Radiology

Incompletely Characterized Incidental Renal Masses:

Emerging Data Support Conservative Management[1]

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With imaging, most incidental renal masses can be diagnosed promptly and with confidence as being either benign or malignant. For those that cannot, management recommendations can be devised on the basis of a thorough evaluation of imaging features. However, most renal masses are either too small to characterize completely or are detected initially in imaging examinations that are not designed for full evaluation of them. These masses constitute a group of masses that are considered incompletely characterized. On the basis of current published guidelines, many masses warrant additional imaging. However, while the diagnosis of renal cancer at a curable stage remains the first priority, there is the additional need to reduce unnecessary healthcare costs and radiation exposure. As such, emerging data now support foregoing additional imaging for many incompletely characterized renal masses. These data include the low risk of progression to metastases or death for small renal masses that have undergone active surveillance (including biopsy-proven cancers) and a better understanding of how specific imaging features can be used to diagnose their origins. These developments support *(a)* avoidance of imaging entirely for those incompletely characterized renal masses that are highly likely to be benign cysts and *(b)* delay of further imaging of small solid masses in selected patients. Although more evidence-based data are needed and comprehensive management algorithms have yet to be defined, these recommendations are medically appropriate and practical, while limiting the imaging of many incompletely characterized incidental renal masses.

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There are established, time-tested guidelines for the image-based evaluation and management of renal masses (1–7). These guidelines are based largely on imaging examinations that provide a thorough evaluation of all features of a renal mass. Indeed, a full evaluation of a renal mass, typically with a renal mass protocol computed tomographic (CT) or magnetic resonance (MR) imaging examination, leads to either a confident diagnosis or an evidence-based assessment of the probability of a diagnosis. However, with the burgeoning use of imaging in medicine today, many renal masses are either too small to characterize fully or are detected incidentally in examinations that are not designed for complete evaluation of renal masses. When an imaging examination demonstrates only some features, and they are not diagnostic, the masses are considered incompletely characterized. Current renal mass management guidelines recommend additional imaging for many of these lesions, typically in the form of a renal mass protocol CT or MR imaging examination (3,5–7). The drive to evaluate incompletely characterized renal masses is predicated in part on the fact that renal cell carcinoma (RCC) is most commonly diagnosed as an incidental finding (4). Moreover, when a renal cancer is found, the patient's prognosis depends largely on detecting the cancer at the organ-confined stage (4,8). However, the recognition of the indolent behavior of many small renal masses, including some that are cancers, is now prompting a less aggressive, conservative approach and one that could include not imaging further many masses that are incompletely characterized. In addition, data available now support making management decisions for many renal masses with less image-based information than was recommended in the past. Specifically, these data support foregoing additional evaluation of some incompletely characterized renal masses, while reserving additional testing for a select few. In this article, we review the rationale for conservative approaches to small renal masses, describe the types of incompletely characterized renal masses, and provide recommendations for management. Knowledge gaps and deficiencies in the data are highlighted to stimulate future research.

Essentials

- Incidental renal masses are considered incompletely characterized with imaging when they are too small to evaluate completely or when they are detected in examinations that are not designed for complete evaluation of them.
- Although most incompletely characterized incidental renal masses are benign, current guidelines do not include a comprehensive set of recommendations as to which masses might indicate further imaging and which would not.
- Several recently recognized factors support the conservative management of incompletely characterized renal masses, including evidence that *(a)* many small solid renal masses are either benign neoplasms or indolent cancers, *(b)* active surveillance of renal masses (including cancers) is safe in selected patients, and *(c)* there is potential for long-term adverse effects, such as chronic kidney disease after nephrectomy.
- There are sufficient data to support foregoing additional imaging of some incompletely characterized renal masses on the basis of identifying specific features, such as masses with homogeneous low (≤20 HU) or high (≥70 HU) attenuation at unenhanced CT; the recommendations provided may help limit unnecessary imaging, with its attendant cost, radiation exposure, and potential morbidity.
- Additional research is needed to understand further the natural history of renal masses, including untreated small cancers, to learn the outcomes of various management strategies and consequently to establish a comprehensive imaging-based algorithm to guide the management of incompletely characterized renal masses.

Rationale for Conservative Approaches to Renal Mass Evaluation

While no single imaging feature can be used to predict accurately the risk of progression and death from renal cancer, the overall approach to renal masses, including those diagnosed as cancers, is now less aggressive than in the past, particularly for those smaller than 3–4 cm (9–11). For renal masses found at imaging, approaches considered conservative, relative to either prompt evaluation or treatment, include ignoring the mass or following it over time with imaging, an approach now known as "active surveillance" (9). Active surveillance is emerging as a viable approach to the management of renal masses, including those diagnosed as renal cancers. The data and experiences learned from active surveillance provide insight into how incompletely characterized renal masses could be managed. The conservative approach to renal masses, including active surveillance, is predicated on five principal, relatively recently recognized factors or developments.

