Role of Percutaneous Needle Biopsy for Renal Masses

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Abstract

Keywords

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The role of percutaneous renal mass biopsy has expanded considerably in the past 10 years. The incidence of incidentally detected small (< 4 cm) solid renal masses is on the rise, and despite a commensurate increase in nephron-sparing treatment, the mortality rate from renal cell carcinoma remains the same. Earlier detection and treatment have not had dramatic effects on population outcome, implying that not all small renal masses will grow to be life-limiting. Indeed, many small solid renal masses are benign, and among those that are malignant, not all share the same malignant behavior. Percutaneous biopsy provides a minimally invasive method for discriminating benign from malignant renal masses, and portends the potential for stratifying malignant risk. With recent improvements in image-guided equipment and technique, percutaneous renal mass biopsy can be performed safely and effectively, with a low complication rate (< 5%) and a high diagnostic yield (> 90%).

Objectives: Upon completion of this article, the reader will be able to describe the established and expanding indications for percutaneous renal mass biopsy.

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Background

Historical concerns regarding safety and efficacy, coupled with an historical clinical paradigm promoting surgical extirpative therapy for all solid renal masses lacking macroscopic fat, once led to consideration of percutaneous renal

mass biopsy as unnecessary and potentially dangerous.^{1,2} However, in the past 10 years, there has been a resurgence of interest in using percutaneous renal mass biopsy to stratify patient-level risk, and to avoid unneeded surgical or ablative therapies.^{2–7} This change in thinking remains in a state of evolution and is driven by several factors.

First, the incidence of clinically detected solid renal masses is on the rise,^{8–10} as is the incidence of renal cell carcinoma (RCC) specifically.^{8–10} Smoking, obesity, hypertension, and increased imaging utilization (ultrasound, computed tomography [CT], magnetic resonance imaging [MRI]) have all contributed to this.^{9–11} Additionally, among renal masses in general, the incidence of small (< 4 cm) solid renal masses is increasing most rapidly.⁸

Second, the use of surgical and ablative therapy for the treatment of renal masses is also on the rise,⁸ indicating that renal masses are being treated more frequently and at earlier stages. However, despite this aggressive approach, mortality from RCC remains relatively unchanged.^{8,10} This raises the possibility that some small solid masses undergoing treatment are not drivers of patient mortality. There are data to support this contention. In a large ($n = 2,770$) surgical series

of patients undergoing radical or partial nephrectomy for a sporadic unilateral nonmetastatic renal mass, a substantial minority of small renal masses (i.e., > 45% of masses measuring < 1 cm) were proven to be histologically benign (e.g., oncocytoma, minimal fat angiomyolipoma [AML]).¹² Similar findings have been replicated in other studies.¹³

In addition to the confounding effects of benign masses, not all histology-confirmed RCCs will behave the same. RCC is a heterogeneous disease with a variety of histologic subtypes and nuclear grades^{13,14}; some are more aggressive than others.¹²⁻¹⁴ Use of percutaneous biopsy to identify which masses are benign, and in some patients which masses are more or less aggressive (for consideration of active surveillance^{6,15,16}), can permit better stratification of patient risk before treatment decisions.

Finally, modern reports have shown a low risk of significant complications following percutaneous renal mass biopsy (< 5% incidence^{17,18}). Although bleeding is common (> 90%¹⁹), it is rarely clinically significant.¹⁷⁻¹⁹ The combination of an increase in perceived benefit and repeated series showing a relatively low risk has led to reconsideration of percutaneous renal mass biopsy as a fundamental component in the diagnostic evaluation of many small solid renal masses.^{3,4}

Indications for Percutaneous Renal Mass Biopsy

There are several established indications for percutaneous renal mass biopsy,³ including the following:

1. **Solid renal mass and known extrarenal primary malignancy:** In this setting, renal mass biopsy is performed to determine whether the renal mass is a second primary malignancy (e.g., RCC), a benign renal mass (e.g., oncocytoma), or a metastasis from the extrarenal malignancy.
2. **Unresectable solid renal mass:** In this setting, renal mass biopsy is performed for tissue confirmation before systemic and/or radiation therapy because there will be no nephrectomy specimen for analysis.
3. **Solid renal mass and significant comorbidities:** In this setting, renal mass biopsy is performed because the risk of biopsy is outweighed by the risk of surgery. The patient likely has minimal physiologic reserve and would not be a good candidate for elective surgery. In addition, if the mass is small and proves to be RCC, it may not affect survival given the other comorbidities. Percutaneous biopsy will allow an informed decision about how aggressively to manage the mass.
4. **Renal mass presumed secondary to infection:** In this setting, renal mass biopsy is performed because of the possibility that the "mass" is focal bacterial pyelonephritis or a developing abscess that can be managed with antibiotics (with or without aspiration) instead of surgery.

