Renal Tumor Biopsy for Small Renal Masses: A Single-center 13-year Experience


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Background: Renal tumor biopsy (RTB) for the characterization of small renal masses (SRMs) has not been widely adopted despite reported safety and accuracy. Without pretreatment biopsy, patients with benign tumors are frequently overtreated.

Objective: To assess the diagnostic rate of RTBs, to determine their concordance with surgical pathology, and to assess their impact on management.

Design, setting, and participants: This is a single-institution retrospective study of 529 patients with biopsied solid SRMs <4 cm in diameter. RTBs were performed to aid in clinical management.

Outcome measurements and statistical analysis: Diagnostic and concordance rates were presented using proportions. Factors that contributed to a diagnostic biopsy were identified using a multivariable logistic regression.

Results and limitations: The first biopsy was diagnostic in 90% (n = 476) of cases. Of the nondiagnostic biopsies, 24 patients underwent a second biopsy of which 83% were diagnostic. When both were combined, RTBs yielded an overall diagnostic rate of 94%. Following RTB, treatment could have been avoided in at least 26% of cases because the lesion was benign. Tumor size and exophytic location were significantly associated with biopsy outcome. RTB histology and nuclear grade were highly concordant with final pathology (93% and 94%, respectively). Adverse events were low (8.5%) and were all self-limited with the exception of one. Although excellent concordance between RTB and final pathology was observed, only a subset of patients underwent surgery following biopsy. Thus it is possible that some patients were misdiagnosed.

Conclusions: RTB of SRMs provided a high rate of diagnostic accuracy, and more than a quarter were benign. Routine RTB for SRMs informs treatment decisions and diminishes unnecessary intervention. Our results support its systematic use and suggest that a change in clinical paradigm should be considered.

Patient summary: Renal tumor biopsy (RTB) for pretreatment identification of the pathology of small renal masses (SRMs) is safe and reliable and decreases unnecessary treatment. Routine RTB should be considered in all patients with an indeterminate SRM for which treatment is being considered.

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1. Introduction

The incidence of kidney cancer is increasing, primarily due to an increase in the detection of small renal masses (SRMs) that are often early stage renal cell carcinomas (RCCs) [1]. This is thought to be in large part related to the greater use of abdominal imaging [2].

Surgical treatment of stage pT1a RCC produces excellent cancer-specific survival rates [3]. Most are incidentally detected as SRMs that are usually solid enhancing masses on imaging and concerning for malignancy [2]. There are currently no clinical or radiographic features that accurately predict histologic diagnosis. Hence surgical series have shown that 20–30% of SRMs are benign on final pathology. Moreover, SRMs found to be malignant are usually of lower nuclear grade than their larger counterparts [4].

Renal tumor biopsies (RTBs) have been proposed as a safe and useful tool for the pretreatment identification of benign tumors. The goal of RTB is to avoid the potential morbidity associated with overtreatment of SRMs [5–8]. Despite their potential benefits, RTBs have not been widely adopted in the management of SRMs [9]. The lag in uptake is likely due to concerns regarding the lack of sufficient tissue for diagnosis, discordance with final pathology, safety, and, most importantly, the lack of perceived impact on clinical management. Several, albeit generally small, studies suggest that these concerns were exaggerated [5–8]. However, large series that demonstrate the benefits of RTB are currently lacking.

In this study, we described the largest single-institution experience with RTB of SRMs, explored factors associated with diagnostic success, and assessed the impact of RTB on clinical management.

2. Methods

2.1. Patient selection

This retrospective single-center study was approved by the institutional review board. Subjects who underwent an RTB for a radiologically indeterminate SRM between January 2001 and December 2013 were identified through a prospectively maintained database. A chart review was performed at the time of radiofrequency ablation (RFA; n = 11), or consisted of a contour abnormality of the renal capsule. The tumor histology was reviewed and correlated to surgical pathology if available. Tumor histology was classified according to the World Health Organization [10]. Tumors in which the subtype was not reported were defined as RCC, unspecified. Fuhrman grade was recorded for clear cell RCC (ccRCC) histology only. If two grades were assigned to a specimen, only the higher Fuhrman grade was recorded. A biopsy was deemed nondiagnostic if there was insufficient material for histology assessment or if nonrenal or unremarkable parenchymal tissue was biopsied.

