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Percutaneous image-guided core biopsy of solid renal masses: analysis of safety, efficacy, pathologic interpretation, and clinical significance

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Abstract

Purpose: To determine the efficacy, safety and clinical utility of CT and US-guided percutaneous renal mass biopsy.

Materials and methods: A retrospective IRB-approved, HIPAA-compliant study of a cohort of 183 consecutive patients who underwent percutaneous, CT or US—guided renal mass biopsy (RMB) from March 2002 through December 2012 was performed. RMB was performed in 183 consecutive patients for suspected solid renal mass of whom 14/183 (7.7%) were excluded because biopsies were performed at an outside institution, medical records were incomplete, or lesions were poorly visualized. Ten patients had multiple biopsies for new growing masses. Using US, CT or CT/US fusion-guidance, a 17G or 19G cannula needle was placed at the margin of the mass and an 18G or 20G core biopsy gun was used to obtain several tissue cores. Renal parenchymal biopsies for medical renal diseases were excluded. Imaging variables (including size, location, and extent of disease), number of core biopsies, patient demographics (age, gender), clinical indication, final pathologic diagnosis, immunohistochemical (IHC) studies, and subsequent final pathological diagnosis on nephrectomy were evaluated.

Results: Of the 169 patients with 184 RMB, 121/169 (71.6%) were male with a mean age of 67.5 years. Of 184 RMB, 126 were malignant [126/184 (68.5%)], 37 [37/184 (20.1%)], were benign, and 21 (21/184 (11.4%) were nondiagnostic. IHC was performed in 131 biopsies (71.1%) and was diagnostic in 88.5% of those cases. Twenty-eight patients underwent subsequent partial nephrectomy; in 27/27 (100%) cases, RMB was concordant with nephrectomy for malignancy and in 21/27 (77.8%) RMB was concordant for subtype of RCC. Overall, the RMB sensitivity for detection of malignancy, specificity, and positive predictive value were 100%. The negative predictive value of benign RMB diagnosis was also 100%. There was a total of 14 (7.6%) complications, 13 minor (7.1%) and 1 major (0.5%). Of the minor complications, ten (5.5%) were postprocedural minor hematomas that resolved conservatively; one (0.5%) postprocedural vasovagal reaction; one (0.5%) episode of hematuria; and one (0.5%) episode of nausea and abdominal discomfort. No cases of renal pseudoaneurysm or tumor seeding attributed to biopsy were identified.

Conclusion: Percutaneous image-guided RMB is safe and highly diagnostic when combined with IHC and supports a greater role of RMB and imaging in evaluating renal masses when rendering appropriate treatments.

Key words: Renal mass biopsy—Renal cell carcinoma—Intervention

Institutional Review Board approval was obtained for this HIPAA-compliant retrospective study.

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In the landmark 2003 study by Frank et al., 12.8% of 2770 resected solid renal masses were benign [1]. The proportion

of benign lesions increased with decreasing mass size; 25% of lesions less than 3 cm, 30% of lesions less than 2 cm, and 44% of lesions less than 1 cm were benign. Thus, up to 20% of small renal masses <4 cm are benign. Renal mass biopsy (RMB) has been advocated to improve preoperative triage for solid renal masses especially those undergoing surgery [2]. The diagnosis of renal tumors is increasing by 2% per year with a incidence of 65, 150 new cases and mortality of 13, 680 deaths estimated in 2013 in the United States; nearly a quarter of these lesions are 3 cm or smaller, and less than 20% are metastatic at diagnosis [3–5]. Traditional single phase imaging protocols have been considered unreliable for characterization, although more recent studies evaluating multiphasic scans for RMB characterization have been promising [6]. Traditionally all solid renal masses were assumed to be renal cell carcinoma (RCC), one of the only solid abdominal masses that did not rely on tissue diagnosis prior to resection. However, up to 25% of nephrectomies are performed for benign disease [7, 8]. This algorithm is changing, and it is increasingly being recognized that prognosis and clinical behavior of malignant lesions are dependent on histologic subtype while benign lesions may be safely followed [9].

