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Solid Renal Masses: What the Numbers Tell Us

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OBJECTIVE. Solid renal masses are most often incidentally detected at imaging as small (≤ 4 cm) localized lesions. These lesions comprise a wide spectrum of benign and malignant histologic subtypes, but are largely treated with surgical resection given the limited ability of imaging to differentiate among them with consistency and high accuracy. Numerous studies have thus examined the ability of CT and MRI techniques to separate benign lesions from malignancies and to predict renal cancer histologic grade and subtype. This article synthesizes the evidence regarding renal mass characterization at CT and MRI, provides diagnostic algorithms for evidence-based practice, and highlights areas of further research needed to drive imaging-based management of renal masses.

CONCLUSION. Despite extensive study of morphologic and quantitative criteria at conventional imaging, no CT or MRI techniques can reliably distinguish solid benign tumors, such as oncocytoma and lipid-poor angiomyolipoma, from malignant renal tumors. Larger studies are required to validate recently developed techniques, such as diffusion-weighted imaging. Evidence-based practice includes MRI to assess renal lesions in situations where CT is limited and to help guide management in patients who are considered borderline surgical candidates.

Keywords: angiomyolipoma, diffusion-weighted imaging, oncocytoma, renal cell carcinoma, renal mass

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In this article, we synthesize the evidence regarding renal mass characterization at CT and MRI, provide diagnostic algorithms for evidence-based practice, and highlight areas of further research needed to drive imaging-based management of renal masses.

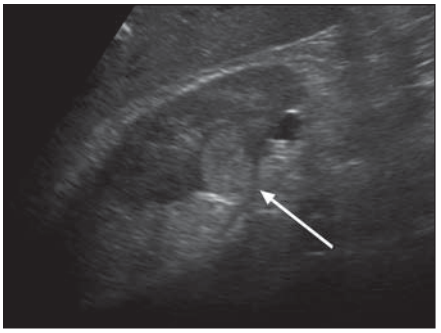
Clinical Vignette

A 68-year-old man presented to his local emergency department with vomiting and right upper quadrant pain. The patient had not experienced symptoms related to urination, fever, or flank pain. He underwent ultrasound examination of the right upper quadrant, which showed cholelithiasis and no findings of cholecystitis. While imaging the right kidney, the sonographer discovered a 2-cm solid right renal mass and notified the radiologist (Fig. 1). The incidental finding prompted further discussion by the emergency department physician with the patient regarding relevant history and a recommendation by the radiologist for a CT to further evaluate the renal mass.

The patient confirmed that he had no known history of malignancy and no symptoms of flank pain or hematuria. Although without severe comorbidities, the patient was taking medications for diabetes and hypertension, and also had a slightly elevated creatinine level. The emergency department physician recommended that the patient schedule a follow-up appointment with a urologist and undergo CT of the abdomen and pelvis for renal mass evaluation. Several weeks later, the patient arrived at the urologist's office after completion of a CT renal mass protocol and resolution of the gastrointestinal symptoms.

The Imaging Question

Growth in utilization of radiologic studies has resulted in increased incidental imaging findings, frequently renal lesions [1, 2]. Most solid renal tumors are incidentally detected as localized lesions less than 4 cm in diameter (stage T1a in the American Joint Committee on Cancer staging system [3]), and most are treated using the current standard of care, nephrectomy, and preferably partial nephrectomy, which has been shown to preserve kidney function and prevent chronic kidney disease [4, 5]. Despite excellent oncologic control with surgical resection, overall survival has not improved in patients with



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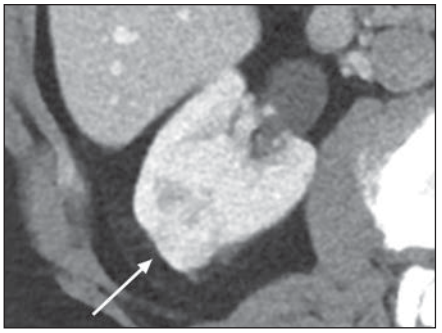

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Fig. 1—68-year-old man with vomiting and right upper quadrant pain who underwent ultrasound.
A, Incidental right upper pole renal mass (*arrow*) is seen.
B, CT renal mass protocol confirmed 2-cm solid enhancing mass without distant abdominopelvic metastases (*arrow*) that was found to represent clear cell renal cell carcinoma at surgical pathology.

small renal cell carcinoma (RCC). In fact, nononcologic mortality in affected patients has paradoxically increased in the past 2 decades, specifically in patients with stage T1a RCC [6]. In recognition of such trends, there may be an increasing need to develop treatment paradigms that better balance oncologic mortality with competing nononcologic and treatment-related risks.

Currently, the major roles of imaging in renal mass management are in characterizing the detected mass, including differentiation of benign from malignant lesions where possible, and in staging and preoperative planning. Multiphase CT is currently the imaging modality of choice for initial diagnosis, staging, and preoperative planning. MRI can be useful in some circumstances to further evaluate a renal mass, but what specific information can it provide, and what is the existing evidence for its added value? Furthermore, how can evidence-based practice be implemented to better evaluate renal lesions and to potentially improve patient-centered management?

Background

Most renal masses are incidentally detected on imaging performed for unrelated symptoms or indications. Although most of these lesions are RCC, most are small (i.e., stage T1a), a substantial portion are benign, and some malignant lesions are indolent [7, 8].

Each of the major imaging modalities offers advantages and drawbacks in renal mass evaluation. Sonography can be helpful in determining the cystic nature of a lesion when a lesion is slightly higher density than fluid on CT. However, its use for characterization is generally hampered by low sensitivity for small lesions, operator dependence, and technical limitations, depending on patient body habitus and bowel gas [9, 10]. CT currently plays a key role in preoperative renal mass evaluation but does not provide accurate discrimination of benign from malignant solid renal lesions in all cases, nor is growth on serial imaging statistically different in benign and malignant lesions [11–13]. As a problem-solving tool, MRI offers diagnostic value in further characterizing some renal masses, and effective utilization may aid management decisions in this generally elderly patient population with competing oncologic and nononcologic mortality risks. The purpose of this review is threefold: first, to summarize and synthesize the evidence regarding renal mass characterization at CT and MRI; second, to provide general diagnostic algorithms for CT and MRI evaluation of small renal masses; and third, to provide recommendations regarding future directions for imaging research to improve diagnostic utility in renal mass evaluation. Our discussion will apply to the more common well-circumscribed small renal cortical tumors and not to lesions displaying clearly aggressive infiltrating growth patterns, as typically seen in urothelial tumors.