2.2. Data

We abstracted the patient demographic characteristics (age, gender, body mass index [BMI], American Society of Anesthesiology [ASA] classification [grade 2–3 vs 1]), lesion characteristics (laterality, location, size, exophytic appearance, histology, Fuhrman grade), and procedural characteristics (year of biopsy, number of previous RTBs performed by the interventional radiologist [IR], type of image guidance, number of biopsy cores, periprocedural morbidity, and type of subsequent intervention). An exophytic lesion was defined as a lesion that caused a contour abnormality of the renal capsule. The tumor histology was reviewed and correlated to surgical pathology if available. Tumor histology was classified according to the World Health Organization [10]. Tumors in which the subtype was not reported were defined as RCC, unspecified. Fuhrman grade was recorded for clear cell RCC (ccRCC) histology only. If two grades were assigned to a specimen, only the higher Fuhrman grade was recorded. A biopsy was deemed nondiagnostic if there was insufficient material for histology assessment or if nonrenal or unremarkable parenchymal tissue was biopsied.

2.3. Biopsy procedure

All RTBs were performed by 1 of the 20 IRs and carried out under imaging guidance. Most RTBs (90%) (Table 1) were performed using a 17-gauge coaxial sheath and an 18-gauge core needle. The number of cores taken at the time of the RTB was left to the discretion of the operator. Postprocedure imaging was routinely performed prior to discharge to rule out a complication.

2.4. Pathologic evaluation

All pathologic specimens were processed according to standard institutional pathologic procedures. Specific immunohistochemical and advanced diagnostic studies were carried out at the discretion of the pathologist. All biopsies were read by one of four dedicated genitourinary pathologists.

2.5. Objectives

The primary objectives were to establish the rates of diagnostic biopsy following the first or second RTB (if performed) and to determine the factors associated with an initial diagnostic RTB. Secondary objectives included assessing whether the diagnostic rate improved over time, measuring the safety of RTBs, and describing the impact of RTB on the management of SRMs. Last, we evaluated the concordance between the RTB pathology and the surgical pathology in patients who underwent surgery.

2.6. Statistical analysis

Continuous variables were reported as medians (interquartile range [IQR]); categorical variables were described with proportions. The baseline characteristics of the patients who had a diagnostic and nondiagnostic RTB were compared using the Wilcoxon rank-sum test for continuous variables and the chi-square or Fisher exact test for proportions. Univariable and multivariable logistic regressions models were generated to test for an association among patient (age, gender, BMI, ASA score), lesion (laterality, location, size, exophytic appearance), procedure-related characteristics (year of biopsy, number of previous RTBs performed by the IR, type of image guidance), and the odds of obtaining a diagnostic biopsy at the time of the initial RTB. The multivariable model was fit with variables significant at p < 0.20 level on univariable analysis. The fit of the model was assessed using the Hosmer-Lemeshow test and the C statistic. Residuals were assessed using a casewise diagnostics method. The odds ratios (ORs) are presented with their 95% confidence intervals (CIs). The Cochran-Armitage test for trend was used to test whether the diagnostic rate of the RTBs increased over the years. Proportions were used to report the safety of RTB and to report the histologic and Fuhrman grade concordance between RTB pathology and definitive surgical pathology. All data were recorded, and statistical analyses were conducted using SAS v.9.3 (SAS Institute Inc., Cary, NC, USA). All tests were two sided, and p values <0.05 were considered statistically significant.
3. Results

A total of 529 biopsied SRMs in 509 patients were included in the analysis. The initial biopsy was diagnostic in 90% ($n = 476$). Of these, 26% ($n = 123$) were of benign histology. The patient, procedure, and lesion characteristics of initial diagnostic and nondiagnostic biopsies are compared in Table 1. Of the 53 nondiagnostic RTBs, a rebiopsy was performed in 24 masses (45%) and was diagnostic in 83% ($n = 20$) of them (Fig. 1). Therefore, the overall diagnostic rate when the first and second RTBs were combined was 94% ($n = 496$). Of these, 26% ($n = 131$) were benign. Most of the malignant lesions were low–Fuhrman grade ccRCC (Table 2). Although the diagnostic rates improved over time, the difference was nonsignificant ($p = 0.06$) (Table 3).

On univariable analysis, age, tumor size, exophytic tumor location, and type of imaging used were significantly associated with the biopsy outcome. However, on multivariable analysis, larger tumor size (OR: 1.71; 95% CI, 1.17–2.50) and an exophytic location (OR: 2.91; 95% CI, 1.56–5.44) were the only factors associated with an initial diagnostic biopsy (Table 4).

