American College of Radiology
ACR Appropriateness Criteria®
Indeterminate Renal Mass

Variant 1: **Indeterminate renal mass. No contraindication to either iodinated CT contrast or gadolinium-based MR intravenous contrast. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
US abdomen with IV contrast	Usually Appropriate	O
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen without and with IV contrast	Usually Appropriate	☢☢☢☢
US kidneys retroperitoneal	May Be Appropriate	O
MRI abdomen without IV contrast	May Be Appropriate	O
CT abdomen with IV contrast	May Be Appropriate	☢☢☢
CT abdomen without IV contrast	May Be Appropriate	☢☢☢
CTU without and with IV contrast	May Be Appropriate	☢☢☢☢
Arteriography kidney	Usually Not Appropriate	☢☢☢
Radiography intravenous urography	Usually Not Appropriate	☢☢☢
Image-guided biopsy adrenal gland	Usually Not Appropriate	Varies
MRU without and with IV contrast	Usually Not Appropriate	O

Variant 2: **Indeterminate renal mass. Contraindication to both iodinated CT and gadolinium-based MR intravenous contrast. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
US abdomen with IV contrast	Usually Appropriate	O
US kidneys retroperitoneal	Usually Appropriate	O
MRI abdomen without IV contrast	Usually Appropriate	O
CT abdomen without IV contrast	May Be Appropriate	☢☢☢
Arteriography kidney	Usually Not Appropriate	☢☢☢
Radiography intravenous urography	Usually Not Appropriate	☢☢☢
Image-guided biopsy adrenal gland	Usually Not Appropriate	Varies
MRI abdomen without and with IV contrast	Usually Not Appropriate	O
MRU without and with IV contrast	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CTU without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant 3: **Indeterminate renal mass. Contraindication only to iodinated CT intravenous contrast. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
US abdomen with IV contrast	Usually Appropriate	O
MRI abdomen without and with IV contrast	Usually Appropriate	O
US kidneys retroperitoneal	May Be Appropriate	O
MRI abdomen without IV contrast	May Be Appropriate	O
CT abdomen without IV contrast	May Be Appropriate	☢☢☢
Arteriography kidney	Usually Not Appropriate	☢☢☢
Radiography intravenous urography	Usually Not Appropriate	☢☢☢
Image-guided biopsy adrenal gland	Usually Not Appropriate	Varies
MRU without and with IV contrast	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CTU without and with IV contrast	Usually Not Appropriate	☢☢☢☢

INDETERMINATE RENAL MASS

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Summary of Literature Review

Introduction/Background

Renal masses are increasingly detected in asymptomatic individuals as incidental findings. Many of these are small renal tumors that vary widely in biological aggressiveness, ranging from benign tumors to high-grade renal cell carcinomas (RCCs). An indeterminate renal mass cannot be diagnosed confidently as benign or malignant at the time it is discovered. Masses that can be definitively characterized on the first imaging test will not be discussed in this review.

CT and MRI with intravenous (IV) contrast and a dedicated multiphase protocol are the mainstays of evaluation for indeterminate renal masses. However, not all incidentally detected renal masses require such a complete assessment. For example, a homogenous mass measuring <20 Hounsfield units (HU) or >70 HU on unenhanced CT is considered benign [1,2] and does not require further imaging characterization. Any mass with density >20 HU and <70 HU as well as any heterogeneous mass on unenhanced CT is considered indeterminate and warrants further evaluation [2,3]. On contrast-enhanced CT, a homogenous renal mass measuring between −10 and 20 HU is considered a benign cyst and does not require further evaluation. Recent evidence suggests that a homogenous renal mass that measures 21 to 30 HU on a portal venous phase contrast-enhanced CT may also be considered as a benign renal cyst and does not require further evaluation [4-7].

Special Imaging Considerations

Dual-energy CT and contrast-enhanced ultrasound (CEUS) are gaining traction in the characterization of indeterminate renal masses.

Several studies have demonstrated that dual-energy CT can improve the differentiation between nonenhancing cysts and low-level-enhancing tumors [8-11]. Dual-energy CT with reconstruction of virtual monochromatic images has been shown to decrease or overcome renal cyst pseudoenhancement [12]. Other studies have shown that dual-energy CT can differentiate between solid tumors and hyperdense cysts incidentally detected on a single-phase postcontrast CT [13-15] and can be useful when a comprehensive multiphase renal protocol CT is not available.

CEUS with microbubble agents is a useful alternative for characterizing renal masses, especially for patients in whom iodinated CT contrast or gadolinium-based MRI contrast is contraindicated. The microbubble agents are not excreted by the kidneys and therefore do not affect renal function. CEUS allows real-time evaluation of microvasculature and has been shown to be valuable for differentiating between cystic and solid renal lesions and for characterizing complex renal cystic lesions and indeterminate renal masses [16-18]. CEUS may result in assignment of a higher Bosniak classification compared to contrast-enhanced CT [19,20]. However, a typical CEUS examination does not result in a complete evaluation of both kidneys for additional renal masses.

