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News and Topics

Renal mass biopsy for the small renal mass

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Abstract

Opponents of premanagement biopsy of small renal masses are not difficult to find. Many urologists contend that the benefits of biopsy do not outweigh the risks, arguing that the results do not influence management substantially and that the most useful information from renal mass biopsy can be attained with advanced imaging. In this article, we develop the counter arguments and demonstrate that renal mass biopsy should be implemented into the small renal mass management algorithm. © 2017 Elsevier Inc. All rights reserved.

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Biopsy of the small renal mass (SRM) (clinical T1a) continues to incite controversy. Those opposed to the performance of renal mass biopsy (RMB) generally attack its safety, accuracy, and lack of use. Proponents of RMB cite accumulating evidence supporting its usage in the evaluation of the SRM that is suspicious for renal cell carcinoma. In this *News and Topics* article, we address popularly stated reasons to forego RMB, review contemporary RMB data, and argue that RMB deserves a role in the evaluation and management of SRMs.

Is RMB necessary? Opponents of RMB contend that a SRM is extremely likely to harbor malignancy, and therefore management options can safely be discussed without a pathologic diagnosis. In actuality, of SRMs (clinical T1a lesions, so <4 cm in maximal diameter), 25% are benign [1]. Many surgical series report a 25% rate of benign tumors, but we feel that a 25% risk of unnecessary surgery is excessive. Inasmuch as RMB can reduce this rate to a more reasonable risk, they are useful. Moreover, although the ability to radiologically differentiate benign and malignant lesions continues to develop, with impressive improvements in radiologic characterization over the years, current technology still is insufficiently accurate to be considered a substitute for histologic diagnosis. Millet et al. [2] performed a retrospective review to determine whether computed tomography characteristics could accurately identify SRM pathology, and concluded that computed tomography was unable to differentiate between benign and malignant lesions. Some success has been demonstrated at discriminating among renal cell carcinoma subtypes [3]. Sun et al. [4] demonstrated that dynamic contrast-enhanced magnetic resonance imaging could differentiate between papillary and clear cell renal cell carcinoma with up to 94% accuracy. Despite this, a serious limitation of radiologic imaging is its inability to differentiate high grade cancers from those that are relatively indolent [5]. This is particularly important given that approximately only 20% of SRMs demonstrate aggressive histology [6] and the ability to reliably differentiate these tumors from indolent ones would reduce both overtreatment and undertreatment.

Is RMB dangerous? Although many have raised concerns about the safety of RMB, modern literature supports the idea that RMB has a low risk of complications [7]. The most common adverse event is hematoma (4.9%), which rarely requires transfusion (0.4%) [8]. Other associated complications with RMB including pain (1.2%), gross hematuria (1.0%), and pneumothorax (0.6%) are similarly minor or rare [8,9]. A potentially disastrous complication of RMB is tumor seeding. In the contemporary literature, only a few cases have been reported when appropriate coaxial technique was used [10,11]. A systematic review of the literature reported no tumor seeding events among 20 studies including 3,113 RMB on 2,979 patients [8].

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A meta-analysis by Marconi et al. [12] similarly noted no RMB tumor seeding for renal cell carcinoma. With the estimated rate of tumor seeding after RMB to be less than 0.01%, this overly emphasized complication can be considered anecdotal [13,14].

Is RMB accurate? With refinements in technique, RMB has grown into a highly accurate diagnostic test. RMB has the ability to differentiate between benign and malignant SRMs, with reported sensitivity of 97.5% to 99.7%, specificity of 96.2% to 99.1%, and positive predictive value of 99.8% in 2 large meta-analyses [8,12]. Patel et al. [8] reported a concerning negative predictive value of 68.5%, however, this is based on the limited number of benign and nondiagnostic biopsies with gold standard surgical pathology. Among 17 studies, only 79 (16.8%) of 468 benign biopsies had surgical pathology, of which 29 (36.7%) were falsely negative. Of these, 19 (65.5%) were concentrated in 2 studies, one of which represented an early experience in RMB using a fine needle aspiration technique, while the other included 6 patients with masses greater than 4 cm [15,16]. Most contemporary studies reveal a substantially lower false-negative rate among benign biopsies [8]. In addition, the false-negative rate of benign RMB is likely subject to selection and verification bias as surgical excision was likely performed in the most concerning of benign renal masses.