Synopsis and Synthesis of Evidence: Summary of Renal Cell Carcinoma Subtype Prevalence and Prognosis

Clear cell carcinoma is the most common of all renal cancer subtypes, accounting for approximately 75% of renal cancers, followed by papillary carcinoma (10%), chromophobe (5%), and other unclassified or undifferentiated subtypes [14]. Interestingly, the histologic subtype has also not been shown consistently to be a significant predictor of prognosis for RCC. A large study by Patard and colleagues [15] showed that TNM stage, Fuhrman grade, and a clinical performance score, but not histologic subtype, were independent prognostic variables for overall survival. A trend of improved prognosis with chromophobe RCC was reported in their study [15]; however, other studies have reported better overall survival in papillary and chromophobe RCC than clear cell RCC [16]. Of note, papillary RCC comprises a heterogeneous subtype of both indolent and also aggressive histologic subtype, and Pignot and colleagues [17] have shown decreased survival in type 2 versus type 1 papillary cancers.

Large studies have shown that the papillary subtype predominates in resected masses smaller than 2 cm, whereas the clear cell subtype appears most commonly among larger tumors [13, 18]. Rothman and colleagues [7] analyzed Surveillance, Epidemiology, and End Results Program data of 19,932 localized RCCs and analyzed the likelihood of each subtype according to size; the incidence of papillary RCC formed a U-shaped curve, where the likelihood decreased with size until lesions reached 10 cm, and then increased in tumors larger than 10 cm.

Significance of Tumor Size and Growth Rate

Risk of Malignancy and Prognosis by Size of Renal Mass

Among the characteristics of a localized renal mass on initial imaging, tumor size is regarded as the single most important predictor of malignancy and aggressive histologic grade [8, 18]. Approximately 80% of small renal masses represent cancers, with clear cell carcinoma accounting for the vast majority of malignant lesions [7, 18]. However, benign lesions increase in prevalence as tumor size decreases. Thompson et al. [8] examined the proportion of benign lesions according to tumor size in 2675 surgically removed renal masses and found benign histologic diagnoses in 56% of lesions 1–2 cm in diameter, decreasing progressively with increasing size to 13% of masses at 6–7 cm. These proportions were similar to values previously reported in a study of 2770 resected renal masses by Frank et al. in 2003 [18]. Furthermore, Frank et al.

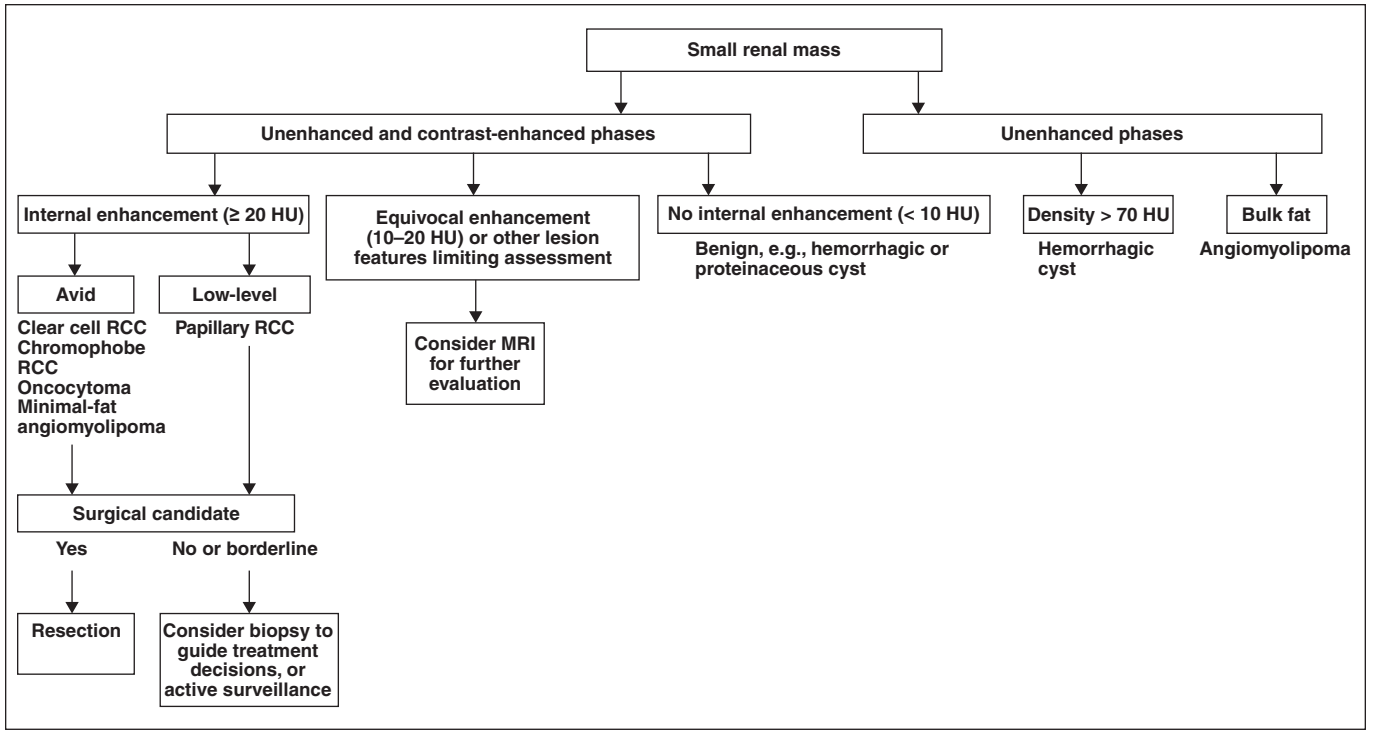

Fig. 2—Diagnostic and management algorithm for small renal mass using CT. RCC = renal cell carcinoma.

reported significant increased odds of clear cell subtype with increasing size, and both studies showed significant increases in aggressive histologic grade with increasing tumor diameter [8, 18].