Many Solid Renal Masses Are Benign

It is well established that most incidentally detected renal masses are benign, and most are benign cysts (12). Many solid renal masses are also benign (13). A benign angiomyolipoma can be diagnosed by the identification of fat in a noncalcified renal mass (3,7,14). Indeed, no single imaging feature is as diagnostically specific as the presence of lesion fat. However, in the past, non–fat-containing solid renal masses were either presumed to be renal cancers or thought to require surgical resection

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Abbreviation:
RCC = renal cell carcinoma

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for diagnosis and cancer exclusion. With this understanding and approach, to determine how often surgically resected masses were benign, a retrospective review of 2770 resections of solid renal masses demonstrated that 12.8% were benign; almost all were oncocytomas and angiomyolipomas (13). Moreover, when stratified by size, the proportion of benign masses was 25% among masses smaller than 3 cm, 30% among masses smaller than 2 cm, and 44% among masses smaller than 1 cm (13). Therefore, although solid renal masses were more likely cancers, many were benign, particularly those that were small. These data demonstrated that among non–fat-containing solid renal masses, the smaller the mass, the more likely they are benign (13). However, size alone is not diagnostic (15), nor are growth kinetics (16). Growth is not diagnostic of a malignancy, because some benign neoplasms grow; for example, renal oncocytomas can grow at a rate similar to that of RCC (17). Lack of growth is not diagnostic of a benign neoplasm, either; RCC may grow little, if at all (10,11,18–21). At present, with respect to developing definitive criteria to distinguish benign from malignant solid renal masses at imaging, additional research is needed, but it is clear that size is an important factor to consider in devising a management plan for renal masses.

Many Small RCCs Are Indolent

In addition to the problems noted in diagnosis, there is no single feature at imaging (or at pathologic examination) that is entirely predictive of the biological behavior of small RCC (22–27). Size does appear to be an important imaging feature; most small RCCs are low grade, and clinical behavior is indolent, manifested by a lack of growth and a low potential for distant metastasis (10,13,16,28). The existence of indolent, nonlethal renal cancers is supported further by the finding of small solid nodules in as many as 50% of kidneys at necropsy; some are indistinguishable from papillary RCC yet are considered "adenomas" on the sole basis of size (smaller than 5 mm) (29). However, size alone is not predictive of biological behavior (11,27,30,31). Beyond size, the relative proportion of solid to cystic components of a renal mass is another imaging feature that appears to predict biological behavior; the more cystic components, the less aggressive the histologic subtype and the lower the nuclear grade (32). Cystic RCC is often less aggressive than solid RCC (33–35). A recent study of 47 cystic RCCs with a mean follow-up of 51 months yielded no growth, local recurrences, or metastases other than one in which a metastasis was found at presentation (36). Another study demonstrated that overall and cancer-specific survival was better among cystic RCCs compared with solid RCCs (37). Of 62 patients with 69 Bosniak category IIF masses and 131 patients with 144 Bosniak category III masses, although many were not resected or proven malignant (the malignancy rate of resected Bosniak category IIF lesions was 25%, and that for Bosniak category III lesions was 54%), no patients that were followed up for at least 1 year developed locally recurrent or metastatic disease (38). The potential to use imaging more effectively to predict genotypes and biological behavior of RCC is an important and active area of investigation (39).

Treatment Is Costly and Potentially Morbid

The use of extirpative surgery (radical or partial nephrectomy) and thermal ablative techniques to treat renal masses is increasing (40). However, surgery for renal masses is costly (41) and may lead to both short- and long-term adverse outcomes (42–44). In addition to complications after surgical (45–48) and imaging-guided percutaneous procedures (49), the concomitant sacrifice of normal nephrons may lead to chronic kidney disease and poor health outcomes (50–52). A recent matched-cohort multi-institutional study involving the Surveillance, Epidemiology, and End Results Medicare data set of cases managed with partial (n = 1471) or radical (n = 4299) nephrectomy for RCC 4 cm or smaller compared with two control groups, one with nonmuscle invasive bladder cancer and the other without cancer, demonstrated that hazard ratios for renal events (eg, hospitalizations related to end-stage renal disease) were increased for both nephrectomy groups compared with control subjects (30). In addition, cardiovascular events were increased for patients undergoing partial and radical nephrectomy compared with patients without cancer (30). Since chronic kidney disease is associated with increased mortality from cardiovascular disease and other causes (52), and since nephrectomy is a marked risk factor for chronic kidney disease (53), the decrease in survival (54) and increased other-cause mortality 5 years (54–56) after radical nephrectomy relative to partial nephrectomy has been attributed to chronic kidney disease. However, the decrease in survival after radical nephrectomy relative to partial nephrectomy has been questioned by others (57) and postulated to result from selection bias in observational studies (58). Since a prospective, randomized trial demonstrated no survival benefit among patients undergoing nephron-sparing surgery compared with radical nephrectomy, some surgeons are less inclined to perform partial nephrectomy (57). Regardless of which surgical approach is optimal or to what degree surgery does harm, the treatment of small renal masses, often presumed to be cancers, may lead to either the unnecessary treatment of a benign neoplasm or the treatment of a cancer that might not have limited the patient's survival. Indeed, one study showed that despite the increasing incidence of small RCC and subsequent treatment, cancer-specific and overall mortality rates increased for each tumor size category (59).

RCC Is an Uncommon Cause of Mortality

RCC is a relatively less common cause of mortality; patients are much more likely to die of other causes (56,60). However, most of the evidence showing that RCC is a rare cause of cancer mortality originates from series of patients who were treated surgically for RCC (61). Thus, the long-term natural history of untreated RCC remains largely unknown

(62). Eighty-five percent of the U.S. population aged 65 and older has one or more chronic conditions; hypertension, heart disease, and diabetes—conditions that increase the long-term risk of chronic kidney disease—are among the most common (63). Therefore, as the population ages, the competing risk of concomitant health problems may be the most important determinant of how to manage an incidentally discovered small renal mass (63).