Tc-99m sestamibi single-photon emission computed tomography (SPECT)/CT has been shown in several studies to be helpful when the diagnosis of a renal oncocytoma is suspected [21-23]. For example, in a study of 31 renal masses imaged with Tc-99m sestamibi SPECT/CT, 91.6% (11 of 12) of oncocytomas had radiotracer uptake above

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adjacent normal renal parenchyma, three hybrid tumors (mixed-type oncocytoma and chromophobe renal cancer) showed tracer uptake, one papillary RCC had a slight tracer uptake, and the remaining 11 RCC were sestamibi negative [23].

CT urography (CTU) is an imaging study that is tailored to improve visualization of both the upper and lower urinary tracts. There is variability in the specific parameters, but it usually involves unenhanced images followed by IV contrast-enhanced images, including nephrographic and excretory phases acquired at least 5 minutes after contrast injection. Alternatively, a split-bolus technique uses an initial loading dose of IV contrast and then obtains a combined nephrographic-excretory phase after a second IV contrast dose; some sites include arterial phase. CTU should use thin-slice acquisition. Reconstruction methods commonly include maximum intensity projection or 3-D volume rendering. For the purposes of this document, we make a distinction between CTU and CT abdomen and pelvis without and with IV contrast. CT abdomen and pelvis without and with IV contrast is defined as any protocol not specifically tailored for evaluation of the upper and lower urinary tracts and without both the precontrast and excretory phases.

MR urography (MRU) is also tailored to improve imaging of the urinary system. Unenhanced MRU relies upon heavily T2-weighted imaging of the intrinsic high signal intensity from urine for evaluation of the urinary tract. IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones. A contrast-enhanced T1-weighted series should include corticomedullary, nephrographic, and excretory phases. Thin-slice acquisition and multiplanar imaging should be obtained. For the purposes of this document, we make a distinction between MRU and MRI abdomen and pelvis without and with IV contrast. MRI abdomen and pelvis without and with IV contrast is defined as any protocol not specifically tailored for evaluation of the upper and lower urinary tracts, without both the precontrast and excretory phases, and without heavily T2-weighted images of the urinary tract.

Initial Imaging Definition

Imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Indeterminate renal mass. No contraindication to either iodinated CT contrast or gadolinium-based MR intravenous contrast. Initial imaging.

Arteriography Kidney

Cross-sectional imaging has replaced arteriography for the evaluation of indeterminate renal masses. There is no relevant literature regarding the use of arteriography in the evaluation of an indeterminate renal mass.

CT Abdomen

CT is the most commonly used modality for evaluating indeterminate renal masses. In a retrospective study of 68 patients with small (≤4 cm) indeterminate renal masses, the diagnostic accuracy of contrast-enhanced CT for predicting RCC was 79.4% [24]. In another retrospective study of 120 patients, the sensitivity and specificity of diagnosing RCC using CT was 94.5% and 27.7%, respectively [25]. Small (≤1.5 cm) renal masses are challenging to evaluate using CT because of the phenomenon of pseudoenhancement [26] and because the partial volume-averaging limits the assessment of the presence of enhancement in a renal mass [27].

Although CT with and without IV contrast is optimal for evaluation of indeterminate renal masses, CT without IV contrast can provide some information. For example, homogenous renal masses measuring <20 HU or >70 HU [1,2] or lesions containing macroscopic fat can be characterized as benign lesions on noncontrast CT. Other studies have also shown that dual-energy CT can differentiate between solid tumors and hyperdense cysts incidentally detected on a single-phase postcontrast CT [13-15] and can be useful when a comprehensive multiphase renal protocol CT is not available.

Cystic Renal Masses

The Bosniak CT classification system for cystic renal masses encompasses the spectrum from simple renal cyst to cystic RCC, with the likelihood of malignancy increasing with the complexity of the mass [28,29]. Because the presence of any enhancing nodules, walls, or thick septa within a cystic mass is key to determining the probability of malignancy using the Bosniak classification, CT without and with IV contrast is usually necessary for evaluating these lesions. One retrospective study of 156 Bosniak IIF lesions showed that 10.9% of the lesions progressed to malignancy between 6 months and 3.2 years [30]. Another retrospective study of 69 Bosniak IIF lesions and 144 Bosniak III lesions showed malignancy rates of 25% and 54%, respectively [31]. In one study of 312 prospectively classified Bosniak lesions, the malignancy rate at pathology was 38% for Bosniak IIF, 40% for Bosniak III, and 90% for Bosniak IV renal lesions [32].