Among localized RCCs smaller than 4 cm, 85% have been reported to represent low-grade tumors, but high-grade disease increases with size, with an odds ratio increase of 13% per centimeter increase in diameter [7]. In another large study, among all lesions up to 4 cm, a minority (≈ 20–25%) showed potentially aggressive features, and approximately 70% of lesions larger than 7 cm also had a low histologic grade [19]. The seemingly disparate finding of a large proportion of tumors larger than 7 cm showing nonaggressive features may be explained partially by selection bias for operative candidates with lesions that may have possessed less inherent aggressive potential (i.e., larger but localized tumors that had not developed metastases).

Despite the importance of tumor size in predicting malignancy and higher histologic grades of RCC, the association of renal mass size with survival remains unclear. One large study from a single institution reported tumor size to be significantly associated with metastasis-free survival when tumors of all sizes were included [20]. In a contradictory study, the size of a small renal mass at presentation was not found to be an independent prognostic factor in survival or metastatic disease [21]. In terms of metastatic disease rates, a large retrospective study by Pahernik et al. [13] reported metastatic rates varying from 2% to 7% in lesions smaller than 3 cm [21], whereas Thompson et al. [20] reported de novo metastases in less than 1% of lesions in the same size group. Furthermore, RCCs measuring 4 cm have been reported to present with synchronous metastases in up to 6% of cases and advanced stage (pT3) in 12% of cases [13, 22]. The disagreement among these large studies is likely at least partially attributable to degrees of selection bias for patients who are operative candidates, with underrepresentation of patients who present with metastatic disease or are observed without surgical management. In a meta-analysis of observed enhancing renal masses, the metastatic disease rate was lower (1%) in lesions smaller than 3 cm [11], which may reflect selection for a more indolent cohort of lesions allowed to remain on imaging surveillance.

Overall, the size of a tumor at initial imaging presentation has been shown to be predictive of malignancy and aggressive histologic grade, with weaker evidence for association with overall survival.

Renal Mass Growth Rate Prediction and Significance

The growth rate of small renal masses monitored with imaging surveillance has been reported as approximately 0.3 cm [11, 19, 23]. In a single series of surgically resected lesions with preoperative serial imaging, the lesion size at presentation did not predict growth rate or histologic grade [23]. Meta-analyses of active surveillance have also reported that initial mean tumor diameter did not differ significantly between positive-growth and zero-growth masses, and that rates of malignancy were comparable between lesions showing positive and zero growth; however, no metastases developed in masses with zero growth [11, 19]. One of these meta-analyses reported that the subgroup of RCCs that were treated had a slightly greater growth rate of 0.4 cm per year, compared with the mean of 0.3 cm [11], and bias in these studies for resection of growing lesions limits definitive correlation of growth rate with likelihood of malignancy and histologic grade, because not all monitored lesions were resected, and the mean follow-up period was generally in the range of 3 years. Therefore, the growth rate of a small renal mass on serial imaging has not been shown to provide reliable prediction of malignancy or benignity, but growing lesions are more likely to be treated during watchful waiting.

CT Assessment of Renal Masses

The renal mass protocol, when performed with CT, varies by institution, but standard imaging includes an unenhanced phase followed by contrast-enhanced images in the nephrographic phase at approximately 90 seconds after contrast injection. The American College of Radiology provides CT as the "most important technique for evaluating the indeterminate renal mass" [24], but recognizes both CT and MRI as appropriate initial studies with comparable performance in identifying lesions that should be surgically managed. The nephrographic phase serves best for detection of a renal mass and also suffices for detection of enhancing components. The corticomedullary (arterial) and urographic (excretory) phases are also often acquired to provide additional anatomic information for presurgical planning and to assess proximity to or involvement of the collecting system. Useful imaging characteristics at CT include the detection of bulk fat, lesion density, and enhancement. However, multiple studies have been performed to assess the performance of enhancement characteristics derived from multiphase imaging in differentiation of renal tumors with limited success [25–29]. A general diagnostic algorithm is presented for CT evaluation, which includes potential circumstances where MRI may provide additional information for management decisions (Fig. 2).

An important consideration for the multiphasic protocol is the increased ionizing radiation exposure to the patient, given recent concerns raised regarding risks of radiation-induced cancers after imaging-related exposures [30–32]. Although the true risk of radiation-induced cancers remains unknown, benefits of deriving further diagnostic information should be balanced with the possible risks and consideration of dose-reduction techniques, including the use of dual-energy CT or patient-centered protocol optimization [33, 34]. Because the median patient age at RCC diagnosis is 64 years, radiation-induced cancer risks in the older patient population are likely minimal relative to other competing mortality risks, such as medical comorbidities [35].

Renal Mass Attenuation

Detection of fat—In general, bulk fat within a solid renal mass detected on CT is a reliable sign of angiomyolipoma. Approximately 5% of angiomyolipomas contain minimal fat and pose a diagnostic challenge because they currently cannot be reliably distinguished from RCCs [36]. Although several studies have reported accurate diagnosis of minimal fat–containing angiomyolipomas using pixel or histogram analyses [37–39], the findings have not been reproducible [40, 41].

Rarely, macroscopic fat may also appear in RCC with osseous metaplasia (usually from the clear cell subtype), cholesterol necrosis, and when a large RCC engulfs perinephric fat [42–44]. In such lesions, calcification within a fat-containing mass should raise suspicion for malignancy [45]. History should also be available to exclude a postprocedural appearance related to prior partial nephrectomy with fat-packing, or prior ablation of a renal mass where the ablation zone evolves to a masslike appearance of bulk fat [46].