Active Surveillance of Renal Masses Is Safe in Selected Patients

Active surveillance has been used to manage selected renal masses for many years; Bosniak category IIF cystic renal masses are followed up (64), and it has been suggested that solid renal masses smaller than 1 cm be followed up (7). Recent data have contributed to the growing acceptance of active surveillance for a larger subset of renal masses (8,27), bolstered further by the acceptance of percutaneous biopsy as a useful test to diagnose both cancers and benign neoplasms (4). Several distinct clinical settings for the role of biopsy in the diagnosis of solid and cystic renal masses were detailed in 2006 (65). That article described the historical indications for renal mass biopsy, such as obtaining a tissue diagnosis in patients with imaging findings of unresectable renal cancer and distinguishing RCC from metastases in patients with extrarenal primary tumors. The article also reviewed emerging indications, now established in our practice, such as renal masses prior to ablation, and renal masses that are hyperattenuating and enhancing and therefore could represent fat-poor angiomyolipomas (65). Since then, the use of biopsy has increased; several reports have shown the accuracy and safety of renal mass biopsy (66–68). As a result, the literature is replete with clinical reports, reviews, and opinion articles on the management of "small renal masses"—a term that could be misconstrued as referring only to solid renal masses or only to RCC (69). In fact, most small renal masses in the reported series were not biopsied; therefore, many of the masses studied were not RCC, and some may not have been solid. This would mirror a clinical scenario in which a renal mass that is not sampled for biopsy (and therefore the diagnosis is not known) is followed up rather than treated. However, the data cannot be used to fully describe the risk of observing an RCC lesion.

When observing patients with a renal mass, the principal risk of active surveillance is progression to metastasis. The evidence suggests that small masses present a low risk of developing metastases during follow-up, particularly those smaller than 3 cm (27,70). Metastases are also rare in the absence of growth (71) but occur in approximately 1.5% of patients undergoing active surveillance (15,20,27,31,72). In the context of active surveillance, a pooled analysis of 880 patients with 936 masses who underwent active surveillance demonstrated that the proportion of masses that progressed to metastasis was small; 18 that progressed to metastatic disease had a higher mean linear growth rate (0.8 cm per year) than nonprogressing masses (0.3 cm per year) and generally progressed after an extended period (mean time to metastases, 40.2 months). Of the 23% of masses that exhibited no growth in that study, none progressed to metastasis. A pooled analysis of six studies (259 patients with 284 masses) also showed that increased age (75 vs 66 years, $P = .03$), initial greatest mass dimension (4.1 vs 2.1 cm, $P < .0001$), initial estimated mass volume (66.6 vs 15.1 cm^3), linear growth rate (0.8 vs 0.3 cm per year, $P = .0001$), and volumetric growth rate (27.1 vs 6.2 cm^3 per year, $P < .0001$) were more common in the progression cohort. Although positive growth appeared to be the strongest predictor for progression to metastasis, the data are inconclusive as to which growth metric is best, which threshold should be used to trigger treatment, and in which patients a surveillance approach should be applied (27).

Percutaneous biopsy, in addition providing a diagnosis of both benign and malignant renal masses, has been suggested as a means to help stratify renal cancers for risk on the basis of tumor histologic subtype and Fuhrman nuclear grade and to select those patients who would benefit from active surveillance (73). In a recent study of 151 patients with small (<4 cm) renal masses (73), biopsy results were divided into favorable, intermediate, and unfavorable categories on the basis of tumor size, subtype, and grade. For example, chromophobe RCC and grade 1 papillary RCC were included in the favorable category, and grades 3 and 4 RCC and sarcomatoid RCC were included in the unfavorable category. A biopsy-directed management algorithm was devised to triage patents to active surveillance or surgery. While the agreement between biopsy and final pathologic result was 92%, final pathologic results showed that 11 patients initially assigned to surveillance should have been assigned to treatment (8.3% of all patients and 31% of those recommended for surveillance), whereas no patients moved from treatment to surveillance. Of the 11 misclassified patients, seven had a biopsy finding indicating grade 1 clear cell RCC; at surgery, five of these tumors were grade 2, and two were grade 3. These results showed that tumor subtype and grade may not be determined accurately. Biopsy is more accurate in predicting RCC subtype (86%–98%) than grade (46%–64%) (74–76). Despite the limitations of biopsy, these results showed that percutaneous biopsy could be used to help select patients for active surveillance in the future.

Finally, recent data now suggest that elderly patients may benefit from active surveillance. A retrospective comparison of active surveillance, radical nephrectomy, and partial nephrectomy among 202 patients with 234 small (<4 cm) renal masses followed up for a median period of 34 months yielded no statistically significant difference in overall or cancer-specific survival among the three groups (77). In another study involving Surveillance, Epidemiology, and End Results Medicare data in 8317 patients older than 66 years, 70% underwent surgery, and 31% underwent surveillance for stage T1a masses (78). During a median follow-up period of 58 months, 25% of patients had more

than one cardiovascular event, and 25% of patients died, including 3% of kidney cancer. Compared with surgery, and controlling for patient and disease characteristics, surveillance had a significantly lower risk of death from any cause (hazard ratio, 0.84; 95% confidence interval: 0.75, 0.94) and a lower risk of experiencing a cardiovascular event (hazard ratio, 0.79; 95% confidence interval: 0.70, 0.89); kidney cancer–specific survival did not differ according to treatment (hazard ratio, 0.89; 95% confidence interval: 0.66, 1.21) (78).