Solid Renal Masses

The presence of macroscopic fat in a noncalcified solid renal mass indicates a benign angiomyolipoma (AML) with virtual certainty. In most cases, the presence of macroscopic fat is readily apparent on CT. However, small amounts of fat may be obscured on contrast-enhanced CT. Therefore, a thin-section unenhanced CT should be used [33]. Some AMLs do not contain macroscopic fat and as such are termed "lipid poor"; definitive differentiation between lipid-poor AMLs from RCCs on CT is not possible. However, renal masses that are hyperattenuating on noncontrast CT and that homogenously enhance following IV contrast administration have been reported to have a higher probability of being a lipid-poor AML [34,35]. In those cases, biopsy of the mass may be useful to make a definitive diagnosis [36].

Oncocytoma is another benign tumor that mimics RCC, and to date there are no specific CT features to reliably differentiate between the two [37]. Enhancement pattern on multiphasic CT has been used to subtype RCC. In a retrospective study of 298 cases of RCC and oncocytoma evaluated with 4-phase CT, multiphasic enhancement threshold helped to discriminate clear-cell RCC from oncocytoma with an accuracy of 77%, clear-cell RCC from papillary RCC with an accuracy of 85%, and clear-cell RCC from chromophobe RCC with an accuracy of 84% [38]. However, no prospective studies have validated the reported enhancement threshold, and accuracies of 77% to 85% may not be sufficient to change clinical management.

CTU

While there is no literature specifically evaluating the performance of CTU for indeterminate renal masses, CTU may be useful in this context. CTU that includes the acquisition of both unenhanced and nephrographic phase images would be expected to provide the same information as CT abdomen without and with IV contrast. The excretory phase images from CTU may provide additional information for differentiating between intrarenal urothelial carcinoma from centrally located RCC [39].

Image-Guided Biopsy Adrenal Gland

Although not generally the initial workup of an indeterminate renal lesion, in recent years the indications for renal mass biopsy have expanded because of the increasing incidence of incidental small renal masses (T1a, ≤4 cm) and the development of minimally invasive treatment and active surveillance strategies for low-risk RCC [40]. Benign renal tumors, such as lipid-poor AML and oncocytoma, mimic RCC at imaging, as seen in one series of 70 renal mass biopsies in which a third were benign [41]. Many small RCCs demonstrate slow growth kinetics with a low rate of progression [42]. The biopsy results can be used to guide decision making aimed at minimizing kidney function loss, with active surveillance being chosen in cases of benign or favorable histology [43]. When there are imaging features suggestive but not diagnostic of a benign mass, such as a fat-poor AML, biopsy should be strongly considered [44]. Decision-modeling studies have also suggested that percutaneous biopsy to guide treatment decisions for small incidentally detected renal tumors can prevent unnecessary surgery in many cases [45,46]. Renal mass biopsy may assist clinical management in patients with limited life expectancy or significant comorbidities [44]. Significant biopsy-related complications are infrequent, with one study of 235 biopsies reporting significant complications in 2 patients (0.9%) [47]. An important limitation of biopsy is the rate of nondiagnostic results, especially for small renal masses. In one study [48] of 345 percutaneous biopsies of renal masses ≤4 cm, the biopsy was diagnostic in 278 cases (80.6%), of which 94.1% were RCC. When repeat biopsy was undertaken in 12 of the initial 67 nondiagnostic samples, a diagnosis was possible in 10 cases (83.3%), and 8 were malignant. The authors suggest that a nondiagnostic biopsy cannot be considered evidence of benignity.

MRI Abdomen

MRI is frequently used to characterize renal lesions. In one retrospective study of 120 patients, the specificity of MRI was significantly higher than that of CT in diagnosing RCC (68.1% versus 27.7%), whereas their sensitivities

were equivalent (91.8% versus 94.5%) [25]. In another study that evaluated 68 patients with small renal masses ≤4 cm, contrast-enhanced MRI showed higher sensitivity (88.1%) for predicting RCC; however, the specificity was low (33.3%) [24]. Renal lesions <1.5 cm may be better characterized using MRI than CT because of its high specificity for small cysts [44] and because MRI is not limited by pseudoenhancement that occurs on CT. MRI has also been shown to be more sensitive to contrast-enhancement for renal masses with indeterminate enhancement at CT [49,50]. A drawback of MRI compared with CT is the limited ability of MRI in detection of calcifications, though calcifications no longer have a significant role in the updated Bosniak Classification system (version 2019) [7].

Ho et al [51] showed that the optimal percentage of enhancement threshold for distinguishing cysts from solid tumors on MRI was 15%. Hecht et al [52] reported that both quantitative and qualitative methods are sensitive in the detection of enhancement in a renal lesion on MRI and that subtracted images enable accurate assessment of tumor enhancement for intrinsically hyperintense lesions using qualitative methods.