Although not yet broadly established, percutaneous renal mass biopsy is also used before thermal ablation so that a histologic diagnosis can be obtained before the tumor is ablated.³ This permits accurate reporting of follow-up data

(i.e., recurrence rates) and ensures that benign masses are not treated unnecessarily.

In addition to the above, there are several evolving/emerging indications for percutaneous renal mass biopsy that directly relate to the mismatch between incidence, treatment, and outcome for patients with a renal mass,^{5,8,20} and some centers are pursuing renal mass biopsy aggressively.^{5,6} The use of renal mass biopsy is expected to increase in the future,^{2,6} where it may be used for stratification of risk not only between benign and malignant tumors but also between various subtypes of RCC⁶ where indolent or lower risk small RCCs may be monitored in active surveillance protocols akin to low-grade low-volume prostate cancer.⁶ At present, such approaches are experimental.

In centers where percutaneous renal mass biopsy is used selectively, some features of a solid mass may help predict a benign histology and encourage the use of a percutaneous biopsy for confirmation. These include the following six scenarios.

Imaging Characteristics that Encourage the Use of Renal Mass Biopsy

1. **Small homogeneous hyperdense avidly enhancing renal mass (CT finding):** Minimal fat AML, which is an AML that lacks evident macroscopic fat on imaging, is a mimicker of RCC. These masses are often homogeneous, small (< 4 cm), hyperattenuating on precontrast CT imaging, and demonstrate homogeneous diffuse avid enhancement.²¹ If these features are present, a benign entity is suggested, and percutaneous biopsy may be useful before extirpative therapy.³
2. **Intracellular lipid-containing T2-hypointense renal mass (MRI finding):** Combinations of features on MRI can predict the presence of a minimal fat AML. Minimal fat AMLs are typically small (< 4 cm), hypointense on T2-weighted imaging (similar to papillary RCC), can contain intracellular lipid (similar to clear cell RCC), and often demonstrate avid arterial enhancement (similar to clear cell RCC).^{22,23} Therefore, a small solid renal mass that is hypointense to normal parenchyma on T2-weighted imaging and contains intracellular lipid is suggestive of a minimal fat AML. This is because the mimickers of those features (papillary RCC and clear cell RCC, respectively) do not share both features together.²² Percutaneous biopsy can be used to confirm the suspected benign diagnosis.
3. **Avidly arterially enhancing T2-hypointense renal mass (MRI finding):** Similarly, a small solid renal mass that is both hypointense to normal parenchyma on T2-weighted imaging and demonstrates avid arterial enhancement is suggestive of a minimal fat AML because the mimickers of those features (papillary RCC and clear cell RCC, respectively) do not share both features together.²² Percutaneous biopsy can be used to confirm the suspected benign diagnosis.
4. **The rapidly developing ill-defined mass in a patient with risk factors for urinary tract infection (CT, MRI, or ultrasound finding):** Not all renal masses are neoplasms. Focal

bacterial pyelonephritis can appear similar to a solid mass on CT, MRI, and ultrasound.²⁴ In patients with risk factors for urinary tract infection who have an ill-defined renal mass, particularly one with an adjacent focal delayed nephrogram and/or inflammation in the surrounding perinephric fat, a trial of antibiotics with repeat imaging may be indicated. If the finding persists, biopsy could be used to determine whether the lesion is infectious or neoplastic.³