Historically, the role of percutaneous renal biopsy has been limited, mainly useful for diagnosing lymphoma, metastatic disease, or patients with increased surgical risk, and by concerns about its safety and accuracy [7, 10]. In the past, critics of RMB have cited a variety of problems including low diagnostic yield, sampling error, and poor correlation with final pathology, arguing that potential risks and complications did not justify the poor yield [7, 11–15]. However, with the development of new pathological techniques such as immunohistochemistry (IHC), diagnostic yields have improved, while complications such as bleeding, and tumor seeding have been rare [10].

In this study, we report our experience with percutaneous image-guided core renal mass biopsy (RMB) with focus on assessment of diagnostic accuracy of our technique combined with immunohistochemical stains (IHC) and impact on clinical management.

Materials and methods

Patients

With Institutional Review Board approval for this HIPAA-compliant retrospective study, we queried our institution's pathology database to derive all solid renal mass biopsies from March 2002 through December 2012. The inclusion criteria were that biopsies and any prior imaging were to be performed at our institution. During the study period, 183 patients underwent percutaneous biopsy of solid renal masses prior to ablation or surgery. Of this cohort, 14 (7.7%) patients were excluded: 6 patients had incomplete records, 5 patients had biopsies performed at outside institutions, 2 patients had no biopsies performed following poor visualization of the mass at the time of procedure, and 1 patient had a biopsy of a non-solid renal mass. In the remaining 169 (91.8%) patients, 184 biopsies were performed. Ten patients had up to 4 additional biopsies, each for a new renal mass. Demographic data were recorded and summarized in Table 1. Imaging variables included size, location and extent of disease, clinical indication, needle gauge,

Table 1. Demographic and clinical information of 184 renal masses

Characteristic	Value
No. of patients queried	183
No. of patients included in study	169
Age (years)	
Mean	67.5
Range	33–93
Gender (male:female ratio)	121 (71.6%):48 (28.4%)
No. of patients who underwent repeat biopsy	10
Bilateral masses	3
Recurrence status post ablation	7
Maximum tumor diameter (cm)	
Mean	3.1
Range	0.7–11.3
Renal mass location	
Left kidney	91 (49.5%)
Right kidney	89 (48.4%)
Transplant	4 (2.2%)
Mean number of cores biopsies	3.8
Biopsy technique	
No. of biopsies with prior recorded imaging results	151 (82.1%)
CT guidance	95 (62.9%)
MR guidance	56 (30.4%)
No. of biopsies with imaging unavailable	33 (17.9%)
No. of biopsies with 17/18 coaxial system	35 (21.6%)
No. of biopsies with 19/20 coaxial system	127 (78.4%)
IHC	
No. of biopsies with immunostains	131 (71.2%)
No. of biopsies without immunostains	53 (28.8%)

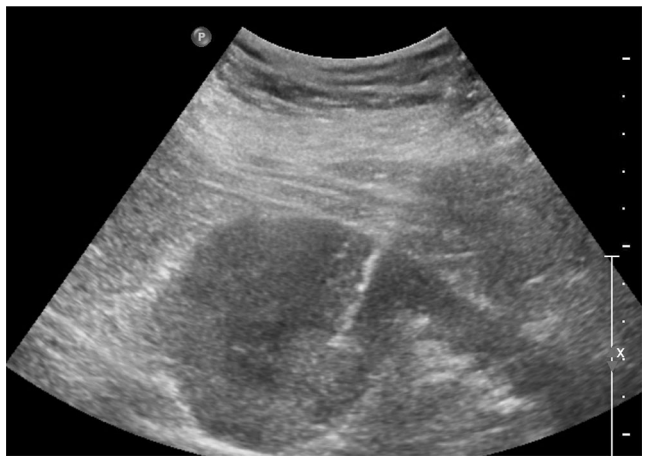

Fig. 1. 65 year old woman found to have incidental bilateral renal masses on cross sectional imaging for evaluation of a urinary tract infection. Ultrasound obtained during biopsy with the patient in anterolateral position shows introducer needle penetrating mass. Biopsy of the right renal mass revealed Fuhrman grade II clear cell renal cell carcinoma.

