Current Role of Renal Biopsy in Urologic Practice

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KEYWORDS

• Accuracy • Diagnosis • Biopsy • Renal mass • Renal cell carcinoma

KEY POINTS

- Renal mass biopsy is safe but not devoid of complications.
- Renal mass biopsy is accurate in differentiating benign versus malignant tumors.
- Renal mass biopsy is imperfect for determination of tumor grade.
- Future efforts to improve renal mass biopsy results must overcome issues with tumor heterogeneity.

INTRODUCTION

Kidney cancer is diagnosed in more than 60,000 new patients in the United States each year and is the cause of more than 13,000 deaths.[1,2] The treatment of renal masses has evolved over the years from radical extirpative surgery, to minimally invasive organ-sparing approaches, to active surveillance (AS) in appropriate patients.[3,4] Yet, issues with overtreatment abound. Studies suggest that 5000 benign renal masses are resected annually,[5] although many patients with proven malignancy are destined to die of other causes.[6] The use of pretreatment renal mass biopsy (RMB) has subsequently become more common,[7,8] but its appropriate use continues to be debated.[8–10] In this article, the authors review and discuss the relevant contemporary urologic literature on RMB.

RENAL MASS BIOPSY TECHNIQUE

Tissue diagnosis of renal tumors can be performed by either fine-needle aspiration (FNA) or core biopsy (CB)[2,11,12] under image guidance (ultrasound, computerized tomography, or MRI). Current data suggest that FNA is inferior in its diagnostic abilities to CB.[11,13] Survey studies have shown that most practicing urologists prefer CB to FNA[14]; however, use of FNA seems to still be commonplace.[11] Unlike sampling with FNA, the cores obtained with CB allow for tissue architecture assessment.[12] Indeed a recent systemic review and meta-analysis of the available data demonstrate that both sensitivity (99.1% vs 93.2%) and specificity (99.7% vs 89.8%) for the diagnosis of malignancy are superior with CB than with FNA.[11] Differentiation between tumor subtype and high versus low tumor grade is also superior with CB.[11,13] Some institutions use both techniques concurrently to improve diagnostic yield and to assist in improved needle placement for CB, once guide sheath placement is confirmed with FNA.[13] However, some investigators maintain that the added utility of FNA is minimal[15]; this is underscored by current guideline recommendations. For instance, the current European Association of Urology's guidelines state "Needle core biopsies are preferable for solid renal masses in comparison with fine needle aspiration (Level of Evidence 2b)."[4]

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SAFETY

In the past, safety was a significant deterrent to widespread adoption of RMB. However, recent reports on RMB highlight its low morbidity. In a systematic review on RMB safety including 2979 patients, Patel and colleagues[2] reported that the most common complications were hematoma (4.9%) and pain (1.2%). Gross hematuria (1.0%), bleeding (0.4%), and pneumothorax (0.6%) were very rare. No events of tumor seeding were documented in this study. In another systematic review, which included 37 studies, 22 series reported at least one complication. The median complication rate was 8.1%, but only 3 cases of Clavien-Dindo grade 2 or greater complications were indexed. Again, the most common complication was hematoma (median 4.3%). Blood transfusion was reported in only 3 studies with a median of 0.7% of cases. Other complications were self-limiting hematuria (median 3.1%) and pain (median 3.0%). One case of urothelial tumor seeding was documented radiographically. However, on final pathologic examination this was not verified.[11] Richard and colleagues[16] reported data from a prospectively maintained largest single dataset of RMB from Princess Margaret Cancer Center and the University of Toronto of 509 patients who underwent 529 RMBs. Adverse events (AEs; n = 48) were carefully prospectively indexed and reported in 42 patients (8.5%). The most common AEs (75%) were perirenal hematoma discovered on postprocedure imaging and bleeding from the puncture sites. All AEs were clinically insignificant (Clavian grade 1) except for one patient requiring angioembolization. In this cohort of largely low-risk lesions, biopsy tract seeding was not identified. Prince and colleagues[17] described a similar AE profile. The investigators reported the results of 565 RMBs and identified only a single Clavian 3a AE (need for angioembolization). Three additional patients required blood transfusion due to bleeding. Older series reveal a much higher complication rate. The most common complication of RMB was hematoma, which may be identified in up to 91% of RMBs if postprocedure imaging is performed. Most of these cases are asymptomatic, and bleeding requiring blood transfusion occurred in only 0% to 5% of cases.[18] The most feared complication of RMB is tumor seeding in the biopsy tract. This complication was described in less than 0.01% of RMBs[13,19] and is considered anecdotal. However, in recent years, 5 case reports on tumor seeding after RMB were published. All cases were renal cell carcinomas (RCCs) (2 clear cell, 3 type-1 papillary). Three of the 4 cases were performed with a coaxial sheath.[20–23] These data highlight that serious long-term risks of RMB are extremely small but do exist.

DIAGNOSTIC VALUE

Nondiagnostic Versus Diagnostic Biopsy

Nondiagnostic biopsy rates are an important issue when interpreting RMB literature. Reasons for nondiagnostic RMB include sampling error and insufficient tissue for pathologic evaluation.[17] Rates of nondiagnostic biopsies range between 0% and 47% in various series.[2,12,24–26] This wide range may be due to different definitions of *nondiagnostic* between studies and on expertise and techniques used at various institutions.[27] Marconi and colleagues[11] have demonstrated an overall nondiagnostic rate of 8% (CB 0%–22% and FNA 0%–32%) in a meta-analysis of RMB studies. Furthermore, Jeon and colleagues[25] retrospectively analyzed the results of 442 RMBs and found an overall nondiagnostic rate of 11.1%. Of interest, as expected, is the fact that the nondiagnostic rate of RMB of cystic lesions was significantly higher compared with solid tumor (25.0% vs 10.4 respectively, $P = .043$). Another retrospective analysis by Prince and colleagues[17] demonstrated similar nondiagnostic rates of RMB (14.7%). However, the nondiagnostic rate was higher for cystic masses (39.8%), nonenhancing or weakly enhancing masses (42.1%), and skin to tumor distance longer than 13 cm (26.9%). Small renal masses (SRMs) (defined as less than 4 cm in all, but one study whereby a cutoff of 5 cm was used) had a slightly higher nondiagnostic rate of RMB (17.4%). The fact that the performing physician or evaluating pathologist experience had no impact on the rates of nondiagnostic RMB is noteworthy. The largest single-center series to date was published by Richard and colleagues[16] and described the results of more than 500 RMBs. The nondiagnostic rate in this series was 10% and decreased to 6% after a repeat biopsy. On multivariable analysis, RMB of an endophytic tumor had a 3-fold higher chance of returning a nondiagnostic result than an RMB of its exophytic counterpart.

Value of Repeat Biopsy

One clinical strategy to manage nondiagnostic RMB is to perform a repeat biopsy. A wide variation in utilization of repeat RMB was reported in a recent meta-analysis whereby it was performed only for 20.4% of patients with primary nondiagnostic RMB.[2] Jeon and colleagues[25] retrospectively analyzed institutional data on RMB and found a similar rate of repeat biopsies for