The postprocedure complication status was available in 492 patients (97%). Among these, a total of 48 adverse events were reported in 42 patients (8.5%). Most of the adverse events (75%) were perirenal hematomas discovered on postprocedure imaging or bleeding through the coaxial sheath. According to the Clavien-Dindo classification [11], the complications were all grade 1 with the exception of one patient who required percutaneous angioembolization (grade 3b). After a median follow-up time of 28 mo (IQR: 11–53), no needle tract seeding had been reported (Table 5).

Following RTB, 175 patients underwent surgery. Surgical pathology was unavailable in three cases (1.7%). Pathology revealed the presence of necrosis in only one case where surgery was performed following a complication after RFA. Therefore, interpretable surgical pathology was available in 171 cases. Four nephrectomies were performed following nondiagnostic biopsies, and all demonstrated malignancy. Three surgeries were performed following RTB showing a benign histology. Two of the biopsy results were confirmed on
final pathology, and one final pathology revealed normal renal parenchyma with an adjacent fat-poor angiomyolipoma in a patient with a benign spindle-cell tumor on RTB histology. There was agreement between biopsy and surgical histology in 93% of the cases (155 of 167). The discordant cases are presented in Supplementary Table 1. RTB correctly identified ccRCC, chromophobe, and papillary RCC compared with surgical pathology in 99% (101 of 102), 100% (15 of 15), and 91% (32 of 35) of cases, respectively (Supplementary Fig. 1). With regard to the patients who were operated and diagnosed with ccRCC on both RTB and surgical pathology, Fuhrman grade was concordant in 63%.

### Table 2 – Histology of benign and malignant tumor obtained through biopsy (n = 496)

<table>
<thead>
<tr>
<th></th>
<th>Benign masses (n = 131)</th>
<th>Malignant masses (n = 365)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td><strong>n (%)</strong></td>
<td><strong>Type</strong></td>
</tr>
<tr>
<td>Oncocytic renal neoplasm, suggesting oncocytoma</td>
<td>80 (61.1)</td>
<td>Clear cell RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fuhrman grade I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fuhrman grade II</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fuhrman grade III</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fuhrman grade IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unspecified</td>
</tr>
<tr>
<td>Fat-poor AML</td>
<td>36 (27.5)</td>
<td>Papillary RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unspecified</td>
</tr>
<tr>
<td>Metanephric adenoma</td>
<td>3 (2.3)</td>
<td>Chromophobe RCC</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>2 (1.5)</td>
<td>RCC (unspecified subtype)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (7.6)</td>
<td>Xp11 translocation RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucinous tubular and spindle cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RCC (unclassified)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mixed clear cell and papillary RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metastasis from other primary</td>
</tr>
</tbody>
</table>

AML = angiomyolipoma; RCC = renal cell carcinoma.
of cases (64 of 101) (Supplementary Table 2). RTB undergraded most of the discordant cases (n = 34 of 37). When grades were pooled into low (1 or 2) and high grades (3 or 4), the biopsy accuracy was 94% (95 of 101). When pooled, six cases had discordant grades, all of which were of lower grade on the RTB compared with definitive pathology.

The histology of lesions managed by AS is illustrated in Supplementary Figure 2. Of these patients, four eventually received definitive treatment because of tumor growth (surgery in three and RFA in one).

4. Discussion

Despite a growing body of evidence, the merits and safety of pretreatment biopsy continue to be debated. This study focused on RTB of SRMs as an aid to treatment decision making. To the best of our knowledge, it is the largest single-institution cohort published on SRM biopsy. We have demonstrated a 90% diagnostic rate with an initial biopsy and an 83% diagnostic rate after a rebiopsy for initially nondiagnostic RTB. Thus RTBs led to a diagnosis in 94% of...
patients with SRMs when the outcomes from the first and second biopsy were combined. Our results are consistent with the higher end of previously reported diagnostic rates varying from 70% to 91% for SRMs in smaller series [5,8,12–18]. Although diagnostic rates increased over time, the improvement was statistically nonsignificant.

In the present study, larger SRMs and exophytic location were significantly associated with increased odds of obtaining a diagnostic biopsy. The odds of obtaining a diagnostic biopsy were almost threefold higher with an exophytic mass compared with a completely endophytic one. Tumor size as a predictor of diagnostic biopsies was previously reported [5,8,17,18]. Neither IR experience nor patient BMI was related to a diagnostic RTB.