Although MRI without and with IV contrast is optimal for renal lesion characterization, MRI without IV contrast can also provide diagnostic information. For example, simple cystic lesions, or even those with thin septations, can often be characterized on noncontrast T2-weighted imaging based on their homogeneous and very high T2 signal intensity. To differentiate between hemorrhagic or proteinaceous cyst and RCC, a retrospective study shows that homogenous high T1 signal intensity lesions with smooth borders and lesion to renal parenchyma signal intensity ratio of >1.6 predicted the lesion as a benign cyst [53]. Another study of 144 T1-hyperintense lesions demonstrated that diffuse and marked T1-hyperintensity achieved accuracies of 73.6% to 79.9% for the diagnosis of T1-hyperintense cysts [54]. An angular interface with the renal parenchyma on T2-weighted imaging has been shown to be 78% sensitive and 100% specific for differentiating benign exophytic renal masses from malignant masses [55]. Diffusion-weighted imaging, although less accurate than contrast-enhanced MRI, may have some ability to differentiate solid RCC from oncocytomas and characterize the histologic subtypes of RCC [56]. New and specialized MRI sequences have been proposed for the purposes of characterizing the vascularity of renal lesions in patients with renal dysfunction. For example, one small study of 17 renal lesions used arterial spin labeling to detect blood flow in renal masses, which correlated with malignancy [57].

Cystic Renal Masses

In a study of 69 cystic renal masses evaluated using the Bosniak classification with CT and MRI, there was CT and MRI agreement in 56 of 69 lesions (81%) and disagreement in 13 of 69 lesions (19%) [29]. CT and MRI were felt to be similar in evaluation of most renal cystic mass lesions. However, MRI may depict additional findings, such as an increase in number of septa, septal or wall thickness, and enhancement. Such findings would result in MRI upgrading cystic lesions and thus might alter patient management [29]. Another study of 33 cystic lesions imaged with both 1.5T and 3.0T MRI showed that there is a greater tendency to upgrade cyst complexity and Bosniak cyst category at 3.0T than at 1.5T and thus suggested that serial follow-up of cystic renal lesions be performed at constant field strength [58].

Solid Renal Masses

Other than AMLs with macroscopic fat, MRI cannot yet reliably differentiate benign from malignant renal tumors. However, several MRI features have been reported to be useful for suggesting types of solid renal tumors. In one multiparametric MRI study, lipid-poor AMLs were characterized by higher T1 signal intensity and lower T2 signal intensity compared to normal renal cortex and by greater arterial-to-delayed enhancement ratio than RCC [59]. Another study showed that the combination of low T2 signal and signal drop on chemical-shift imaging is specific for lipid-poor AMLs but lacks sensitivity, and the combination of low T2 signal intensity and high area under the contrast-enhanced MRI curve is sensitive and specific for lipid-poor AMLs [60]. Although both papillary RCC and lipid-poor AMLs can have low signal intensity on T2-weighted images, the presence of intratumoral hemorrhage seen on T1-weighted images was suggested to be a specific feature of papillary RCC [61]. Nonetheless, MRI findings of lipid-poor AMLs overlap with various RCC subtypes and remain difficult to prospectively diagnose [60].

Findings on MRI that suggest a lipid-poor AML may warrant a biopsy for definitive diagnosis. Sun et al [62] reported that tumor signal intensity changes on the corticomedullary phase MRI were the most effective in distinguishing clear-cell and papillary RCC, the two most common subtypes of RCC, with area under the receiver operating characteristic curve (AUC) of 0.99. Hotker et al [63] showed that the combination of parameters' apparent diffusion coefficient, peak enhancement, and downslope achieved a high diagnostic accuracy (AUC 0.889–0.907) for the identification of clear-cell RCC. A recent multileader study showed that a standardized MRI-based

diagnostic algorithm had diagnostic accuracy of 81% (88 of 109) and 91% (99 of 109) in the diagnosis of clear-cell RCC and papillary RCC, respectively, while achieving moderate to substantial inter-reader agreement among 7 radiologists [64].

MRU
There is no relevant literature regarding the use of MRU in the evaluation of indeterminate renal masses.

Radiography Intravenous Urography
There is no relevant literature regarding the use of IV urography (IVU) in the evaluation of indeterminate renal masses.

US Abdomen with IV Contrast
CEUS using microbubble agents is emerging as a useful way to characterize previously indeterminate renal lesions [16-18]. In a study of 1,018 indeterminate renal lesions, CEUS had a per patient sensitivity of 100% (126 of 126 patients), specificity of 95% (132 of 139 patients), positive predictive value of 94.7% (126 of 133 patients), and negative predictive value of 100% (132 of 132 patients) for classifying benign versus malignant renal masses [16]. In that study, any echogenic masses with enhancement equal to or greater than normal renal cortex and wash-out, and any masses with blood flow, were considered malignant. In another study, CEUS successfully classified 95.7% (90 of 94) previously indeterminate lesions and has an accuracy of 90.2% (37 of 41 lesions) when compared with the reference standard, including histopathology and follow-up [18]. In the subgroup analysis, CEUS was definitive for 94.4% (17 of 18) of cases referred because of equivocal enhancement at CT [18]. In that same study, CEUS was able to classify lesions in 100% (10 of 10) of the cases in which the lesions were indeterminate on prior MRI [18]. Another study of CEUS in 83 CT indeterminate renal masses reported that the accuracy of characterization by CEUS was 95.2% compared with 42.2% using unenhanced US [17].