Therefore, the preponderance of current evidence suggests that an active surveillance approach can be safe and potentially beneficial in selected patients. However, a consensus has not been reached as to precisely which patients and which renal masses should undergo surveillance (79). To our knowledge, there are no data as to whether ultrasonography (US), CT, or MR imaging should be used or how often (79). In addition, "focused" surveillance protocols have not been described. In lieu of such data, we use renal mass protocol CT or MR imaging to follow up patients undergoing active surveillance, typically on an annual basis. The role of active surveillance in the management of renal masses is a fertile area for radiology research. Improved imaging methods to assess the biological aggressiveness of renal masses, including size and growth assessment tools, improved percutaneous biopsy methods to both target and procure specimens that demonstrate tumor grade, and development of better tissue markers of biological aggressiveness, are all needed. Although patient accrual would be challenging, a prospective, randomized trial of active surveillance versus treatment, ideally in which the diagnosis of each mass is known, would also help address which patients should undergo surveillance. Until more data emerge, we agree with other authors and recommend restricting active surveillance to patients with a limited life expectancy, patients with medical comorbidities that increase the risk of invasive treatments,

Figure 1

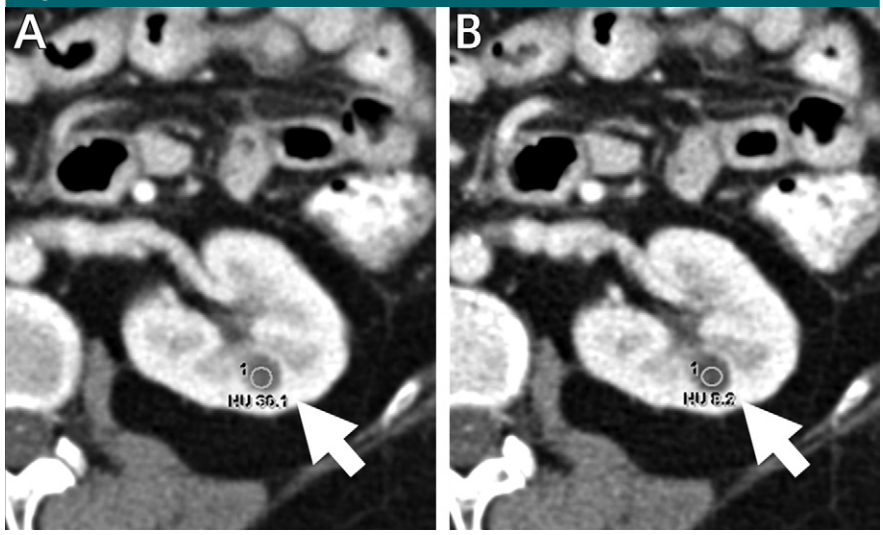

Figure 1: *A,* Axial 5-mm-thick contrast-enhanced CT image in a 49-year-old woman demonstrates an incompletely characterized incidental 8-mm left-sided renal mass (arrow) with an attenuation of 30 HU. The mass cannot be characterized completely because the mass is smaller than twice the section thickness. The findings could be due to a volume-averaged simple cyst, a proteinaceous cyst, or a solid neoplasm. *B,* Axial contrast-enhanced 3-mm-thick CT image reconstructed from the same acquisition data as in *A* demonstrates that the mass (arrow) has a homogeneous attenuation of 8 HU; the features are diagnostic of a simple cyst.

and patients with limited renal reserve who are therefore at risk for the necessity of renal replacement therapy (27,30,42,51,52,63). The rationale for active surveillance can be used to support conservative approaches to the management of renal masses that are not completely characterized with imaging.

Definition of an Incompletely Characterized Renal Mass

A "completely characterized" renal mass is one in which the imaging features are diagnostic, such as a classic angiomyolipoma at CT or MR imaging or a simple cyst at US, contrast material–enhanced CT, or contrast-enhanced MR imaging, or one in which the imaging features allow a full probabilistic assessment on the basis of current evidence, such as Bosniak cysts and solid masses at renal mass protocol CT or MR imaging (3,5–7). The important CT and MR imaging technical aspects of these include image acquisitions before and after intravenous contrast material administration, the acquisition of nephrographic phase data, and reconstructions with 3–5-mm section thickness (3,5–7). Important additional technical aspects of renal mass protocol MR imaging include obtaining T1-weighted, T2-weighted, and chemical-shift images and fat-suppressed T1-weighted images before and at several time points after intravenous contrast material administration, including subtraction images (3,5–7). Diffusion-weighted imaging may be added (80). Although a specific diagnosis may not be possible for many "completely characterized" renal masses, the imaging assessment is considered complete, and management recommendations can be rendered. Incompletely characterized renal masses comprise the remainder encountered with imaging. There are two sources of incomplete characterization: masses that are "too small to characterize" and masses that are imaged with an imaging protocol that is not designed for evaluation of all relevant features—that is, the protocol does not include

