole, lower pole, and other regions), necrosis, calcification, maximum tumor size, needle groups due to needle size and type, and number of needle pass. Their role in diagnostic yield was investigated after excluding patients diagnosed suspected malignant from the analysis and accuracy rates. All the masses were detected solid by US. Necrotic parts were defined as marked posterior acoustic enhancement whereas calcifications were marked posterior acoustic shadow. The largest size in any plane was accepted as maximum size. Two groups were divided with needle size and type: large needle group with 18G cutting needles and small needle group with 20G aspiration needles. Chi-square test, Student-t test, and binary logistic regression analyses were used for statistical analysis; p value of < 0.05 at 95% confidence interval was statistically accepted as significant. Predictor values were obtained at multivariable logistic regression analysis.

Results

The most frequent findings were lumbar pain and tenderness (n=83; 69.2%), anemia (n=32; 26.7%), hematuria (n=16;

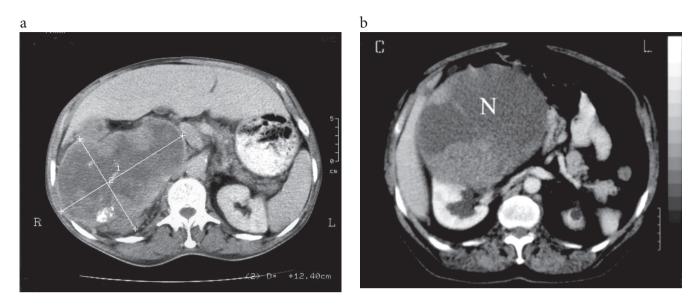




Figure 2. CT appearances of perirenal involvement are seen in various patients with renal cell carcinomas. a. CT in a patient shows solid hypodense mass with peripheral contrast enhancement, widespread necrosis, and calcifications in the right kidney. It also demonstrates that vena cava inferior is displaced. b. The same features of the former except calcifications are seen in the right renal mass of another patient. N: large necrosis. c. CT shows a necrotic mass (M) with peripheral contrast enhancement and apparent perirenal invasion (P) in the upper pole of the left kidney.

13.3%), and shortness of breath (n=5; 4.2%). 40-year-old male patient with operated cerebellum hemangioblastomas applied for cystic malformations of the pancreas and bilateral renal masses. The patient was diagnosed as von Hippel-Lindau syndrome (Figure 1).

Demographic features of 120 patients are summarized in Table 1. The mean maximum size of the solid renal masses was 8.8 ± 4.9 cm. Maximum size was < 3 cm in 9 (1 cm in 2), 3-6 cm in 35, and > 6 cm in 76 patients. Of them, 67 (55.8%) and 53 (44.2%) were in the right and left kidneys, respectively. Locations in kidneys were upper pole (n=50, 41.7%), lower pole (n=28, 23.3%), and other regions (n=42, 35.0%). Necrosis were detected in 38 (31.7%), calcification in 10 (8.3%), and >one needle pass in 35 (29.2%) patients. Needle pass in large needle

group was 2 (n=33 patients) and 3 (n=2) while the remaining biopsies had one needle pass. Table 2 and Table 3 show biopsy and surgical diagnosis of renal masses dividing as malignant or benign lesions, respectively.

Seventeen patients were inoperable due to poor medical conditions. Forty-seven renal masses had metastases in the other sites initially, in addition, 18 with primary malignity and 21 with invasion on imaging (Figures 2a-c). Three masses were seen in solitary kidneys, 2 operated due to renal cell carcinomas and one operated with renal tuberculosis. Bilateral renal masses were detected in 4 patients; 2 with lymphomas, both one with chronic pyelonephritis and hemorrhagic solidified cysts. The mean follow-up time was 9.4±13.4 months, range; 6-118 months. Follow-up times of small and large needle

Characteristics		Value
Age (years)		57.1±11.8 ª
Gender	Women	36 (30.0%) ^b
	Male	84 (70.0%)
Primary malignity	Negative	102 (85.0%)
	Positive	18 (15.0%)
Side	Right kidney	67 (55.8%)
	Left kidney	53 (44.2%)
	Upper pole	50 (41.7%)
Location	Lower pole	28 (23.3%)
	Other ^c	42 (35.0%)
Necrosis	No necrosis	82 (68.3%)
	Necrosis	38 (31.7%)
Calcification	Negative	110 (91.7%)
Calcincation	Positive	10 (8.3%)
Maximum size (cm)		8.8±4.9
Needle	Small aspiration	84 (70.0%)
Needle pass	Large cutting	36 (30.0%)
	1	85 (70.8)
	>1	35 (29.2%)

Table 1. Demographic features of 120 patients

^a Mean±2SD

^b Number (percent)

° Mid region and/or mixed regions

groups were $10.2\pm15,7$ months and 7.7 ± 4.2 months, respectively (p=0.189).