These results have also shown that histologic subtypes diagnosed with RTB had a high concordance (94%) with surgical pathology. Such rates were stated in a 2012 review article to be between 86% and 98% [19]. As previously reported [19–21], RTB seems to be less accurate in determining Fuhrman grade with a tendency to undergrade compared with the final surgical pathology. Fuhrman grades have been often pooled into low (1 and 2) and high (3 and 4) to improve the prognostic value of grade in ccRCC [22]. The prognostic utility of such pooling in SRMs is unknown, but if it were to be applied, substantial agreement would be observed (94%). Furthermore, studies have shown that ccRCC masses <3 cm are low grade in >90% of cases [23]. The controversy regarding grade heterogeneity in SRMs is pertinent to programs where initial AS is offered and should be acknowledged as a shortcoming of the technique.

As we learn more of the natural history of SRMs managed by AS [24] and the greater likelihood of older and infirm patients dying from other causes [25], RTB to determine pretreatment histology may become more relevant to treatment decisions. It is generally believed that low-grade ccRCC, papillary type 1, and chromophobe tumors carry more favorable prognoses [26]. Thus if AS was offered as initial treatment for low-grade malignancies, definitive therapy could be avoided in even more individuals following RTBs.

As previously reported [19], this study confirms the safety of RTBs with significant complications occurring in <1% of cases. Although needle tract seeding remains a concern, none of the patients biopsied experienced such an event. Moreover, since the use of coaxial biopsy techniques, no such cases have been reported in the literature [19].

This study is not devoid of limitations. First, it is possible that noncaptured variables may have affected the biopsy success rates, such as the lesion's echogenicity, anterior versus posterior location, and amount of adipose tissue. Likewise, given the fact that periprocedural complications were captured retrospectively, it is likely that complications were underestimated. The small number of patients who underwent a rebiopsy following an initial nondiagnostic RTB also limited our ability to assess the value of rebiopsy. Nonetheless, given the relatively high diagnostic rate after a repeat biopsy (83%) and the high benign rate among these (40%), it seems worthwhile.

Finally, although we have demonstrated a good correlation between biopsy and final pathology, the fact remains that only a subset of patients underwent surgery. For example, it is possible that a subset of patients labeled as harboring a benign oncocyctic renal neoplasm are in fact actually harboring a chromophobe RCC or a mixed tumor. Due to this concern, we routinely follow these patients with regular imaging despite the presence of a favorable RTB pathology.

In experienced hands, RTB is associated with a high diagnostic yield, high pathologic correlation with definitive surgical pathology, and low morbidity. Moreover, based on the biopsy results, treatment was avoided or could have been avoided in at least 25% of patients because of benign histology by RTB. In addition to preventing unnecessary interventions, studies have also shown RTBs to be cost effective [27]. RTBs may also help better define candidates for AS. As such, RTBs may help avoid unnecessary treatment and its related morbidity. Renal surgery is associated with morbidity including but not limited to hemorrhage (<10%), urine leak (<3%), acute renal insufficiency (<2%), flank bulge or hernia (approximately 5%), and a low but nonetheless real risk of perioperative mortality (<1%) [28,29].

As such, in our opinion, it seems very difficult to continue justifying performing potentially morbid surgery for SRMs based only on imaging findings because RTB is safe and has a diagnostic yield in >90% of cases.

5. Conclusions

Although the evidence in favor of routine RTB to characterize SRMs is compelling, critics have continued to argue against the practice because of the previously enumerated concerns. Our results demonstrate that each of these concerns is exaggerated. In view of our results, it seems difficult to continue to justify a timid uptake of routine SRM biopsies and the use of this information to implement treatment strategies. Indeed RCC is one of the very few tumors where indications for surgery are based on imaging only. Given the current evidence, it is our strong belief that it is now time to shift the clinical paradigm. We believe that RTB should be considered the initial step in the management of patients with radiographically indeterminate SRMs in whom a therapeutic approach is being considered. In an era where overdiagnosis and overtreatment of favorable cancers is gaining worldwide attention, routine RTB for SRM should lead to diminished intervention. Furthermore, with biomarker discovery RTB could ultimately facilitate the personalization of care.

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Author contributions: Antonio Finelli had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Finelli, Jewett, Kachura, Evans, Zlotta.

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Analysis and interpretation of data: Richard, Finelli, Jewett, Evans.

Drafting of the manuscript: Richard, Jewett, Bhatt, Kachura, Evans, Herrmanns, Juver, Zlotta, Finelli.
Critical revision of the manuscript for important intellectual content: Richard, Jewett, Bhatt, Evans, Hermanns, Zlotta, Finelli.

Statistical analysis: Richard, Finelli.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eururo.2015.04.004.

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