5. *The infiltrative renal mass (CT, MRI, or ultrasound finding):* RCC is typically a cortically based mass. If a renal mass has an infiltrative pattern of growth that preserves the reniform shape of the kidney, urothelial carcinoma and lymphoma are more likely than RCC.²⁵ Because the management of these entities differs dramatically from both one another and that of traditional solid renal masses, percutaneous biopsy can be used to determine the most effective treatment.
6. *Multiple solid renal masses without macroscopic fat (CT, MRI, or ultrasound finding):* This scenario raises the possibility of lymphoma²⁵ as well as a variety of hereditary syndromes (e.g., Birt-Hogg-Dubé syndrome, hereditary leiomyomatosis and renal cell cancer syndrome, familial renal oncocytoma, etc.).²⁶ Percutaneous biopsy of the largest and/or most suspicious-appearing renal mass(es) can help determine the type and aggressiveness of management. Syndromes predisposing to multifocal RCC are usually approached with nephron-sparing strategies.²⁷ Biopsy results can direct which masses (if any) require near-term management versus active surveillance.

Imaging Characteristics that Oppose the Use of Renal Mass Biopsy

Renal masses seen on single time-point imaging are often inconclusive. Bi-phasic (with and without contrast) imaging is often required for complete assessment.⁴ Potential pitfalls of renal mass imaging related to the consideration of renal mass biopsy include the following five scenarios:

1. *Pseudoenhancement (CT pitfall):* Pseudoenhancement is an artifactual increase in attenuation (typically 1–25 HU) within a nonenhancing renal cyst on postcontrast CT imaging simulating true enhancement.^{28,29} It is caused by a computational failure in the CT scanner to properly account for beam hardening artifact.²⁹ It is commonly seen with small (< 2 cm), endophytic cysts adjacent to brightly enhancing renal parenchyma.^{28,29} If these features are present, and pseudoenhancement is suspected, MRI can be performed to determine whether the enhancement is real. Biopsy in the setting of pseudoenhancement will likely lead to a nondiagnostic histologic specimen, which will prompt a variety of difficult decisions that may lead to inappropriate management.
2. *Hemorrhage and protein content (CT, MRI, and ultrasound pitfall):* Hemorrhage and protein content within a complicated cyst can simulate solid tissue on ultrasound, CT, and MRI. On ultrasound, hemorrhage/protein content will

cause the cyst to appear hypoechoic (instead of anechoic). Grayscale and Doppler imaging will be unable to consistently and reliably differentiate this from solid tissue, although ultrasound contrast agents (not FDA approved in the United States) may be a solution.³⁰ On CT, hemorrhage/protein content will cause the cyst to measure greater than simple fluid attenuation (> 20 HU, “hyperdense cyst”). Performing pre- and postcontrast imaging will allow proper discrimination in most cases, provided there is no pseudoenhancement. On MR, hemorrhage/protein content will cause the cyst to appear hyperintense to simple fluid on precontrast T1-weighted imaging, rendering postcontrast imaging difficult to interpret. Subtraction imaging, in which the precontrast imaging data are “subtracted” from the postcontrast imaging data, will allow determination of solid enhancement in most cases, provided there is no substantial motion artifact between the two sequences.³¹ Similar to biopsy in the setting of pseudoenhancement, biopsy of a hemorrhagic cyst can lead to inappropriate management.

3. *Macroscopic fat (CT pitfall):* The presence of macroscopic fat within a solid renal mass is diagnostic of a benign renal AML in the absence of calcifications or aggressive behavior. If these conditions are met, biopsy is unneeded.³² However, postcontrast and thicker-section (i.e., 5+ mm) CT imaging is less sensitive for the detection of macroscopic fat than is precontrast and thinner-section (2–3 mm) CT imaging.^{31,33} If an obviously enhancing renal mass (e.g., 160 HU) is seen only on postcontrast CT imaging, unenhanced thin-section (2–3 mm) precontrast imaging is still helpful to determine whether macroscopic fat is present (which would obviate biopsy).
4. *Intracellular lipid (MRI pitfall):* Although macroscopic fat is diagnostic of AML in almost all cases, intracellular lipid detected with chemical shift MRI is not—it can be seen with both clear cell RCC and AML.²³ Intracellular lipid is characterized by central diffuse signal loss on opposed-phase imaging, while macroscopic fat is characterized by peripheral India ink artifact.³⁴ Knowledge of this distinction can avoid this pitfall.
5. *The hypervascular renal mass (CT and MRI pitfall):* Determination of solid tissue on CT and MRI is made based on the presence or absence of enhancement. However, vascular masses (e.g., pseudoaneurysm, arterial-venous fistula) can also demonstrate enhancement. If a mass enhances similar to blood pool (i.e., follows the appearance of the aorta on all postcontrast sequences), a vascular mass should be suspected.³⁵ Biopsy of a vascular mass can cause massive hemorrhage and is contraindicated. Use of flow-sensitive MR pulse sequences (e.g., time of flight), identification of MRI flow voids, and/or application of Doppler ultrasound can establish the correct diagnosis.^{36,37}