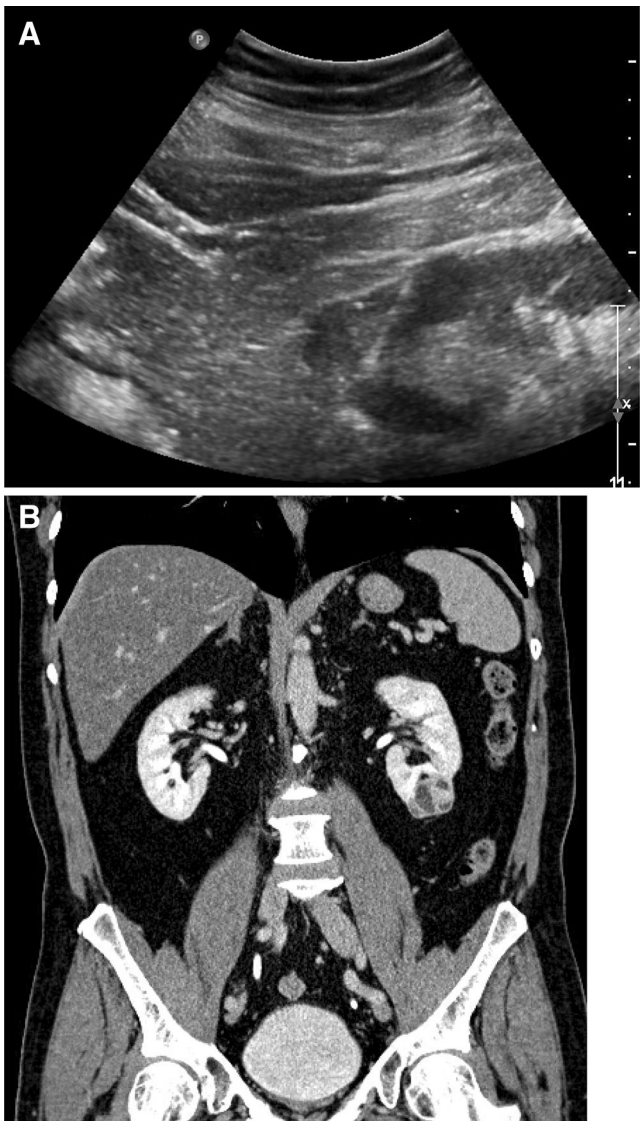

Fig. 2. **A** 72-year-old man with monoclonal gammopathy and thyroid cancer found to have questionable left renal mass arising from the inferior pole on surveillance imaging. Ultrasound of the left kidney demonstrates the introducer needle in within the lesion. Biopsy of the mass was nondiagnostic as benign renal parenchyma was found on the pathologic specimen. **B** Coronal contrast-enhanced CT demonstrates a mixed solid and cystic enhancing renal mass arising from the left inferior pole. Subsequent follow-up ultrasound and cross sectional imaging demonstrated stability of the lesion for 3 years.

number of core biopsies taken, and the histopathologic subtype of the primary tumor. For patients who underwent nephrectomy, the pathologic diagnosis was recorded. For patients who did not undergo surgery, the subsequent treatment, such as radiofrequency ablations or chemotherapy, was recorded. Patients with metachronous multifocal lesions were included if new lesions were biopsied or resected. Biopsy results were compared with surgical or clinical follow-up (Figs. 1, 2, 3).

CT/US guided biopsy

Informed consent was obtained from patients, and risks including bleeding, infection, and seeding were discussed. Prior to the procedure, platelet counts and coagulation status were checked to be $>50{,}000/\text{mm}$ [3] or INR <1.5, respectively, at the time of biopsy. Biopsies were generally performed with patients under conscious sedation except when performed with radiofrequency ablation, for which general anesthesia was used. All biopsies were performed using standard sterile techniques and local anesthesia. Biopsies were generally performed under real time ultrasound (US) guidance alone or in combination with intermittent CT guidance or in a few cases with US–CT fusion guidance (PercuNav, Philips Medical Systems). During the duration of the study, a variety of CT and US scanners were used. Patient position depended on the location of the mass with the patient typically placed prone for posterior lesions or in the lateral decubitus position for anterolateral lesions.