Nondiagnostic biopsies, in which biopsy resulted in insufficient tissue, normal kidney parenchyma, fibrosis, or necrosis, occurs in 10% to 20% of RMB [8]. This rate can be significantly improved upon with repeat biopsy. Another attempt at RMB yields diagnostic results at a rate of approximately 80%, thus decreasing the frequency of nondiagnostic RMB to less than 10% [17]. In one series, 22.3% of nondiagnostic RMB went on to definitive surgery and 90.4% of these masses were malignant [8]. Although diagnostic accuracy of RMB continues to improve, these results suggest that management of nondiagnostic RMB should proceed with caution.

As data suggest RMB to be accurate with a low rate of adverse events, we argue that it deserves an integral role in the management of SRMs. Our group has previously published a SRM algorithm implementing RMB-influenced risk stratification [18]. Reviewing 133 patients with both RMB and surgical pathology from an excised SRM, we evaluated whether RMB pathology allowed accurate risk assignment and treatment as compared to the "ideal management" as determined by surgical pathology. RMB incorrectly assigned 4 of 133 (3.0%) patients, all of which were incorrectly assigned to surveillance. Accuracy of RMB-guided management was quite high, as it demonstrated a sensitivity for treatment of 96%, specificity for surveillance of 100%, a positive predictive value of treatment of 100%, and a negative predictive value of surveillance of 86%. Although this analysis excluded patients with benign and nondiagnostic RMB, it provided accurate treatment assignment of malignant RMB results when compared to final surgical pathology. A multi-institutional retrospective study by Rahbar et al. [19] of 1,175 robotic partial nephrectomy specimens reported that up to 52% of surgeries in their cohort could have been avoided had they known the pathology prior to surgery. Although based on the theoretical assumption of 100% concordance between RMB and surgical pathology, it suggests that surgical treatment (and associated risks) of many SRMs could be avoided with the implementation of RMB-based risk stratification.

RMB-guided management has also been shown to be superior to other risk-stratification nomograms. RENAL nephrometry score (RNS) nomograms have been used to predict malignancy and risk-stratify patients [20]. In 281 patients, Osawa et al. [21] evaluated whether an RMB-based algorithm was superior to RNS nomograms in accurately predicting and risk-stratifying SRMs. RMB demonstrated superior accuracy in predicting malignancy (99% vs. 29% concordance) as well as high-risk malignancy (67% vs. 61% concordance). The addition of RNS, as well as age and gender, to RMB and tumor size did not improve the accuracy of a risk-stratification algorithm previously published by Halverson et al. [18,22].

One area of concern is with RMB false-negatives. This is primarily based on lower rates of nuclear grade concordance, with most studies demonstrating RMB under-grading. Tumor heterogeneity and hybrid histology have been put forth as contributing reasons for inaccuracy [13,23]. A risk of RMB-based risk stratification is incorrectly assigning a patient with a high-risk tumor to surveillance when they should be treated. This danger can be mitigated if patients with adverse pathology who are (incorrectly) assigned to surveillance can be identified and diverted to delayed intervention without compromising outcomes. Hawken et al. [24] described 495 SRMs treated with surgical excision. A period of surveillance followed by delayed intervention was performed for 94 patients (median = 386 days, IQR: 272–702), whereas the remaining 401 underwent early intervention (median = 84 days, IQR: 59–121). Delayed intervention was not associated with adverse pathology ($P = 0.8$). Interestingly, greater annual SRM growth demonstrated a modest but significant association with adverse pathology for patients on surveillance (odds ratio = 1.2, 95% CID: 1.03–1.3 mm/y, $P = 0.02$). This supports the often-applied practice (heretofore based on clinical principle rather than evidence) of using growth as a determining factor for delayed intervention for patients on active surveillance. Outcomes of these patients were no worse than for those whom underwent early intervention, thus assuaging some of the concerns about false-negative RMB.

With increasing amounts of data supporting the diagnostic ability of RMB, current debate is centered around its clinical use [25]. Some proponents of RMB implore its use in the majority of SRMs [17,26], whereas others argue for a more limited role [25]. The appropriate usage of RMB is