Lesion density—The attenuation of the renal parenchyma typically ranges from 30 to 40 HU; a hyperattenuating renal mass usually measures between 40 and 90 HU on unenhanced CT images [47]. Lesions with homogeneous unenhanced density of more than 70 HU have been reported to represent hemorrhagic cysts more than 99% of the time [48]. However, hemorrhagic cysts may also have density less than 70 HU and are best confirmed as nonenhancing lesions with unenhanced and contrast-enhanced imaging. A high-density lesion (40–70 HU) is most commonly RCC, but the differential diagnosis also includes minimal-fat angiomyolipoma, metanephric adenoma, leiomyoma, oncocytomas, and other mesenchymal and metanephric lesions that overlap in appearance with RCC [50]. Prior studies support consideration of a minimal-fat angiomyolipoma when evaluating an enhancing high-attenuation lesion at CT

TABLE 1: Summary Comparison of Studies Examining Differentiation of Renal Cell Carcinoma (RCC) From Oncocytoma

Reference	Imaging Modality	Comparison RCC Subtype	Imaging Criteria	Reported Results	Characteristics of Tumors
Young et al. [25]	CT	Clear cell	Threshold attenuation values in three phases	84% accuracy (81/97)	All sizes
Wildberger et al. [57]	CT	Clear cell	Qualitative features: solid, well-demarcated, central scar, spoke wheel pattern, hypodense after contrast agent administration	12.2% (6/49) observations correct for oncocytoma	All sizes
Bird et al. [58]	CT	All subtypes	Attenuation in three phases, percentage change	$p < 0.05$, using Student t test for RCC vs oncocytoma	< 4 cm, RCC group: 60% clear cell
Davidson et al. [59]	CT	All subtypes	Homogeneous enhancement and central sharply marginated scar	No difference in small and large tumors, 33% called RCC	All sizes
Zhang et al. [26]	CT	Clear cell	Qualitative features, enhancement in two phases	No difference	All sizes, with small number oncocytoma
Cornelis et al. [68]	MRI	Clear cell	Segmental inversion after 5-min delay, and tumor-to-spleen signal intensity ratio	55% sensitivity, 97% specificity, 86% PPV, 88% NPV	All sizes
Rosenkrantz et al. [67]	MRI	Chromophobe	Qualitative features, segmental inversion after 3-min delay	10% of chromophobe, oncocytoma with segmental inversion	All sizes, most < 4 cm
Taouli et al. [69]	MRI	All subtypes (solid tumors only)	DWI in addition to contrast-enhanced MRI, ADC cutoff of $\leq 1.66 \times 10^{-3}$ mm^2/s (at b values 0, 400, 800)	90% sensitivity, 83% specificity, AUC 0.854 for solid RCC	All sizes ≥ 1 cm

Note—PPV = positive predictive value, NPV = negative predictive value, DWI = diffusion-weighted imaging, ADC = apparent diffusion coefficient, AUC = area under the curve.