18 patients had primary malignancies; 2 had two primaries (one with lymphoma and nasopharynx carcinoma, the other with breast and ovary carcinomas). The remaining 16 had one primary malignity. Of them, 5 (27.8%) and 13 (72.2%) had benign and malignant renal masses, respectively. These 13 malignant renal masses were lymphoma (n=2), metastasis (n=3), and renal cell carcinoma (n=8). 13 of 15 patients (86.7%) and 75 of 92 (81.5%) with/without primary malignancies were accurately diagnosed, respectively.

The nondiagnostic cytology was detected in 15 of 120 lesions (12.5%). Nondiagnostic rates were 8.3% (3/36) in large needle group and 14.3% (12/84) in small needle group. The most frequent site of them was left kidney location, 12 (80.0%) vs. 3 (20.0%). Six patients underwent repeat biopsies (one with 2 repeat biopsies); nondiagnostic biopsies (n=3), renal cell carcinomas (n=2), and benign (n=1).

Among 120 patients, 15 (12.5%) and 105 (87.5%) had benign or malignant solid masses, respectively. Among 105 patients, 95 patients (90.5%) and 10 patients (9.5%) were diagnosed as renal cell carcinoma and other malignancies, respectively. Renal cell carcinomas were clear cell type (n=86 patients), chromophobe type (n=3), and papillary type (n=6). Other malignancies were non Hodgkin lymphomas (n=3) and metastases (n=7). Fifteen of 95 patients with renal cell carcinomas went through radical nephrectomies whereas none of the other malignancies experienced operation. In-

Table 2. Diagnostic correlation of 120 renal tumors in biopsy cohort

Costale visul must	Diagnosis		T-4-1	
Cytological results	Benign	Malignant	Total	
Benign	15 (78.9%) ^a	4 (21.1%)	19 (15.8%)	
Indeterminate ^b	0 (0%)	13 (100%)	13 (10.8%)	
Malignancy	0 (0%)	73 (100%)	73 (60.8%)	
Nondiagnostic	0 (0%)	15 (100%)	15 (12.5%)	
Total	15 (12.5%)	105 (87.5%)	120 (100%)	

^a Number (percent)

^b Atypical lymphoid cells or suspected malignant

Table 3. Surgical correlation of biopsy cohort in 16 renal tumors

Cytological results	Surgical diagnosis		Total	
	Benign N			
Benign	1 (50.0%) ^a	1 (50.0%)	2 (12.5%)	
Indeterminate ^b	0 (0%)	4 (100%)	4 (25.0%)	
Malignancy	0 (0%)	8 (100%)	8 (50.0%)	
Nondiagnostic	0 (0%)	2 (100%)	2 (12.5%)	
Total	1 (6.3%)	15 (93.8%)	16 (100%)	

^a Number (percent)

^b Atypical lymphoid cells or suspected malignant

stead, they were treated with chemotherapy. Fifteen benign masses were oncocytomas (n=2), hematomas (n=4), type 4 hydatid cyst (n=1), infections (n=3, one pyelonephritis and 2 other), and other benign lesions (n=5). One patient with primary uroepithelial carcinoma of bladder was operated for the left kidney mass; his diagnosis was oncocytoma in operation similar to the biopsy. Sixty-six of 95 renal cell carcinomas were accurately diagnosed as malignant whereas 12, 13, and 4 were suspected malignant, nondiagnostic, and falsely benign in biopsies, respectively.

Nephrectomy was avoided in 58 non operated renal cell carcinomas with a malignant diagnosis. Eight of non operated other 10 malignancies were correctly diagnosed. Ten of 15 patients with definite benign masses had no primary malignity. So, clinical management was altered by avoiding operation in total 76 of 120 (63.3%) patients, which were 58 renal cell carcinomas, 10 benign lesions without any primary malignity, and 8 other malignancies,.

Variables affecting accuracy in 107 patients are seen in Table 4 after excluding 13 suspected malignancies. The only predictor affecting accuracy was side of involved kidney (p=0.002). Small and large needles did not differ in accuracy, as 80.3% vs. 87.1% (p=1.000). Sensitivity and negative predictive values were 77.6% and 37.5% in small needles and 84.0% and 60.0% in large needles, respectively. Technical success was detected 100%. Positive and negative predictive values, sensitivity, specificity, and accuracy rates were detected as 100% (73/73), 44.1% (15/34), 79.3% (73/92), 100% (15/15),