Using real time US guidance, the 17G or 19G introducer needle was advanced to the margin of the lesion and a 18G or 20G core biopsy gun was used to obtain several (usually 4–5) tissue core biopsies. When possible, the outer cannula was guided to the margin of the mass via the renal parenchymal approach. After the cores were acquired, two to three 0.5 cm gelfoam pledgets were advanced through the introducer needle to obtain hemostasis. The core biopsies were sent to pathology for further analysis. All patients were hemodynamically monitored in the postprocedural recovery room for at least 3 h and any complications were recorded. Imaging was not routinely performed for postprocedural hematomas, but all episodes of hemorrhage identified by postprocedural imaging or by clinical symptoms were reported in complications. Subsequent imaging was used to review any delayed complications including tumor seeding. Complications were categorized per the guidelines published by the Society of Interventional Radiology [16]. Minor complications were defined as those resulting in self-limited gross hematuria or perinephric hematoma that was managed conservatively. Major complications were those requiring further intervention such as transfusion of blood products or any angiography and embolization, surgery, acute renal obstruction or failure, sepsis, or death [16].

All specimens were prepared with hematoxylin and eosin (H&E) staining and 131 of the 184 (71.1%) adequate specimens also underwent immunohistochemical (IHC) staining. The decision to perform immunohistochemical staining was made by the reviewing pathologist. For this study, diagnostic samples were interpreted as benign if a specific benign diagnosis was made and as malignant if a specific malignant diagnosis was made. The remainder was classified as nondiagnostic if normal

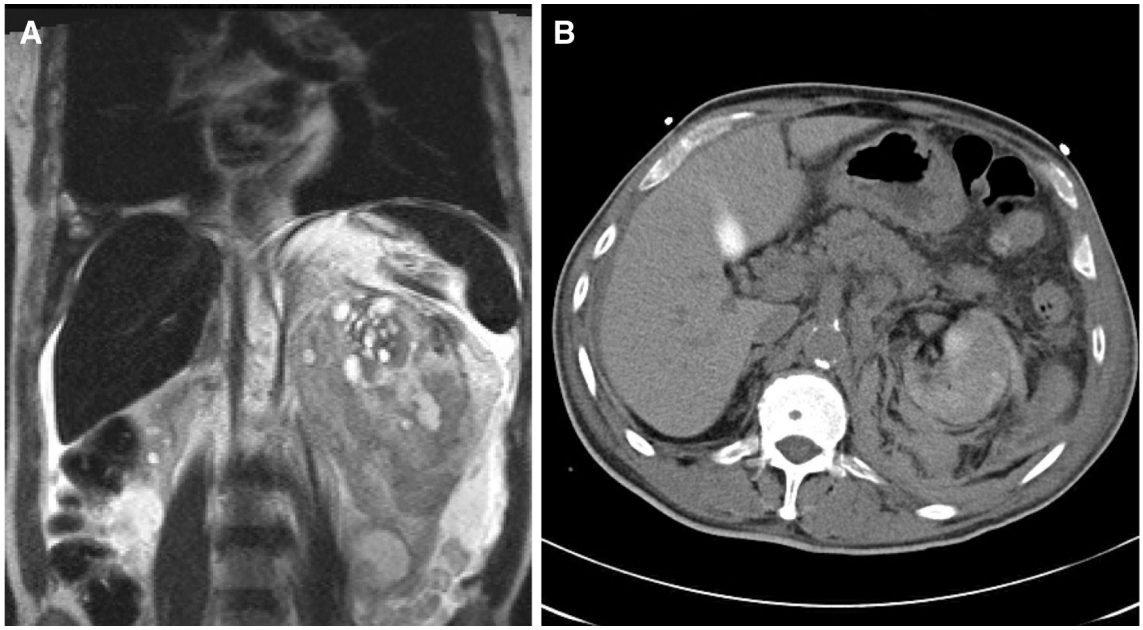

Fig. 3. 63-year-old man with chronic renal failure, on hemodialysis found to have left renal mass on prior CT. Patient had undergone percutaneous US/CT guided biopsy and ablation. **A** Delayed MRI was obtained given the patient's unstable hemodynamics in the postprocedural recovery room. Coronal T2 HASTE image shows 10 × 12 cm left sided intraparenchymal/retroperitoneal hematoma. The patient then underwent a left renal angiogram, which revealed a small arteriovenous fistula that was subsequently embolized. **B** Noncontrast axial CT demonstrating large left renal intraparenchymal hematoma with extension into the retroperitoneum.

renal parenchyma was obtained or if the amount of tissue was inadequate to render a pathologic diagnosis.

Statistical analysis

Sensitivity, specificity, positive predicative value (PPVs) and negative predicative value (NPVs) were calculated for core biopsies. In patients undergoing surgery, post-biopsy histopathologic results were compared and biopsy accuracy was determined.