Figure 2

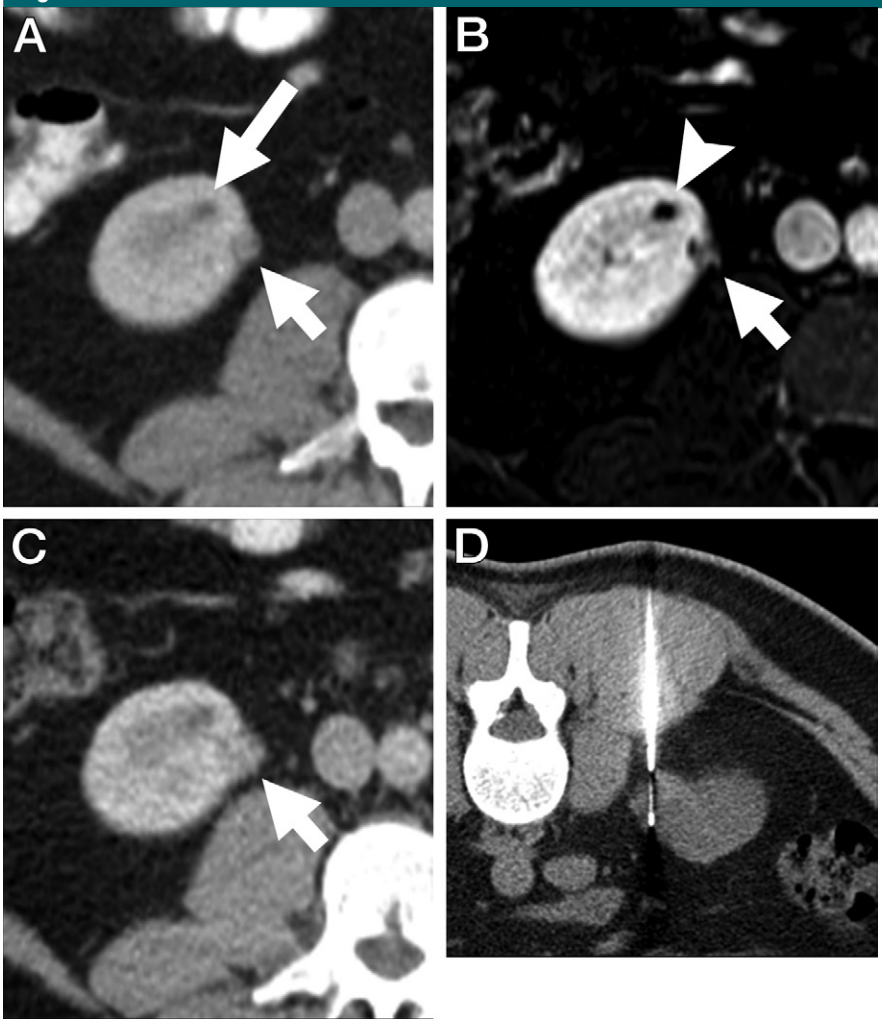

Figure 2: *A,* Axial contrast-enhanced CT image demonstrates an incompletely characterized incidental 7-mm left renal mass (short arrow) with an attenuation of 40 HU and a second smaller mass (long arrow) in a 46-year-old man with Hodgkin disease. *B,* Subtraction image from a subsequent renal mass protocol MR imaging examination confirmed that the 7-mm mass was enhancing (arrow) and was therefore a solid neoplasm. The second mass (arrowhead) was shown to be a simple cyst. *C,* CT image obtained 1 year later showed that the 7-mm mass (arrow) grew to 1 cm. *D,* Percutaneous biopsy demonstrated grade 1 clear cell RCC, and the tumor was ablated. This patient demonstrates the appropriate imaging confirmation of a subcentimeter hyperattenuating renal mass as a solid neoplasm, followed by safe active surveillance and a diagnostic biopsy when the mass grew to 1 cm. Images also show how MR imaging can be used to confirm a subcentimeter mass as a cyst.

the important technical aspects used for renal mass protocol examinations.

Incompletely Characterized Renal Masses That Are Too Small

Renal masses that are too small to characterize completely are so small that their features cannot be assessed even when using an imaging protocol designed to characterize them. Because these masses are highly likely to be benign (on the basis of small size) and evaluation of them is often inconclusive, additional imaging has not been recommended (1,7,81). Most are benign cysts (1,79,82). Such masses are typically smaller than 1 cm, but the definition of a mass that is "too small to characterize" is best related to technique. At CT or MR imaging, the diameters of such lesions are less than twice the reconstructed section thickness. Therefore, to minimize partial volume averaging effects and obtain a section principally through the mass in question, the diameter of the mass should be larger than or equal to twice the reconstructed section thickness (5). For example, if 5-mm reconstructions are used, only renal masses 10 mm and larger can be assured of being imaged principally through the mass. If 3-mm reconstructions are used, only masses 6 mm and larger can be assured of being imaged principally through the mass. These theoretical principles were demonstrated in a CT study; of 44 renal masses between 5 and 10 mm, 39 (89%) were characterized as cysts by using 3-mm sections (with a 50% overlap), compared with only 13 (30%) that were characterized as cysts by using 5-mm sections (with no overlap) (82). By using 3-mm reconstructions, renal masses 5 mm or smaller are too small to characterize but can still be reported to likely be benign cysts. The statistical likelihood that cystic lesions smaller than 1 cm are benign has been suspected for many years (7,81), but using thin reconstructions increases confidence (Fig 1). However, if the sections are too thin, image noise may inhibit the analysis. Therefore, some renal masses will remain too small to characterize completely, despite using an appropriate section thickness for the size of the mass. Although 3-mm reconstructions have been recommended (7), characterizing renal masses between 6 and 10 mm completely with CT may still be difficult. In our experience, the superior contrast resolution of MR imaging by using T2-weighted images and fat-suppressed contrast-enhanced T1-weighted images often allows cysts as small as 1–3 mm to be diagnosed confidently, even though the diameter of the mass is less than twice the reconstructed

Table 1

Management Recommendations for Patients with Incompletely Characterized Incidental Renal Masses at Contrast-enhanced CT