Studies have shown CEUS to be more sensitive than contrast-enhanced CT in characterizing cystic renal masses [19,65]. In a study of 31 cystic renal masses evaluated by both CT and CEUS using the Bosniak classification, 26% of the lesions were upgraded by CEUS [19]. In a prospective CEUS study of 94 solid renal lesions excluding lipid-rich AML, hypovascularity of small solid renal masses relative to the cortex in the arterial phase has 100% specificity for detecting malignancy, especially for detecting papillary RCC [66]. Quantitative analysis of CEUS has also been reported to be useful to stratify RCC and benign renal tumors [67,68].

US Kidneys Retroperitoneal
US can detect and characterize renal masses. The criteria for US diagnosis of renal cysts are well defined. To diagnose renal cysts via US, the mass must be sonolucent, demonstrate good through-transmission of the sound waves with posterior enhancement, and have a thin, well-defined wall. US has been shown to be useful in further characterizing hyperattenuating cysts presenting as indeterminate hyperattenuating renal lesions on CT [69]. Complex masses without detected Doppler flow and that do not fulfill the criteria of cysts on US are considered indeterminate and require further evaluation, usually by contrast-enhanced CT or MRI. However, a recent retrospective study of 161 hyperechoic renal lesions measuring ≤1 cm at US showed that 98.1% of them were considered clinically insignificant, suggesting that such lesions may not require additional imaging [70].

Variant 2: Indeterminate renal mass. Contraindication to both iodinated CT and gadolinium-based MR intravenous contrast. Initial imaging.

Arteriography Kidney
Cross-sectional imaging has replaced arteriography for the evaluation of indeterminate renal masses. There is no relevant literature regarding the use of arteriography in the evaluation of indeterminate renal masses. Arteriography typically requires IV administration of iodinated contrast.

CT Abdomen
Iodinated CT contrast is contraindicated in some patients with severe allergy to the CT contrast or patients who are at high risk for contrast-induced nephropathy. For more details, please refer to the ACR *Manual on Contrast Media* [71]. The inability to utilize IV contrast to evaluate a renal mass markedly limits whether it can be classified as benign or malignant on CT, but it does provide some information if calcifications, nodules, or septations are visible. Homogenous renal masses measuring <20 HU or >70 HU [1,2] or lesions containing macroscopic fat can be characterized as benign lesions, but all other small lesions cannot be characterized using CT without IV contrast. Large lesions with calcifications and necrosis may not need further characterization, but detection of venous invasion and metastases is also limited.

CTU
There is no relevant literature regarding the use of CTU in the evaluation of indeterminate renal masses.

Image-Guided Biopsy Adrenal Gland
Invasive sampling is not generally the initial workup of indeterminate renal masses. However, in recent years, the indications for renal mass biopsy have expanded because of the increasing incidence of incidental small renal masses (T1a, ≤4 cm), the development of minimally invasive treatment, and active surveillance strategy for low-risk RCC [40]. Benign renal tumors, such as lipid-poor AML and oncocytoma, mimic RCC at imaging, as seen in one series of 70 renal mass biopsies in which a third were benign [41]. Many small RCCs demonstrate slow growth kinetics with a low rate of progression [42]. The biopsy results can be used to guide decision making aimed at minimizing kidney function loss with active surveillance being chosen in cases of benign or favorable histology [43]. When there are imaging features suggestive of a benign mass, such as a fat-poor AML, biopsy should be strongly considered [44]. Decision-modeling studies have also suggested that percutaneous biopsy to guide treatment decisions for small incidentally detected renal tumors can prevent unnecessary surgery in many cases [45,46]. Renal mass biopsy may assist clinical management in patients with limited life expectancy or significant comorbidities [44]. Significant biopsy-related complications are infrequent, with one study of 235 biopsies reporting significant complications in 2 patients (0.9%) [47]. An important limitation of biopsy is the rate of nondiagnostic results, especially for small renal masses. In one study [48] of 345 percutaneous biopsies of renal masses ≤4 cm, the biopsy was diagnostic in 278 cases (80.6%), 94.1% of which were RCCs. When repeat biopsy was undertaken in 12 of the initial 67 nondiagnostic samples, a diagnosis was possible in 10 cases (83.3%), and 8 were malignant. The authors suggest that a nondiagnostic biopsy cannot be considered evidence of benignity.