Results

Subjects

Of the 169 patients, 121 (71.6%) were male and 48 (28.4%) were female with a mean age of 67.5 years (range 33–93 years). In 169 patients, 184 renal mass biopsies were performed; ten patients had between 2 and 4 renal mass biopsies for metachronously arising masses. These 184 RMBs were performed using coaxial 18 or 20-gauge core needle technique; patient and mass characteristics are summarized in Table 1. Furthermore, 131 biopsies (71.1%) had immunohistochemistry, which was much more common in the past 7 years. All renal masses arose in native kidneys except for 4 lesions that arose from transplant kidneys.

Sensitivity for detection of malignancy

In 184 renal mass biopsies, 126 (68.5%) were diagnosed as malignant, 37 (20.1%) were benign, and 21 (11.4%) were nondiagnostic (Table 2). The benign biopsies included 24 (13.0%) oncocytomas, 6 (3.2%) lipid poor angiomyolipomas, 5 (2.7%) fibrosis, and 2 (1.1%) inflammations (Table 2).

In 11.4% of cases, biopsy samples were considered pathologically nondiagnostic either due to insufficient tissue (4.3%) or sampling of benign renal parenchyma (7.1%) Lesion size for these nondiagnostic samples ranged from 1.4 to 5.5 cm (average 2.6 cm). No difficulties were noted at the time of biopsy in these cases. Furthermore, nearly all patients underwent radiofrequency ablation concomitantly after biopsy and no repeat biopsies were performed. No new lesions subsequently arose in these patients during the follow-up period.

In 28 patients who underwent partial nephrectomy after biopsy, 27/27 (100%) masses diagnosed as malignant on biopsy were also confirmed to be malignant on the partial nephrectomy specimen. In this subset, the sensitivity, specificity, and positive predictive value for detection of malignancy was 100%. In 21/27 (77.8%) cases, biopsy was concordant with the surgical specimen for subtype of RCC. In 2 cases, RMB diagnosis of clear cell RCC was changed to papillary type 2 and in one

Table 2. Results of 184 renal mass biopsies

Biopsy result	No. of cases
Total	184
Malignant biopsies	126 (68.5%)
RCC	116 (63.0%)
Clear cell	85 (46.2%)
Papillary, type 1	15 (8.2%)
Oncocytic neoplasm	5 (2.7%)
Not otherwise specified	4 (2.2%)
Chromophobe	3 (1.7%)
Papillary, type 2	2 (1.1%)
Clear cell-papillary RCC	1 (0.5%)
Collecting duct	1 (0.5%)
Sarcomatoid features	1 (0.5%)
Lymphoma	5 (2.7%)
Metastases	2 (1.1%)
Carcinoma not otherwise specified	1 (0.5%)
Urothelial cancer	1 (0.5%)
Benign biopsies	37 (20.1%)
Oncocytoma	24 (13.0%)
Angiomyolipoma	6 (3.2%)
Fibrosis	5 (2.7%)
Inflammation	2 (1.1%)
Nondiagnostic biopsies	21 (11.4%)
Inadequate tissue	8 (4.3%)
Renal parenchyma	13 (7.1%)

Table 3. Complications from 184 renal mass biopsies

SIR complication classification	No. of cases
SIR complications	14/184 (7.6%)
Major	1/184 (0.5%)
Retroperitoneal hematoma requiring IR embolization	
Minor	13/184 (7.1%)
Postprocedural hematomas	10 (5.5%)
Episodic hematuria	1 (0.5%)
Vasovagal reaction	1 (0.5%)
Nausea/abdominal discomfort	1 (0.5%)

case, RMB diagnosis of papillary type 1 RCC was changed to unclassified RCC. In one case, biopsy diagnosis of unclassified RCC was changed to clear cell RCC; while in another case, the initial diagnosis of unclassified RCC on biopsy was changed to chromophobe. One case of RMB was changed from papillary type 1 RCC to papillary type 2.

In one of the 28 biopsied cases with surgical pathology, core biopsy initially showed predominantly fibrous tissue with focal areas of myxoid change. Microscopic differential diagnosis included normal kidney vs. oncocytoma but no pathologic diagnosis was offered due to insufficient amount of tissue. At partial nephrectomy, the resected lesion was diagnosed as a solitary fibrous tumor. No benign RMB was subsequently proven malignant and the negative predicative value of a benign biopsy to exclude malignancy was 100%.