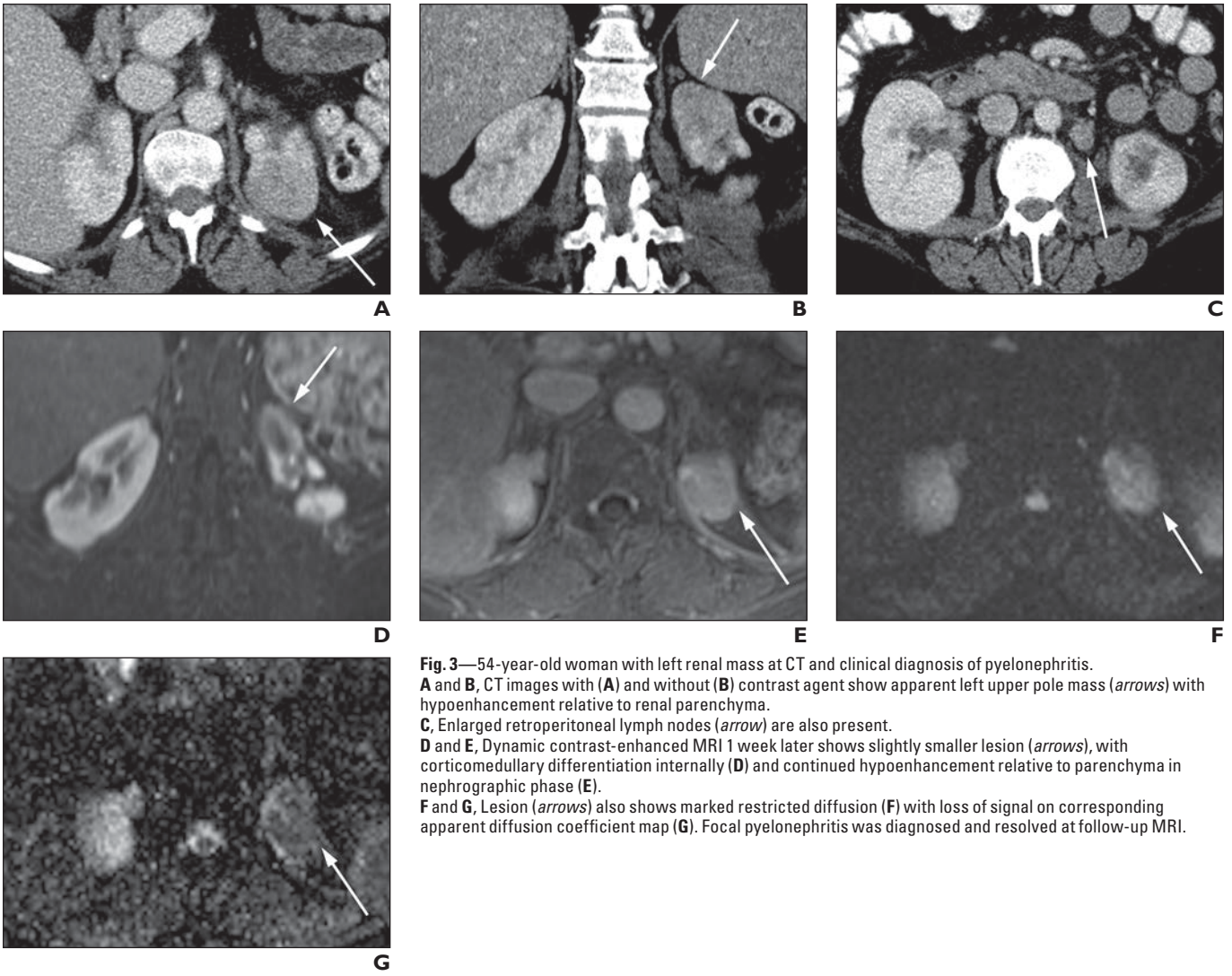

Fig. 3—54-year-old woman with left renal mass at CT and clinical diagnosis of pyelonephritis.
A and **B**, CT images with (**A**) and without (**B**) contrast agent show apparent left upper pole mass (*arrows*) with hypoenhancement relative to renal parenchyma.
C, Enlarged retroperitoneal lymph nodes (*arrow*) are also present.
D and **E**, Dynamic contrast-enhanced MRI 1 week later shows slightly smaller lesion (*arrows*), with corticomedullary differentiation internally (**D**) and continued hypoenhancement relative to parenchyma in nephrographic phase (**E**).
F and **G**, Lesion (*arrows*) also shows marked restricted diffusion (**F**) with loss of signal on corresponding apparent diffusion coefficient map (**G**). Focal pyelonephritis was diagnosed and resolved at follow-up MRI.

[36, 52]. Still, biopsy remains necessary at this time to determine the diagnosis because of an overlap in appearance with RCC [53].

Lesions that appear lower density than the renal parenchyma include renal cystic lesions, focal pyelonephritis, abscess, and papillary RCCs. In such cases, where clinical history is not informative or may be confounding, MRI may aid in further differentiating among these benign and malignant diagnoses (Fig. 3).

Qualitative and Quantitative Enhancement

Enhancement is defined as an increase in attenuation by 20 HU or more on contrast-enhanced images compared with unenhanced images because lesser degrees of change in attenuation value may be attributable to pseudoenhancement [54]. The phenomenon of pseudoenhancement is known to be significantly associated with central location and also with masses smaller than 1 cm, limiting CT assessment in such cases [55]. When the attenuation change falls within 10–20 HU, subtraction imaging at MRI may be useful if available [56].

Perhaps the most clinically relevant imaging challenge for the localized small renal tumor remains distinguishing RCC from benign solid lesions, particularly oncocytomas and minimal-fat angiomyolipomas. Though multiple investigations have examined qualitative and quantitative methods of analyzing enhancement to distinguish RCC from oncocytoma, no enhancement characteristics have been shown to accurately and reproducibly distinguish oncocytoma from RCC [25, 26, 57–59] (Table 1). Furthermore, the degree of heterogeneity of protocols and study design prevent a meta-analytic approach to synthesize the available published data.

Some similarities and differences in enhancement peaks and patterns have been reported among oncocytomas and RCC subtypes and are summarized here. In a study of 298 renal tumors of varying size, both clear cell RCC and oncocytomas peaked in the corticomedullary phase [25]. In terms of enhancement pattern, oncocytomas have been reported to show a "segmental inversion" pattern on enhanced phases [60], but these findings have not been consistently reproducible [61–63]. Furthermore, a central scar is present in the minority of cases [64]. To date, to our knowledge, no qualitative imaging features have been shown to reliably diagnose oncocytomas at CT.

Absolute peak attenuation values have also been studied for discrimination of RCC from oncocytomas. Young et al. [25] found that clear cell RCC was differentiated from

oncocytoma with an accuracy of 77%, sensitivity of 86%, and positive predictive value of 85% using attenuation thresholds of 106 HU in the corticomedullary phase, 92 HU in the nephrographic phase, and 68 HU in the excretory phase. The authors' institution used a four-phase CT protocol and did not limit the size of the evaluated lesions [25]. Given the lack of a standardized protocol across institutions, quantitative use of enhancement should be examined in a larger study to further evaluate the diagnostic value of absolute attenuation changes.

RCC is also not reliably distinguished from minimal-fat angiomyolipomas using enhancement characteristics. In addition to being adipose rich or poor, angiomyolipomas vary in composition of smooth muscle and vascular and epithelioid elements, which leads to a variable imaging appearance [65]. In several small series, minimal-fat angiomyolipomas have been described to show homogeneous enhancement in addition to hyperdensity relative to renal parenchyma [36, 51, 52]. Although some differences have also been described in enhancement kinetics among RCC subtypes and minimal-fat angiomyolipomas, Yang and colleagues [53] examined the potentially predictive imaging variables and found that unenhanced high density was the only examined variable that consistently and significantly differentiated minimal-fat angiomyolipomas from RCC. Despite the inability to completely exclude RCC with homogeneous enhancement and intrinsic hyperattenuation, minimal-fat angiomyolipoma may be important to specify in the differential diagnosis because surveillance or biopsy may be under consideration for poor surgical candidates.

Among RCC subtypes, papillary RCC has been found to show lesser degrees of enhancement than other subtypes of RCC and, in some cases, may be mistaken for renal cysts because of low-level enhancement [66]. In a study examining differentiation of the clear cell from the papillary subtype, attenuation less than 100 HU in the corticomedullary phase of enhancement was 95.7% specific after normalization for aortic enhancement [29]. Both papillary and chromophobe RCC have been shown to peak in the nephrographic phase, later than clear cell RCC [25]. Qualitatively, papillary RCCs have been reported to show variable patterns of either homogeneous or heterogeneous enhancement [26–28].

Overall, CT assessment can provide limited information to assess the likelihood of certain RCC subtypes according to the degree of enhancement and inherent density, but, in cases without bulk fat, cannot discriminate benign from malignant tumors. When initial characterization with CT leaves a question about the presence of enhancing components or a nontumorous lesion, as summarized in the provided diagnostic algorithm (Fig. 2), MRI may offer further problem-solving capability.