Recommendation	Finding
Probably benign cyst, additional imaging probably not necessary	Renal masses that are smaller than 1 cm or smaller than twice the section thickness and have homogeneously low attenuation (≤20 HU), renal masses that are smaller than 1 cm or smaller than twice the section thickness and have homogeneous attenuation higher than 20 HU due to volume averaging*
Possibly malignant, additional imaging may be warranted†	Renal masses that are heterogeneous and no regions contain fat (less than −10 HU)‡, renal masses that contain fat (less than −10 HU) and calcification§, renal masses with attenuation that measures more than 20 HU in any part (not due to partial volume averaging)*

* Estimation of the contribution of partial volume averaging can be aided by relating mass size, mass attenuation (in Hounsfield units), and section thickness. To minimize partial volume averaging, the diameter of the mass should be larger than or equal to twice the reconstructed section thickness.

† Among masses smaller than 1 cm, consideration can be given to delaying additional imaging for 3–6 months.

‡Renal mass protocol CT or MR imaging of masses that are heterogeneous (and likely enhancing) would both confirm enhancement and be used to evaluate for fat that might be masked by intravenous contrast material.

§ RCC may rarely contain fat cells; these neoplasms typically contain calcification.

Table 2

Management Recommendations for Patients with Incompletely Characterized Incidental Renal Masses at Unenhanced CT

Recommendation	Finding
Probably benign cyst, additional imaging probably not necessary	Renal masses of any size, with homogeneously low attenuation (≤20 HU)*; renal masses that are smaller than 1 cm or smaller than twice section thickness, with homogeneous attenuation higher than 20 HU due to volume averaging†; renal masses that are homogeneously hyperattenuating (≥70 HU)
Possibly malignant, additional imaging may be warranted‡	Renal masses that contain fat (less than −10 HU) and calcification§, renal masses with attenuation that measures more than 20 HU in any part (not due to partial volume averaging) and less than 70 HU, renal masses that are heterogeneous, renal masses that are non–simple cyst–appearing (masses are that heterogeneous, attenuation of more than 20 HU in any part, or masses that contain septa, wall thickening, mural nodules, or calcification)

* Also known as "simple cyst–appearing renal masses," these masses contain no septa, thick wall, mural nodules, or calcification.

† Estimation of the contribution of partial volume averaging can be aided by relating mass size, mass attenuation (in Hounsfield units), and section thickness. To minimize partial volume averaging, the diameter of the mass should be larger than or equal to twice the reconstructed section thickness.

‡ Among masses smaller than 1 cm, consideration can be given to delaying additional imaging for 3–6 months.

§ RCC may rarely contain fat cells; these neoplasms typically contain calcification.

section thickness. Also, MR imaging is not subject to pseudoenhancement, a phenomenon that results in artificially high attenuation values, principally with small, intrarenal masses (83). From a practical standpoint, when encountering renal masses smaller than 1 cm at CT, an analysis of the images could relate the reconstruction thickness to the attenuation of the mass. For example, if contiguous 3-mm sections are reconstructed, the attenuation of simple cysts 6 mm and larger generally measures 20 HU or less. If not, the mass may be solid. If contiguous 5-mm sections are reconstructed, the attenuation of simple cysts 10 mm and larger generally measures 20 HU or less. If not, the mass may be solid. Subcentimeter renal masses that may be solid, such as masses with attenuation values higher than 20 HU at contrast-enhanced CT (not thought to be due to partial volume averaging or pseudoenhancement), can be reported as hyperattenuating, and a differential diagnosis of a proteinaceous cyst or a small neoplasm such as an RCC or a benign neoplasm could be considered (Fig 2). A renal mass protocol CT or MR imaging examination can be performed after a 3–6-month delay to evaluate whether a subcentimeter mass is enhancing and to assess any interval growth. When completely characterized and shown to be enhancing, the differential diagnosis can be narrowed to either a small RCC or a benign neoplasm, such as an oncocytoma or a fat-poor angiomyolipoma (14). If the mass does represent an RCC, it is likely indolent, given its small size (7) (Fig 2). In scenarios in which solid renal masses smaller than 1 cm are followed, active surveillance not only appears to be low risk but can be used to obtain an estimate of growth (9,11,12,14–22,69–72). Since renal masses that are too small to characterize completely may be encountered in any cross-sectional imaging examination, including renal mass protocol CT and MR imaging, additional recommendations depend on the type of examination with which they have been detected (Tables 1, 2).