Complications

Complications occurred in 14 of 184 (7.6%) cases (Table 3); 1 (0.5%) major and 13 (7.1%) minor. One patient (0.5%) (Table 3) with end stage renal disease on hemodialysis who underwent concurrent RFA with RMB for 2 cm left renal mass experienced a retroperitoneal hematoma requiring transfusion and arterial embolization of a post-procedure arteriovenous fistula. One month follow-up imaging revealed resolution of the retroperitoneal hematoma and no evidence of arteriovenous fistula.

Thirteen patients (7.1%) had minor complications based on the SIR classification. Of these patients, ten (5.5%) had postprocedural hematomas, all of which were managed conservatively. On follow-up, there were no reports of tumor seeding in the areas of hematoma. Contrast-enhanced postprocedural MRIs were obtained in all patients with postprocedural hematomas and were reviewed prior to patient discharge to fully assess the extent of devascularization and confirm stability of the collection. Follow-up clinic visits with MR renal imaging in 1 month showed resolution of hematomas in these cases.

One patient (0.5%) experienced episodic hematuria in the recovery room and was observed overnight prior to discharge. One patient (0.5%) had postprocedural lightheadedness and another (0.5%) experienced postprocedural nausea and abdominal discomfort that resolved without intervention.

Discussion

The role of percutaneous image-guided renal mass biopsy has evolved considerably with a decrease in traditional controversy due to questions over its sensitivity, reliability, and safety for detection of malignancy. Traditionally, patients underwent surgical resection of non-fatty renal masses though nearly 20–30% of surgically resected stage T1a masses are histopathologically benign [8, 14]. In this study, we reviewed our institutional experience of percutaneous image-guided core needle biopsy for diagnosis of renal masses and found it to be highly effective with a very favorable risk profile. Almost 90% of all lesions biopsied yielded a definitive diagnosis.

We found that percutaneous image-guided RMB had a sensitivity and specificity of 100% for detection of malignancy, and compared favorably with contemporary series (range of 89–100% sensitivity) [3, 7, 17–19]. These results also refute older studies that reported poor sensitivity of fine needle aspiration (FNA) for the detection of malignancy (as low as 50%) and a high rate of nondiagnostic biopsies (up to 33%) [7, 13, 15]. Our results are due to many factors including improved CT and/or US guidance technologies, operator experience, and improved biopsy techniques, larger sample size obtained with increased use of 18- or 20-gauge core biopsy needles, use of coaxial technique, and advances in pathological and IHC analysis [7]. In our series, percutaneous image-guided renal mass biopsy was diagnostic in 88.5% of

cases. Using surgical specimen as reference standard, 100% of malignant biopsy specimen were accurately confirmed as malignant on surgical specimen with over 76.9% concordance between biopsy and surgical subtyping of RCC.

In our series, we had 21 nondiagnostic biopsies with a wide range of sizes. No discrete pattern for these failures was observe, unlike that previously reported in several studies where smaller lesions (<3–4 cm) had worse diagnostic outcomes [7, 13]. One of the main arguments against routine biopsy has been the high rate of nondiagnostic material reported in older studies [8]. However, based on our study and several other more recent studies, true false negatives are uncommon and in these cases, one could consider re-biopsy, given the low rate of complications. In the Wood study, a 6% false negative rate was reported in 79 biopsies while in the Neuzillet study a 5.6% false negative rate was reported in 56 biopsies [17, 20]. Most of these false negative results may be attributed to insufficient tissue material. Patient management was altered due to biopsy results in over 40% of patients in both studies [17, 20].