suspected mang	inumeres			
Variable		True	False	p valueª p value ^b
Age (years)		56.7±11.6°	56.7±15.2	0.998^{a} 0.352^{b}
Gender	Women	27 (81.8%) ^d	6 (18.2%)	0.939ª
	Male	61 (82.4%)	13 (17.6%)	0.884^{b}
Side	Right kidney	54 (93.1%)	4 (6.9%)	0.001 ^a
	Left kidney	34 (69.4%)	15 (30.6%)	0.002 ^b
	Upper pole	34 (77.3%)	10 (22.7%)	0.0014
Location	Lower pole	19 (79.2%)	5 (20.8%)	0.301ª 0.350 ^b
	Other	35 (89.7%)	4 (10.3%)	0.550
Necrosis	No necrosis	61 (84.7%)	11 (15.3%)	0.336ª
	Necrosis	27 (77.1%)	8 (22.9%)	0.811^{b}
Calcification	Negative	81 (82.7%)	17 (17.3%)	0.659ª
	Positive	7 (77.8%)	2 (22.2%)	0.926 ^b
Maximum size		8.6±5.0	9.5±4.9	0.472ª
(cm)		0.0±3.0		0.481^{b}
Needle	Small aspiration	61 (80.3%)	15 (19.7%)	0.401ª
	Large cutting	27 (87.1%)	4 (12.9%)	0.785 ^b
Needle pass	1 pass	62 (80.5%)	15 (19.5%)	0.455ª
	>1 pass	26 (86.7%)	4 (13.3%)	0.807^{b}

Table 4. Variables affecting accuracy in 107 patients after excluding 13 suspected malignancies

^a Univariate p value (upper value)

^b Multivariable p value (lower value)

^c Mean±2SD

^d Number (percent)

and 82.2% (88/107), respectively. Also, false negative and false positive rates were 55.9% (19/34) and 0% (0/73), respectively. Any major complication and tumor seeding was not seen in the series.

Discussion

Traditionally, imaging-guided percutaneous biopsy has played a limited role in the treatment of suspicious renal masses because the safety, reliability, and accuracy of this procedure have been questioned and understudied [2]. In some cases, such as small incidental tumors, locally advanced or metastatic renal cell carcinomas and other metastatic malignancies, pretreatment evaluation could be useful for appropriate management [5].

A 10% to 22% incidence of benign tumors has been reported in several studies [7]. One large surgical series of 2,770 patients showed that 13% of all renal masses treated by radical nephrectomy were benign and 46% of renal masses smaller than 1 cm were benign [8]. These benign incidence rates were found 12.5% in all tumors of the present series and 50% if their sizes < 1 cm.

It is recommended for biopsy of patients with solid renal tumors that do not have the typical radiologic features of renal cell carcinoma and that do not require surgery, such as renal metastases, lymphomas, and benign tumors [5]. An exact tissue diagnosis may be valuable preoperatively, and biopsy results change clinical management in many cases [9]. If a preoperative diagnosis could be made with certainty some patients, such as those with significant co-morbid conditions and those with large benign renal masses who would normally undergo radical nephrectomy, would be better served with a nephron sparing operation or nonoperative management [7].

In the last decade, there has been renewed interest in nephron sparing operations for appropriately sized solid renal masses because it is well recognized that not all solid renal masses are malignant and radical excision is not always necessary for satisfactory long-term results [7]. The information provided by biopsy has altered management in 60% rate in Maturen et al.'s series as an important and substantive change in the care of many patients, particularly those who avoid nephrectomy by means of biopsy diagnosis [3]. This alteration which significantly impacted treatment method was at a similar rate of 63.3% in our study.

However, the negative predictive value of percutaneous biopsy is not as high; a range of values, from 38% to 100% has been reported, depending on the method of imaging guidance, biopsy needle gauge, and size of renal mass [8]. Nevertheless, we found this rate as 44.1% in low limits and detected at higher rate in large needles than small needles, 60% vs. 37.5%. The low negative predictive value implies that negative results should be handled suspiciously and leads to re-evaluation of the patient's status and risk for malignancy and consideration of resection of the mass as opposed to continued clinical and imaging follow-up [10]. We reached at malignant definite diagnoses in this manner. Among 19 false diagnoses, 3 patients were operated and diagnosed as malignant, as well.

Reported percutaneous biopsy techniques have mainly involved fine-needle aspiration [2]. Up to 60% of fine needle aspirations have an insufficient amount of material for pathologic analysis [2]. Our low negative predictive value has been mainly caused by nondiagnostic cytology of 12.5%. Recent investigations using core needle biopsy have shown high accuracy rates, while no statistically significant difference was detected in diagnostic yield in a series [8]. Our nondiagnostic cytology was to some extent higher in small needles than large ones, 14.3% vs. 8.3%. We consider that this could be caused from that cytopathologist was not present in any biopsy procedure. Core biopsy was reported slightly more sensitive than fine needle aspiration in a series [9], similarly, this was seen in our series. In this condition, we recommend 18G needles for relatively high negative predictive value.