Although the technical success rate of percutaneous biopsy is excellent for solid renal masses, the data are not as robust for complex cystic masses, specifically Bosniak III cystic masses.³ Use of biopsy in this setting is controversial, with some centers advocating its use and others arguing against

it.^{3,38} Nondiagnostic biopsy results are more common in this setting due to a lack of viable tissue for sampling,^{39–41} and nondiagnostic results do not affect management.^{3,40} Biopsy of Bosniak IV cystic masses are 95% likely to be malignant, while Bosniak IIF cystic masses are much less commonly so (< 15% malignant).⁴² Therefore, use of percutaneous biopsy for Bosniak IV and Bosniak IIF complex cystic masses is generally not recommended.

Technical Considerations of Percutaneous Renal Mass Biopsy

Before image-guided biopsy, a review of previous cross-sectional imaging studies is needed to determine the safest approach to the targeted lesion. As with all percutaneous procedures, the shortest distance to the lesion without crossing additional organs, large vessels, or vital structures is optimal. Percutaneous renal mass biopsies are typically performed using either CT or ultrasound guidance. The choice of which imaging modality used is dependent on several factors including availability and physician preference. In general, lesions that are not well visualized on ultrasound, usually due to overlying bowel gas or a large patient body habitus, may be better accessed using CT guidance. For endophytic renal masses, the use of intravenous contrast may be transiently useful when utilizing CT guidance. Advantages of using ultrasound guidance include multiplanar real-time imaging, lack of ionizing radiation, and lower cost. To date, there has been no prospective study comparing the accuracy of renal mass tumor biopsies using different imaging modalities, but Rybicki et al did note in a single-center retrospective study that the choice of imaging modality used (CT or ultrasound) when performing renal mass biopsies did not affect the sensitivity or the negative predictive value for identifying malignancy.³⁹

As renal masses may be difficult to approach anatomically, a coaxial method may be useful because this method allows for multiple specimens without having to repeatedly position the needle. The coaxial technique has been shown to improve the biopsy success rate while decreasing procedure time.⁴³ Using this method, a larger gauge needle or cannula is advanced to the renal mass, and once adequately positioned a smaller gauge needle is placed through the larger cannula to obtain tissue. Tissue can be obtained either by fine needle aspiration or core biopsy. Fine needle aspiration uses small needles (21 gauge or smaller) through which aspiration can be applied while rapidly advancing and retracting the needle into the lesion via the outer cannula. When performing the aspiration technique, care must be taken not to further advance the outer cannula deeper into the patient. Tissue samples obtained using fine-needle aspiration technique should be evaluated by a cytopathologist at the time of the procedure to ensure the adequacy of the sample. Core needle biopsies are larger, usually 18 gauge, and are used to procure tissue samples for histologic analysis. A variety of needle systems can be employed including automatic side-cutting needles that can produce 8- to 17-mm core specimens, which can be sent to the pathology laboratory in formalin for analysis.

The reported sensitivity of fine needle aspiration for diagnosing malignancy is varied, ranging from 64 to 97%,^{44–52} and is highly dependent on whether the aspirate was sufficient and upon the interpretive skills of the cytopathologist. Early investigations reported insufficient sample rates as high as 5 to 16%, with false-negative rates of 8 to 36%, usually indicating that the aspirates did not provide sufficient material for cytologic analysis.^{44–47} Core needle biopsy has been shown to have sensitivities for malignancy ranging from 79 to 100%,^{17,53,54} and false-negative rates of 0 to 21%. An advantage of core biopsy over needle aspiration is the larger sized specimen, which can be used with immunohistochemistry for RCC subtyping and genomic analysis.