Another common argument against percutaneous core biopsy is missing high grade tumor due to lesion heterogeneity [21]. Routine H&E staining is less useful in differentiating among eosinophilic tumors with limited tissue samples. The use of immunohistochemical stains improves diagnostic specificity and in distinguishing among RCC subtypes. For example, Shah et al. described malignant lesions with areas of classic oncocytic features occurring chromophobe or type 2 papillary RCC subtypes. In such cases, they recommended the use of Hale's colloidal iron and contemporary IHC panel, in particular IHC analysis for cytokeratin 7 in adequate samples, to support their impression of oncocytic neoplasm, favoring oncocytoma with the caveat that rarely areas mimicking oncocytoma may occur in some RCCs [22]. In the series by Lebret et al., the correlation between histological diagnoses on biopsy and in surgical specimens was 86%. They cite advances in IHC studies allowed for better identification of specific tumors, namely for clear cell RCC, (pancytokeratin+, vimentin+, CD10+, EMA+ and CK7±), chromophobe RCC (Hale+, CK&+, P504S+, EMA+, CD10± and vimentin), and oncocytoma (CK7-, pancytokeratin± and EMA±) [23]. Furthermore, in their series, they found that cases of eosinophilic tumor IHC positivity with P504s, CK7 and vimentin is specific for papillary RCC; a CK7 and CD117 positivity profile was observed in chromophobe RCC; and a vimentin and CD10 positivity profile was noted with clear cell RCC. Moreover, they observed weaker Fuhrman nuclear grade correlation (0.46) of biopsy results with surgical specimens [23]. In our series the use of contemporary IHC panels was diagnostic of malignancy in 88.5% of biopsies and was useful in correctly subtyping RCC in 77.8% of patients (21/27) who underwent nephrectomy and is in alignment with previous reported conclusions in literature [23]. With advances in cytology, cytogenetics and immunocytochemistry, percutaneous renal mass biopsy can correctly subtype RCC at rates of 91% with core biopsy and 85% with fine needle aspiration thus supporting the case that biopsies are adequate for rendering a definitive diagnosis in most cases of renal mass lesions when indicated [3, 17, 24–27].

Our experience also shows that renal mass biopsy is safe with a major complication rate of 0.5% and a minor complication rate of 7.1%, most of which were self-limited hematomas, requiring no escalation of care [7, 13]. One patient with underlying renal failure and possible secondary coagulopathy did experience delayed retroperitoneal hemorrhage bleed secondary to arteriovenous fistula formation following radiofrequency ablation after biopsy. Our standard procedure is to generally keep the patient for at least 6 h of observation, following biopsy and ablation with imaging. None of the patients experienced any other long-term complications, namely tumor seeding in surgical pathology specimens or on follow-up imaging or pseudoaneurysmal formation. The risk of bleeding and hematomas was minimal in our series and may be minimized with the use of 19G needles and gelfoam embolization of the tract after biopsy [28]. Tumor tract seeding is of special interest given that many critics cite the fear of seeding to avoid biopsy. Although tumor seeding has been in one much older study, [29] no contemporary recent studies have reported tumor seeding complications after long follow-up [3, 7, 17, 20, 30]. The risk of needle track seeding is increased with biopsy of transitional cell carcinoma and may occur more often with non-cutting needles than with cutting needles. [8] In our coaxial biopsy technique, the 19G outer cannula needle is inserted through normal kidney when possible to the margin of the mass, enabling only the inner biopsy gun to sample mass without tracking cells outside the mass. Others have also argued that coaxial techniques may aid in preventing tumor seeding outside Gerota's fascia [3, 7].

Limitations of the study include the absence of surgical confirmation on all the biopsies. However, the subset of patients with surgical specimen was highly correlated, and thus, this may reflect the possible accuracy of the remaining cohort with no surgical specimen. Second, it is possible that the number of complications was under assessed due to the lack of non-routine post-biopsy imaging, a limitation noted in other studies [23]. Thus, asymptomatic intrarenal hematomas and other similar complications may have been missed in the immediate period, though routine clinic follow-up showed no evidence any lingering complications in all cases. Finally, the increased use of radiofrequency ablation following percutaneous biopsy at our institution

may have limited use in following up nondiagnostic biopsies, thereby not allowing for accurate assessment of some renal lesions through core biopsy.

Despite these limitations, we have shown in this large single institution observational cohort study that percutaneous image-guided biopsy for renal masses is highly safe and effective. In 88.5% of cases, it enabled a confident diagnosis of malignancy or benignity. The percentage of nondiagnostic biopsies was small, and there was a very favorable risk profile with minimal complications. Categorization among the subtypes of RCC is facilitated with use of IHC, given tumor heterogeneity, and sampling-related issues. In summary, percutaneous renal mass biopsy is safe and accurate method of differentiating among solid renal masses that may potentially prevent unnecessary surgery for a significant subset of patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with animals performed by any of the authors.

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