MRI Assessment of Renal Masses

MRI most often complements CT in renal mass characterization, although it may also be used as the initial dedicated study for evaluation of a renal mass under current American College of Radiology guidelines [24]. Compared with CT, patient-level factors, such as the ability to tolerate longer scan time and cooperate with breath-holding, may lead to more potential variability in diagnostic quality. Just as with CT, the detection of internal enhancing soft tissue is of primary importance. Routinely performed sequences in the MRI protocol for renal mass evaluation include T2-weighted imaging, T1-weighted opposed-phase imaging (in-phase and out-of-phase sequences), and fat-suppressed T1-weighted gradient-echo acquisition before and after administration of IV gadolinium-based contrast medium in corticomedullary, nephrographic, and urographic phases of enhancement. Diffusion-weighted imaging (DWI) can improve diagnostic confidence, and the use of apparent diffusion coefficient (ADC) values for discriminating between benign and malignant lesions and among RCC subtypes is also under active investigation.

MRI offers problem-solving capability in some scenarios where CT may be limited in identifying enhancing soft tissue and can provide an accurate diagnosis of a cyst or solid mass through synthesis of signal characteristics and subtraction imaging [56]. In primary lesion assessment, the combination of lesion characteristics across multiple sequences can suggest the differential diagnosis, as presented in a general diagnostic algorithm (Fig. 4). However, just as with CT, MRI cannot yet differentiate benign and malignant tumors, aside from classic angiomyolipomas.

Enhancement

In lesions with intrinsically T1-hyperintense components, subtraction can be helpful to determine the presence of enhancement [56]. Enhancement kinetics have also been studied for differentiating tumor types at MRI; just as with CT, clear cell carcinomas and angiomyolipomas tend to show early enhancement in the corticomedullary phase followed by lower level enhancement in later phases, and low-level late enhancement is more typical of papillary RCC [25, 66]. Studies examining the differentiation of clear cell and chromophobe RCC from oncocytomas using enhancement characteristics have reported variable results [67–69], but as in studies using CT, small lesions may be less likely to show the reported features that differentiate RCC from oncocytoma (Table 1). The heterogeneity of study design and MRI techniques among these small studies does not support performance of meta-analysis.

Complex cystic renal lesions and papillary RCCs may have a similar appearance at CT, due to hypoattenuation, minimal appreciable heterogeneity, and enhancement; more distinctive features at MRI can aid in delineating the tumor types and specifically identify enhancing tissue (Fig. 5). The distinction may be useful in poor surgical candidates to assess prognostic implications, or to better identify a specific portion of tumor to target in biopsy if pretreatment diagnosis is desired [70–72].

Unenhanced Sequences

T2-weighted imaging—T2 signal intensity can be somewhat helpful if it is used in a solid renal mass to assess the likelihood of a papillary RCC or minimal-fat angiomyolipoma because of low T2 signal. T2 hyperintensity is typically seen in clear cell tumors but is not specific, because this characteristic can also be seen in oncocytomas and in a minority of chromophobe carcinomas [67]. Hindman et al. [73] examined the ability to distinguish between minimal-fat angiomyolipoma (< 25% lipid content at histopathology) and clear cell RCC and found that low T2 signal was the only imaging feature, aside from small size, that predicted minimal-fat angiomyolipoma in multivariate logistic regression. In another study of clear cell and papillary RCC, low T2 signal was 100% specific in discriminating papillary RCC from the clear cell subtype; thus, low T2 signal is not a specific indicator of benign histologic subtype [74].

T1-weighted imaging—The detection of bulk fat on MRI is accomplished through T1-weighted imaging with and without fat suppression, or T1-weighted in-phase and out-of-phase imaging using the India ink artifact [75]. Microscopic fat detected as loss of signal on out-of-phase imaging cannot be used reliably to discriminate between