MRI Abdomen
Because of the risk for nephrogenic systemic fibrosis [72], certain gadolinium-based contrast agents may be contraindicated in patients with renal failure. Another contraindication is severe allergy to gadolinium agents. For more details, please refer to the ACR *Manual on Contrast Media* [71]. In the absence of contrast, unenhanced MRI has some advantages over unenhanced CT in the characterization of renal masses. Simple cystic lesions or even those with thin septations can often be characterized on noncontrast T2-weighted imaging based on their homogeneous and very high T2 signal intensity. To differentiate between hemorrhagic or proteinaceous cysts and RCC, a retrospective study shows that homogenous high T1 signal intensity lesions with smooth borders and lesion to renal parenchyma signal intensity ratio of >1.6 predicted the lesion as a benign cyst [53]. Another study of 144 T1-hyperintense lesions demonstrated that diffuse and marked T1-hyperintensity achieved accuracies of 73.6% to 79.9% for the diagnosis of T1-hyperintense cysts [54]. An angular interface with the renal parenchyma on T2-weighted imaging has been shown to be 78% sensitive and 100% specific for differentiating benign exophytic renal masses from malignant masses [55]. Diffusion-weighted imaging, although less accurate than contrast-enhanced MRI, may have some ability to differentiate solid RCC from oncocytomas and characterize the histologic subtypes of RCC [56]. New and specialized MRI sequences have been proposed for the purposes of characterizing the vascularity of renal lesions in patients with renal dysfunction. For example, one small study of 17 renal lesions used arterial spin labeling to detect blood flow in renal masses, which correlated with malignancy [57]. A drawback of MRI compared with CT is the limited ability of MRI for detection of calcifications.

MRU
There is no relevant literature regarding the use of MRU in the evaluation of indeterminate renal masses.

Radiography Intravenous Urography
There is no relevant literature regarding the use of IVU for the evaluation of indeterminate renal masses. IVU requires IV administration of iodinated contrast.

US Abdomen with IV Contrast
CEUS using microbubble agents is emerging as a useful way to characterize previously indeterminate renal lesions [16-18]. It is not limited by renal or hepatic failure. In one study of 1,018 indeterminate renal lesions, CEUS had a per patient sensitivity of 100% (126 of 126 patients), specificity of 95% (132 of 139 patients), positive predictive value of 94.7% (126 of 133 patients), and negative predictive value of 100% (132 of 132 patients) for classifying benign versus malignant renal masses [16]. In that study, any echogenic masses with enhancement at least of normal renal cortex and wash-out as well as any masses with blood flow were considered malignant. In another study, CEUS successfully classified 95.7% (90 of 94) of previously indeterminate lesions and has an accuracy of 90.2% (37 of 41 lesions) when compared with the reference standard, including histopathology and follow-up [18]. In the subgroup analysis, CEUS was definitive for 94.4% (17 of 18) of cases referred because of equivocal enhancement

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For patients with contraindication to either iodinated CT contrast or gadolinium-based MRI contrast, US is useful for characterization of renal masses. The criteria for US diagnosis of renal cysts are well defined. To diagnose renal cysts via US, the mass must be sonolucent, demonstrate good through-transmission of the sound waves with posterior through-transmission, and have a thin, well-defined wall. US has been shown to be useful in further characterizing hyperattenuating cysts presenting as indeterminate hyperattenuating renal lesions on CT [69]. Complex masses not fulfilling the criteria of cysts on US are considered indeterminate and require further evaluation, usually by contrast-enhanced CT or MRI. However, a recent retrospective study of 161 hyperechoic renal lesions measuring ≤1 cm at US showed that 98.1% of them were considered clinically insignificant, suggesting that such lesions may not require additional imaging [70].

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Arteriography Kidney
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CT Abdomen
Iodinated CT contrast is contraindicated in some patients with severe allergy to the CT contrast or in patients who are at high risk for contrast-induced nephropathy. For more details, please refer to the ACR *Manual on Contrast Media* [71]. The inability to utilize IV contrast to evaluate a renal mass markedly limits whether it can be classified as benign or malignant on CT, but it can provide some information. Homogenous renal masses measuring <20 HU or >70 HU [1,2] or lesions containing macroscopic fat can be characterized as benign lesions, but all other small lesions cannot be characterized using CT without IV contrast. Large lesions with calcifications and necrosis may not need further characterization, but detection of venous invasion and metastases is also limited.

CTU
There is no relevant literature regarding the use of CTU in the evaluation of indeterminate renal masses.