Nondiagnostic specimens and false-negative biopsies can be due to several factors including insufficient tissue procurement and sampling error. Unsuccessful biopsies are more common with smaller masses and masses with internal necrosis. Thus, constant or repeated visualization of the needle as it enters the mass is recommended so that the needle can be directed to the more solid components within the mass (►Fig. 1A, B). Imaging can be used to confirm the needle location for more precise needle placement and a better core specimen. It is also useful to obtain multiple specimens from different locations within the mass, if possible. The minimum number of specimens needed to provide an

Figure 1 (A) Axial contrast-enhanced computed tomography shows a partially cystic neoplasm in the posterior aspect of the lower pole of the right kidney (arrow). (B) Ultrasound-guided percutaneous biopsy of the mass was directed to the solid component of the renal tumor (guide lines), revealing papillary clear cell carcinoma.

adequate specimen has not been determined, although an improvement in subtype accuracy has been found with several cores versus one core biopsy specimen.⁵⁵ Nondiagnostic biopsies should be regarded with caution because repeat biopsies in this setting often yield malignant results.^{53,56}

Complications of Percutaneous Renal Mass Biopsy

Reported complications associated with percutaneous renal mass biopsy include hemorrhage and needle track seeding.^{53,56–58} Hemorrhage after this procedure is common; Ralls et al⁵⁸ found that small postbiopsy hematomas were seen after 91% of percutaneous renal biopsies. However, clinically significant hematomas or bleeding is unusual; if severe, these can be treated with blood transfusions, volume expansion, and/or angiography with embolization. Needle track seeding is a potential risk with any percutaneous procedure; fortunately, it is a rare occurrence in this patient population¹ with an estimated risk of less than 0.01%. There have been seven reports of track seeding associated with renal biopsies of RCCs, uroepithelial malignancies, and renal sarcoma^{58,59}; however, recent series report no cases of tumor seeding. This may be due to improved practices such as the use of coaxial technique. Both pseudoaneurysm and arteriovenous fistula formation are well-recognized complications of percutaneous renal biopsy.⁶⁰ Typically, they are clinically silent, but occasionally can cause retroperitoneal bleeding that may require arterial embolization.

Diagnostic Yield of Percutaneous Renal Mass Biopsy

Percutaneous renal mass biopsy has been shown to be safe and effective, with diagnostic accuracy rates routinely reported above 90%.^{2,17,39,54,57} However, it is important to note that accuracy can be defined in several ways, including the ability to identify malignancy, the ability to correctly identify the tumor type, and the ability to grade neoplastic tissue. The technical success rate of percutaneous renal mass biopsies with respect to procuring sufficient tissue for histologic analysis ranges from 78 to 100%. Higher success rates have been reported by operators utilizing a larger number of biopsy specimens, although an exact number is not specified.^{48,55} The ability of percutaneous renal mass biopsy to diagnose malignancy ranges from 53 to 100% taking into account the false-negative, false-positive, and indeterminate pathologic diagnoses. In a literature review by Lane et al² of more than 2,000 renal mass biopsies, the authors reported an overall technical failure rate of 5%, sensitivity for malignancy of 92%, and specificity of 90%.

Recent literature has focused on the success rates of percutaneous biopsy for small (< 4 cm) solid renal masses. The probability of malignancy within a small solid renal mass has been found to be inversely related to renal tumor size, with up to 22% of such masses measuring 1 to 4 cm proving benign. In addition, malignancies found in these smaller

masses tend to be lower grade and more indolent than those found in larger masses.¹² In a recent study, Halverson et al⁶ retrospectively evaluated 151 small renal masses that underwent both percutaneous renal mass biopsy and subsequent partial or radical nephrectomy. For diagnosing malignancy, there was complete concordance between the histology rendered from core biopsy and that rendered by surgery. Histologic concordance was 94% and Fuhrman nuclear grade concordance was 65%. Similar results have been reported by others with histologic subtyping accuracy ranging from 88 to 94%, and grading accuracy ranging from 64 to 70%.^{61,62} Lack of concordance was largely attributed to tumor heterogeneity, which is undoubtedly present in many tumors.

Conclusions

Image-guided percutaneous renal mass biopsy is a highly accurate procedure with minimal morbidity that can be used to detect benign disease, differentiate primary from secondary renal masses, and decrease the number of unnecessary extirpative therapies. Image-guided biopsy will likely continue to aid in the management of incidentally detected renal masses, in particular for patients undergoing active surveillance algorithms and/or minimally invasive therapy.

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