Figure 3

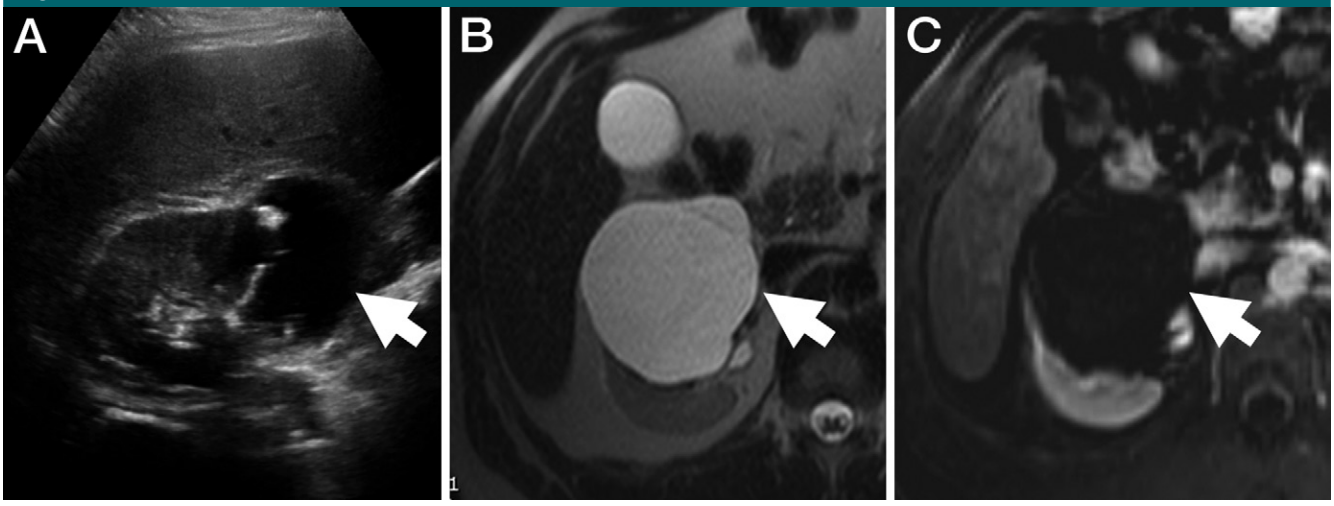

Figure 3: *A,* US image demonstrates an incompletely characterized incidental 7.3-cm septated right renal mass (arrow) in a 46-year-old man. *B,* Axial T2-weighted MR image demonstrates a hyperintense mass (arrow) with a few thin septa. *C,* Axial T1-weighted fat-suppressed contrast-enhanced MR image demonstrates a hypointense mass (arrow) with a few enhancing thin septa. These features fulfill all criteria for a benign complicated cyst.

Incompletely Characterized Renal Masses Detected with Imaging Examinations Not Designed for Evaluation of All Relevant Features

The remaining incompletely characterized renal masses are those that are detected with imaging examinations that are not designed for evaluation of all the relevant features. On the basis of current guidelines, renal mass protocol CT and MR imaging examinations are designed to allow examination of all relevant features of a renal mass (3,5–7). Therefore, a renal mass identified at US, contrast-enhanced CT, unenhanced CT, or unenhanced MR imaging may be incompletely characterized.

US Evaluation

While the US evaluation of a simple cyst is considered "complete," the degree to which US can be used to completely characterize other renal masses is not known. Although some have suggested that US can be used to diagnose benign complicated cysts (Bosniak category II cysts) with confidence (84), renal mass protocol CT or MR imaging is generally recommended to further characterize nonsimple cystic renal masses (3,5–7) (Fig 3). Use of Doppler US and the implementation of U.S. Food and Drug Administration–approved intravenous contrast agents may allow more cystic renal masses to be characterized fully (85,86). US may also be used to identify solid renal masses, particularly when Doppler imaging or intravenous contrast material is used to show that the mass has a blood supply (86,87). One multireader study of 40 cystic renal masses showed that contrast-enhanced US performed after the intravenous injection of sulfur hexafluoride–filled microbubbles was 80%–83% accurate in the discrimination of malignant from benign masses, compared with 63%–75% for CT and only 30% for US without the use of contrast material (85). These results are promising, but more studies will be needed to confirm these results. US can also be used to offer a probable diagnosis of a solid renal mass; however, CT or MR imaging typically follows to confirm the diagnosis and stage renal cancers (3,5–7). For example, since there is no US feature that is specific for angiomyolipoma, a definitive diagnosis requires CT or MR imaging when a hyperechoic renal mass is encountered (7). Therefore, in our current practice, renal mass protocol CT or MR imaging is generally performed for renal masses that are not simple cysts. Future studies will help define better the role of US, with or without the use of contrast material, in managing solid and cystic renal masses (beyond simple cysts), particularly since US is less costly than CT and MR imaging and uses no ionizing radiation.

Contrast-enhanced CT

Incompletely characterized renal masses found at contrast-enhanced CT can be divided into those for which additional imaging is probably not necessary and those that may warrant additional imaging (Table 1). As discussed earlier, renal masses smaller than 1 cm (or a size that is less than twice the section thickness) can be analyzed as they would when detected with renal mass protocol CT. Masses smaller than 1 cm at contrast-enhanced CT that have attenuation less than or equal to 20 HU and are homogeneous are likely cysts. When these masses have attenuation values higher than 20 HU, an analysis relating the size of the mass to section thickness can determine whether the high attenuation value is likely due to partial volume averaging effects or not. Masses (of any size) that are homogeneous and measure higher than 20 HU at contrast-enhanced CT (and are not thought to be due to partial