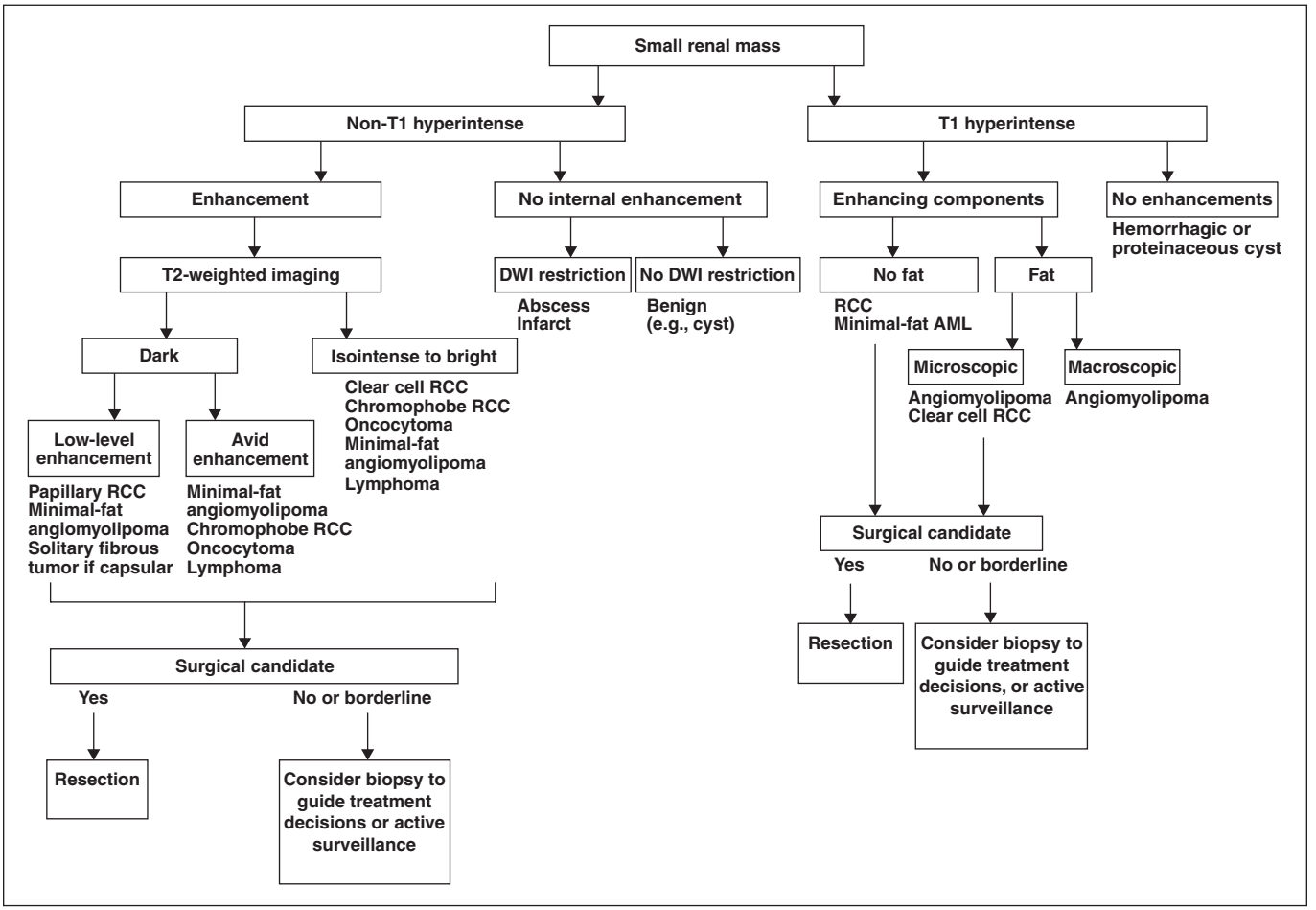

Fig. 4—Diagnostic and management algorithm for small renal mass using MRI, provided diagnoses are favored given lesion characteristics; however, overlap remains between benign lesions and renal cell carcinoma (RCC) and among RCC subtypes. AML = angiomyolipoma; DWI = diffusion-weighted imaging.

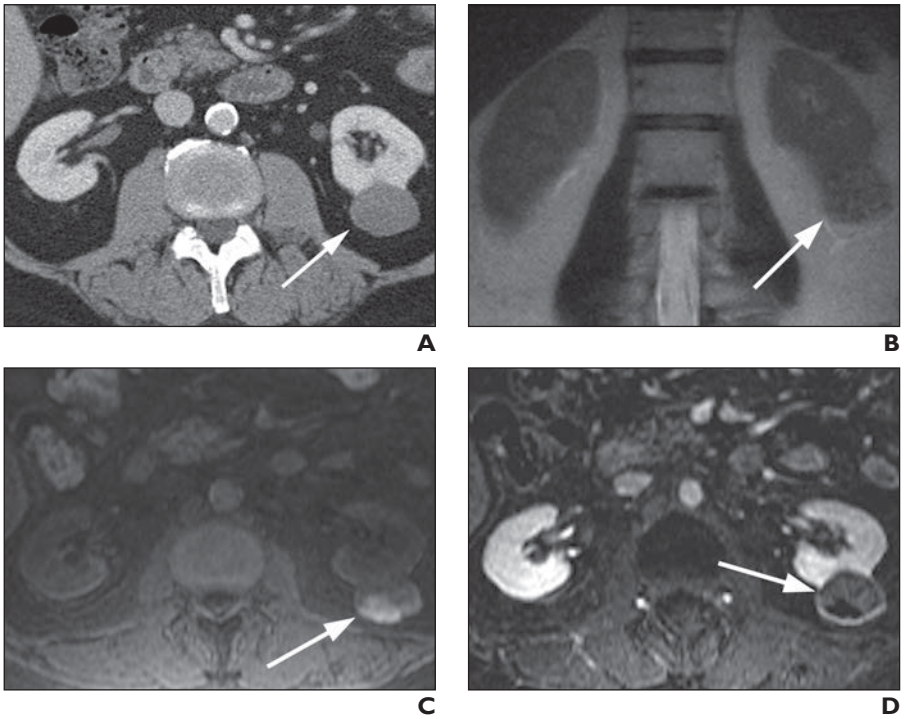

Fig. 5—67-year-old man with hypoattenuating left renal mass at CT who underwent further evaluation with MRI.
A, Contrast-enhanced CT shows hypoattenuating (25 HU) left renal mass (*arrow*), with borderline enhancement internally.
B, At MRI, coronal HASTE shows lesion (*arrow*) to be predominantly T2 dark.
C, Axial T1-weighted image shows hyperintense layering posterior component (*arrow*).
D, MRI subtraction image shows anterior enhancing soft tissue and confirms nonenhancing posteriorly layering hemorrhage (*arrow*). Papillary renal cell carcinoma was diagnosed at surgical pathology.

angiomyolipomas containing minimal fat, because clear cell RCCs may also contain microscopic fat [73].

Lesions that are intrinsically T1 hyperintense but show no evidence of fat are most likely hemorrhagic or proteinaceous cysts, and subtraction imaging can be helpful to assess for underlying enhancing components. Among solid lesions, both benign and malignant lesions can show T1 hyperintensity because of blood products or proteinaceous contents; hemorrhage is seen in RCC (particularly within the clear cell and papillary subtypes) but may also be seen in benign solid neoplasms, such as oncocytomas, metanephric tumors, or angiomyolipomas [72, 76]. In addition, the presence of hemorrhage or hemosiderin within a mass with enhancing soft tissue is not a distinguishing characteristic among RCC subtypes [67, 74].