Other known limitations of aspiration include the inability to diagnose oncocytomas and angiomyolipomas, two benign solid renal neoplasms that on occasion can mimic renal cell carcinoma [2]. We successfully used 18G cutting needles in oncocytomas, also did not experience biopsy in any angiomyolipoma because of mainly high predictive value of imaging (US and CT) in this entity. Immunocytochemistry, immunophenotyping, and molecular techniques have been well recognized to aid in the diagnosis [12]. They provide a distinction between oncocytoma and angiomyolipoma, as well. Advances in monoclonal antibody technology have also had a major impact on the ability to diagnose and classify renal neoplasm [8]. Novel technologies have increasingly been used in the other tumors, e.g. to evaluate nodal status in the papillary thyroid cancer with reverse transcription – polymerase chain reaction [12]. Similarly, more sensitive markers would inevitable improve the sensitivity and negative predictive value of percutaneous renal mass biopsy [11].

The high sensitivity (90%) of the biopsy results in patients with a known primary cancer strongly supports the use of percutaneous renal mass biopsy to identify those patients with renal cell carcinoma who need surgery [11]. Likewise, our results compare favorable with this conclusion. Diagnosing primary malignancy or metastasis, we determined whether chemotherapy or surgery could be indicated in these patients. Also, high sensitivity of percutaneous renal biopsy was reported in patients who were not surgical candidates whose imaging findings suggested a resectable renal cell carcinoma [11]. This was observed in our study, as well.

Some authors have noted diminished sensitivity for the detection of malignancy and loss of accuracy in tumor grading in small lesions (< 3-4 cm) and in predominantly cystic lesions [3, 5, 10, 11]. Lechevallier et al. reported that the median size of the tumors in which biopsy failed was significantly lower than that of the tumors in which biopsy results were positive [5]. They attributed the failures to the mobility of small tumors, which were pushed away by the biopsy needle instead of being penetrated by it [5, 10]. Nevertheless, we did not find size as a predictor in accuracy; this may be caused from small number of < 3 cm tumors. Also, accuracy can be reduced in large (> 6 cm) tumors because of necrosis. This may possibly be due to sampling error, described as in the literature [11].

Age, gender, necrosis, calcification, location in kidney, and number of needle pass were not detected as predictors in accuracy. Upper lobe location led to slightly more false results, but this did not reach at a significant level. The only predictor of the series was location of left kidney. Difficulty in left renal biopsy may have a role in this low accuracy, although upper lobe location was not detected efficient in accuracy. We propose this should be examined prospectively, although a prior study did not find side of kidney as predictor [5]. We believe that US guidance can mostly be performed rather than CT guidance in left upper pole tumors. But, CT guidance can be selected in repeat biopsy after a nondiagnostic result.

Renal biopsy related complications have been described in as many as 13% of patients, the rate of minor complications being 6.6%, the rate of major complications, 6.4%, and the mortality 0.1% [6]. Also, perinephric hematoma has been found 24-72 hours after biopsy in more than 90% of cases evaluated prospectively [6].

Any major complication and mortality was not recorded in the present study. Minor subcapsular bleeding has been reported in recent series where control CT was routinely taken after biopsy [10]. We did not perform CT in this way, so minor hemorrhagic complications could not be documented. Instead, we observed patients 3 hours after biopsy without CT if any sign or symptom was not found. This may lead to complication rate to be found at a lower rate. Conversely, routine post-procedure or delayed imaging might reveal higher rates of hemorrhage, but without compromise of hemodynamic stability the clinical significance is questionable [3].

Needle seeding is a very rare complication and is mostly reported with transitional cell carcinoma [10]. We did not detect any seeding on routine control CT. This can be caused from that no transitional cell carcinoma was not found in the series and that we approached directly by avoiding tracts traversing other organs, described as in the literature [10]. In fact, seeding is very rare complication in spite of frequently discussed [8].

Our restriction is that retrospective nature of study has potential limitations in which surgery was not mostly performed in benign lesions since avoiding it and follow-up times were relatively low. Minor complications may not be verified due to not performing control CT immediately after biopsy. The other restriction was the absence of tumor grading in renal cell carcinoma

In summary, percutaneous ultrasonography-guided needle biopsy of solid renal masses is effective and safe method with large size cutting needles and small aspiration needles. Change in clinical management was 63.3% by avoiding nephrectomy. Diagnostic yield was low in left kidney relating to right kidney, 69.4 vs. 93.1, while upper lobe location did not lead to significant false result. Repeat biopsies can be taken under CT guidance after nondiagnostic yield in solid tumors of left kidney. All the needles including large cutting type was found safe.

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