Image-Guided Biopsy Adrenal Gland
Invasive sampling is not generally the initial workup of indeterminate renal masses. However, in recent years, the indications for renal mass biopsy have expanded because of the increasing incidence of incidental small renal masses (T1a, ≤4 cm), the development of minimally invasive treatment, and active surveillance strategy for low-risk RCC [40]. Benign renal tumors, such as lipid-poor AML and oncocytoma, mimic RCC at imaging, as seen in one series of 70 renal mass biopsies in which a third were benign [41]. Many small RCC demonstrate slow growth kinetics with a low rate of progression [42]. The biopsy results can be used to guide decision making aimed at minimizing kidney function loss with active surveillance being chosen in cases of benign or favorable histology [43]. When there are imaging features suggestive of a benign mass, such as a fat-poor AML, biopsy should be strongly considered [44]. Decision-modeling studies have also suggested that percutaneous biopsy to guide treatment decision for small incidentally detected renal tumors can prevent unnecessary surgery in many cases [45,46]. Renal mass biopsy may assist clinical management in patients with limited life expectancy or significant comorbidities [44]. Significant biopsy-related complications are infrequent, with one study of 235 biopsies reporting significant complications in 2 patients (0.9%) [47]. An important limitation of biopsy is the rate of nondiagnostic results, especially for small renal masses. In one study [48] of 345 percutaneous biopsies of renal masses ≤4 cm, the biopsy was diagnostic in 278 cases (80.6%), of which 94.1% were RCC. When a repeat biopsy was undertaken in 12 of the initial 67 nondiagnostic samples, a diagnosis was possible in 10 cases (83.3%), and 8 were malignant. The authors suggest that a nondiagnostic biopsy cannot be considered evidence of benignity.

MRI Abdomen

MRI is frequently used to characterize renal lesions. In one retrospective study of 120 patients, the sensitivity and specificity of MRI without and with IV contrast for diagnosing RCC were 91.8% and 68.1%, respectively [25]. In another study that evaluated 68 patients with small renal masses ≤4 cm, contrast-enhanced MRI showed a sensitivity of 88.1% for predicting RCC; however, the specificity was low (33.3%) [24]. Renal lesions <1.5 cm may be better characterized using MRI than CT because of its high specificity for small cysts [44]. A drawback of MRI compared to CT is the limited ability of MRI in detection of calcifications.

Ho et al [51] showed that the optimal percentage of enhancement threshold for distinguishing cysts from solid tumors on MRI was 15%. Hecht et al [52] reported that both quantitative and qualitative methods are sensitive in the detection of enhancement in a renal lesion on MRI and that subtracted images enables accurate assessment of tumor enhancement for intrinsically hyperintense lesions using qualitative methods.

Although MRI without and with IV contrast is optimal for renal lesion characterization, MRI without IV contrast can also provide diagnostic information. For example, simple cystic lesions or even those with thin septations can often be characterized on noncontrast T2-weighted imaging based on their homogeneous and very high T2 signal intensity. To differentiate between hemorrhagic or proteinaceous cysts and RCC, a retrospective study shows that homogenous high T1 signal intensity lesions with smooth borders and lesion to renal parenchyma signal intensity ratio of >1.6 predicted the lesion as a benign cyst [53]. Another study of 144 T1-hyperintense lesions demonstrated that diffuse and marked T1 hyperintensity achieved accuracies of 73.6% to 79.9% for the diagnosis of T1-hyperintense cysts [54]. An angular interface with the renal parenchyma on T2-weighted imaging has been shown to be 78% sensitive and 100% specific for differentiating benign exophytic renal masses from malignant masses [55]. Diffusion-weighted imaging, although less accurate than contrast-enhanced MRI, may have some ability to differentiate solid RCC from oncocytomas and characterize the histologic subtypes of RCC [56]. New and specialized MRI sequences have been proposed for the purposes of characterizing the vascularity of renal lesions in patients with renal dysfunction. For example, one small study of 17 renal lesions used arterial spin labeling to detect blood flow in renal masses, which correlated with malignancy [57].

Cystic Renal Masses

In a patient who cannot receive iodinated contrast, MRI without and with IV contrast is a good alternative. MRI may depict findings like an increase in number of septa, septal or wall thickness, and enhancement; these may result in MRI upgrading cystic lesions and thus might alter patient management [29]. Another study of 33 cystic lesions imaged with both 1.5T and 3.0T MRI showed that there is a greater tendency to upgrade cyst complexity and Bosniak cyst category at 3.0T than at 1.5T and thus suggested that serial follow-up of cystic renal lesions be performed at constant field strength [58].