Diffusion-weighted imaging—DWI may particularly be helpful in lesion detection and evaluation when gadolinium-based contrast medium cannot be administered. It can also aid in differentiating some benign and malignant lesions [77–79]. Visual inspection of DWI can assist with lesion detection and, for certain lesions, reinforce the likelihood of a pseudolesion. Although investigators have examined the use of ADC values to predict RCC subtypes and separate benign from malignant lesions, their use is limited by the fact that that there is substantial inter- and intrascanner variability in ADC measurement, and ADC values depend on selected b values that vary across institutions and protocols [9, 10, 79]. That said, ADC has been shown to be significantly lower in renal disease (both malignant and nonmalignant processes such as infection) than in normal renal parenchyma [80–82]. Small studies have shown the potential value of DWI for helping to differentiate between benign and malignant masses [69, 78]. Kim et al. [77] also showed improved accuracy with the addition of DWI in differentiating benign from malignant T1-hyperintense lesions at unenhanced MRI.

Studies have also examined the use of ADC values in discriminating among RCC subtypes. A lower ADC has been reported in the papillary subtype of RCC compared with other subtypes at both 1.5 and 3 T [69, 80], whereas clear cell RCC showed a significantly higher ADC than other subtypes at 3 T [80, 82]. ADC has also been found to be significantly lower in high-nuclear-grade (III and IV) than in low-nuclear-grade (I and II) clear cell tumors at 1.5 T [83] and between grades at 3 T [82]. Although the current nonuniformity of techniques for DWI limits the routine use of ADC values, findings suggest potential value for improving the clinical performance of MRI and warrant larger, ideally multiinstitutional, studies with standardized parameters and b values to establish the reliability of ADC values across scanner types.

Evidence-Based Guidelines

Recognizing that management of early-stage renal cancers with uniformly aggressive treatment has not improved patient health outcomes, imagers may offer helpful guidance to patients and referring physicians through knowledge of how CT, MRI, or biopsy can best inform decision making. We offer general guidelines for using MRI as a problem-solving tool for renal mass evaluation, with the caveat that the decision requires consideration of patient-level factors in the management of renal masses. Although CT and MRI offer similar abilities for diagnosis, staging, and preoperative anatomic delineation, MRI may offer more sensitive and specific evaluation when the patient cannot receive iodinated contrast agent or when the lesion has features limiting assessment at CT, such as endophytic property, small size (≈ 1 cm), equivocal enhancement, or confluent areas of dense calcification [55, 54] (Fig. 2). In such cases of low-level or unclear enhancing components, subtraction images at MRI may allow ascertainment of a benign cyst, precluding the need for surgery.

MRI can offer incremental value after CT when patients may not be strong candidates to undergo standard surgical treatment. When a possible diagnosis of minimal-fat angiomyolipoma is suggested at CT, supportive findings for the same diagnosis at MRI may prompt biopsy and avoid surgery. Similarly, a mildly complex questionably enhancing low-density lesion at CT may be a predominantly cystic lesion or a papillary RCC, and enhancement and T2 characteristics at MRI may inform the decision to perform biopsy or monitor a mass in select patients. For borderline or poor surgical candidates in particular, substantial changes in the posttest probability of a benign or indolent lesion may influence the pursuit of biopsy, active surveillance, or percutaneous ablative therapy.

Renal mass biopsy was not historically favored by urologists because of perceived risks of tract-seeding, sampling error, inability for pathologic diagnosis in a substantial proportion of cases, and risk of periprocedural complications such as hemorrhage [84–86]. With improvements in imaging-guided percutaneous techniques and cumulative reported experience in the literature, data support a minimal risk of tract seeding and an up to 99% rate of pathologic diagnoses with biopsy [87, 88]. Given these favorable findings and considering the older population in which small renal masses are usually discovered, renal mass biopsy may play an increasingly integral role in the near future if greater emphasis is placed on patient-centered management.

Further advances in immunohistochemical analysis may also support improved management decisions using renal mass biopsy. Historically, the distinction of epithelioid angiomyolipoma from sarcomatoid RCC may have been problematic at pathology, but current immunohistochemical evaluation makes the diagnosis with high accuracy [89]. The diagnosis of chromophobe carcinoma or oncocytoma remains a challenge at pathology, however, because of the overlap in features.

Outstanding Issues That Warrant Research

The radiologic discrimination of benign, indolent, and aggressive malignant renal masses remains the diagnostic challenge of high clinical relevance. The current need for tissue-based diagnosis and prevalent treatment pattern of nearly nondiscriminatory extirpation encourage key areas for research in imaging evaluation of the small renal mass. These key areas include reliable diagnosis of the most common benign lesions and the ability to predict tumor aggressiveness in malignancies. Positive findings in these areas have been reported in relatively small studies with highly variable imaging techniques, limiting application of the evidence at this time. The incremental value of recently developed quantitative techniques, such as DWI including intravoxel incoherent motion or arterial spin labeling [90, 91], warrant larger studies because morphologic characteristics and quantitative assessment derived from conventional imaging have been well studied and have not performed reliably in distinguishing benign and malignant tumors. Larger, multiinstitutional studies would better establish the performance of CT and MRI and address these questions of high clinical relevance.

Targeted imaging agents may also in the future allow greater sensitivity and specificity in lesion characterization; one such targeted agent for PET/CT of clear cell RCC has

already undergone testing in patients [92]. In the absence of reliable imaging markers of aggressiveness, renal mass biopsy may be further studied as a more frequently used guide in treatment selection. In addition to providing histologic subtype, biopsy specimens may in the future allow testing for specific protein expression or genetic mutations and guide targeted chemotherapy and prognostication more so than the morphology-based Fuhrman grading system.

Conclusion

Considerable challenges remain in the imaging of small renal mass. Given the incidental nature of many lesions, overall indolence of small renal masses, and lack of improved outcomes for this older patient population, despite downward stage migration in renal cancer, imaging evaluation may play an increasingly important role for decision makers in the selection of treatment. CT and MRI provide similar assessment of renal masses, but MRI may better depict enhancing components in some circumstances. MRI can also potentially provide incremental value after CT findings when a benign mass or pseudolesion is questioned, or for soft-tissue targeting in biopsy for a low-attenuation lesion. Larger studies must be conducted to determine the diagnostic performance of newer imaging techniques for predicting benignity and metastatic potential, and thus more definitively establish the role of imaging-based management in shifting renal mass treatment paradigms and improving patient health outcomes.

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