Solid Renal Masses

Other than AMLs with macroscopic fat, MRI cannot yet reliably differentiate benign from malignant renal tumors. However, several MRI features have been reportedly useful for suggesting certain types of solid renal tumors. In one multiparametric MRI study, lipid-poor AMLs were characterized by higher T1 signal intensity and lower T2 signal intensity, compared with normal renal cortex, and greater arterial-to-delayed enhancement ratio than RCC [59]. Another study showed that the combination of low T2 signal and signal drop on chemical-shift imaging is specific for lipid-poor AMLs but lacks sensitivity, and the combination of low T2 signal intensity and high AUC contrast-enhanced MRI curve is sensitive and specific for lipid-poor AMLs [60]. Although both papillary RCC and lipid-poor AMLs can have low signal intensity on T2-weighted images, the presence of intratumoral hemorrhage seen on T1-weighted images was suggested to be a specific feature of papillary RCC [61]. Nonetheless, MRI findings of lipid-poor AMLs overlap with various RCC subtypes and remain difficult to prospectively diagnose [60]. However, findings on MRI that suggest a lipid-poor AML may warrant a biopsy for definitive diagnosis. Sun et al [62] reported that tumor signal intensity changes on the corticomedullary phase MRI were the most effective in distinguishing clear-cell and papillary RCC, the two most common subtypes of RCC, with AUC of 0.99. Hotker et al [63] showed that the combination of parameters' apparent diffusion coefficient, peak enhancement, and downslope achieved a high diagnostic accuracy (AUC 0.889–0.907) for the identification of clear-cell RCC. A recent multireader study showed that a standardized MRI-based diagnostic algorithm had a diagnostic accuracy of 81% (88 of 109) and 91% (99 of 109) in the diagnosis of clear-cell RCC and papillary RCC, respectively, while achieving moderate to substantial inter-reader agreement among 7 radiologists [64].

MRU

There is no relevant literature regarding the use of MRU in the evaluation of indeterminate renal masses.

Radiography Intravenous Urography
There is no relevant literature regarding the use of IVU for the evaluation of indeterminate renal masses.

US Abdomen with IV Contrast
CEUS using microbubble agents is emerging as a useful way to characterize previously indeterminate renal lesions [16-18]. In one study of 1,018 indeterminate renal lesions, CEUS had a per patient sensitivity of 100% (126 of 126 patients), specificity of 95% (132 of 139 patients), positive predictive value of 94.7% (126 of 133 patients), and negative predictive value of 100% (132 of 132 patients) for classifying benign versus malignant renal masses [16]. In that study, any echogenic masses with enhancement at least of normal renal cortex and wash-out, as well as any masses with blood flow, were considered malignant. In another study, CEUS successfully classified 95.7% (90 of 94) previously indeterminate lesions, and had an accuracy of 90.2% (37 of 41 lesions) when compared with the reference standard, including histopathology and follow-up [18]. In the subgroup analysis, CEUS was definitive for 94.4% (17 of 18) of cases referred because of equivocal enhancement at CT [18]. In that same study, CEUS was able to classify lesions in 100% (10 of 10) of the cases in which the lesions were indeterminate on prior MRI [18]. Another study of CEUS in 83 CT indeterminate renal masses reported that the accuracy of characterization by CEUS was 95.2% compared with 42.2% using unenhanced US [17].

In a prospective CEUS study of 94 solid renal lesions, excluding lipid-rich AML, hypovascularity of small solid renal masses relative to the cortex in the arterial phase has 100% specificity for detecting malignancy, especially for detecting papillary RCC [66]. Quantitative analysis of CEUS has also been reported to be useful to stratify RCC and benign renal tumors [67,68].

US Kidneys Retroperitoneal
US plays an additionally important role in the detection and characterization of renal masses in patients who cannot receive iodinated contrast. The criteria for US diagnosis of renal cysts are well defined. To diagnose renal cysts via US, the mass must be sonolucent, must demonstrate a good through-transmission of the sound waves with posterior enhancement, and have a thin, well-defined wall. US has been shown to be useful in further characterizing hyperattenuating cysts presenting as indeterminate hyperattenuating renal lesions on CT [69]. Complex masses not fulfilling the criteria of cysts on US are considered indeterminate and require further evaluation, usually by contrast-enhanced MRI in these patients. However, a recent retrospective study of 161 hyperechoic renal lesions measuring ≤1 cm at US showed that 98.1% of them were considered clinically insignificant, suggesting that such lesions may not require additional imaging [70].

Summary of Recommendations

- **Variant 1:** CT abdomen without and with IV contrast, MRI abdomen without and with IV contrast, or US abdomen with IV contrast is usually appropriate for the initial imaging of an indeterminate renal mass in patients without contraindications to either iodinated CT contrast or gadolinium-based MR IV contrast. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2:** US abdomen with IV contrast, US kidneys retroperitoneal, or MRI abdomen without IV contrast is usually appropriate for the initial imaging of an indeterminate renal mass in patients with contraindications to both iodinated CT and gadolinium-based MR IV contrast. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 3:** US abdomen with IV contrast or MRI abdomen without and with IV contrast is usually appropriate for the initial imaging of an indeterminate renal mass in patients with contraindications to iodinated CT IV contrast. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).

Supporting Documents
The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [73].

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

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