Figure 4

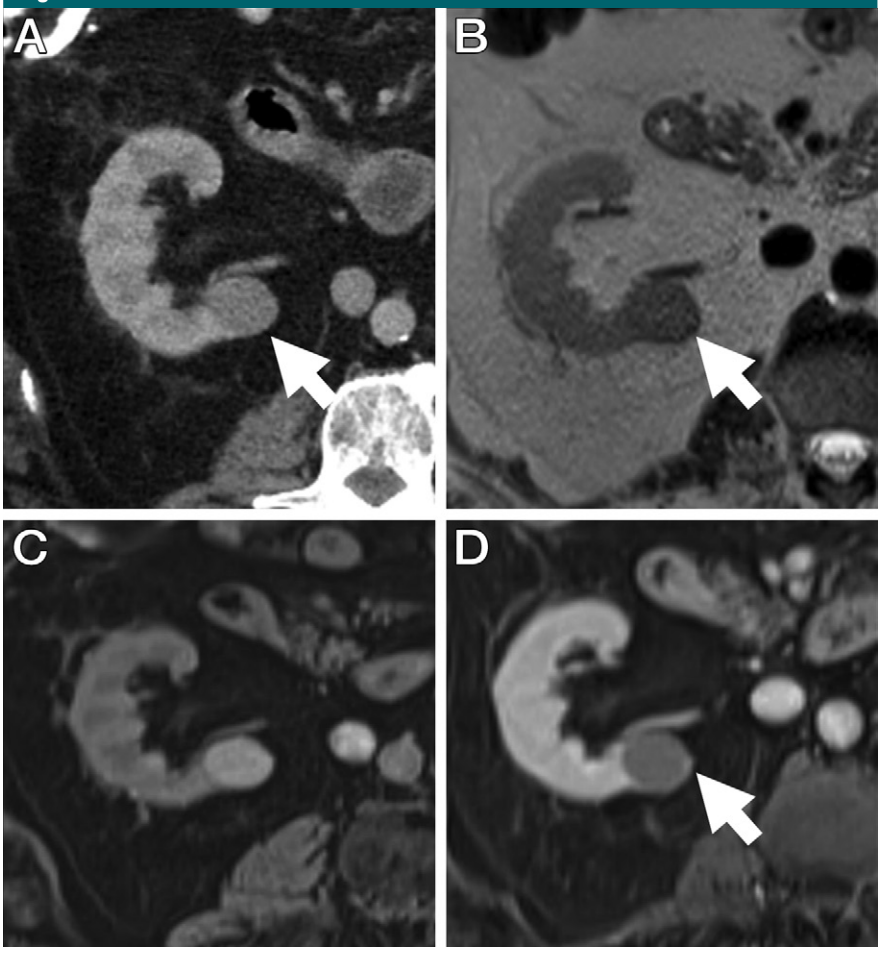

Figure 4: *A,* Axial 5-mm-thick contrast-enhanced CT image in a 75-year-old man with colon cancer demonstrates an incompletely characterized incidental hyperattenuating (53-HU) 2.5-cm right renal mass (arrow) that could represent a solid benign or malignant neoplasm or a benign proteinaceous cyst. *B,* Axial T2-weighted MR image demonstrates that the mass (arrow) is homogeneously hypointense. *C, D,* Axial fat-suppressed T1-weighted MR images acquired before (*C,* signal intensity of 114 arbitrary units [au]) and after (*D,* signal intensity of 118 au) administration of intravenous contrast material demonstrate no enhancement within the mass (arrow on *D*). The features are diagnostic of a benign proteinaceous cyst.

volume averaging or pseudoenhancement) could be either enhancing solid masses or proteinaceous cysts. Among masses with attenuation higher than 20 HU, those that are homogeneous and 3 cm or smaller are probably proteinaceous cysts; however, RCC (typically papillary subtype) remains a possibility (1–3,5,7,85). Indeed, since the unenhanced attenuation of a renal mass is not known at contrast-enhanced CT, definitively discriminating between a cyst and a solid mass would necessitate evaluation with US or renal mass protocol CT or MR imaging (Fig 4). Dual-energy CT scans have been proposed as a way to discriminate high-attenuation cysts from solid masses (88–90). Preliminary experience suggests that a dual-energy CT–based iodine subtraction technique can be used to discriminate nonenhancing high-attenuation cysts that contain no iodine from enhancing solid neoplasms that do. Attenuation values on virtual unenhanced CT images have been shown to be comparable to those obtained with actual unenhanced acquisitions. However, further studies will be needed to learn how broadly contrast-enhanced CT can be applied and its precise role.

Excluding recent hemorrhage in a cyst, a heterogeneous mass at contrast-enhanced CT is suspicious for an enhancing solid renal neoplasm, rather than a proteinaceous cyst. Therefore, unless there is evidence of fat in the mass and an angiomyolipoma can be diagnosed, renal mass protocol CT or MR imaging is warranted to both confirm enhancement and evaluate for fat that might have been masked by intravenous contrast material (Fig 5). Renal masses that contain calcifications in addition to fat may represent RCC, and, thus, biopsy would be needed to differentiate angiomyolipoma from RCC (7,65).

Unenhanced CT

Incompletely characterized renal masses are found commonly in unenhanced CT examinations (Table 2). Renal masses with unenhanced attenuation higher than 20 HU are considered hyperattenuating (3,7). Historically, when masses with attenuation higher than 20 HU were detected at unenhanced CT, additional imaging with either *(a)* renal mass protocol CT or MR imaging or *(b)* US was often suggested so that the established criteria could be met. By using CT, the established criteria for a benign, hyperattenuating cyst required that the mass be small (≤3 cm), homogeneously hyperattenuating, and nonenhancing (3,7,91). However, a retrospective analysis of 54 RCCs (size range, 1.3–11.2 cm) and 52 hyperattenuating renal cysts (size range, 1.0–6.1 cm) showed that homogeneous renal masses with unenhanced CT attenuation of 70 HU and higher had a 99.9% chance of being a benign hyperattenuating cyst (92) (Fig 6). These findings formed the basis, in part, for a subsequent study of 3001 patients undergoing screening CT colonography (93). Among all patients screened, 433 (14.4%) had renal masses 1 cm and larger with a mean diameter of 2.5 cm. Among these, all were simple cyst–appearing

Figure 5

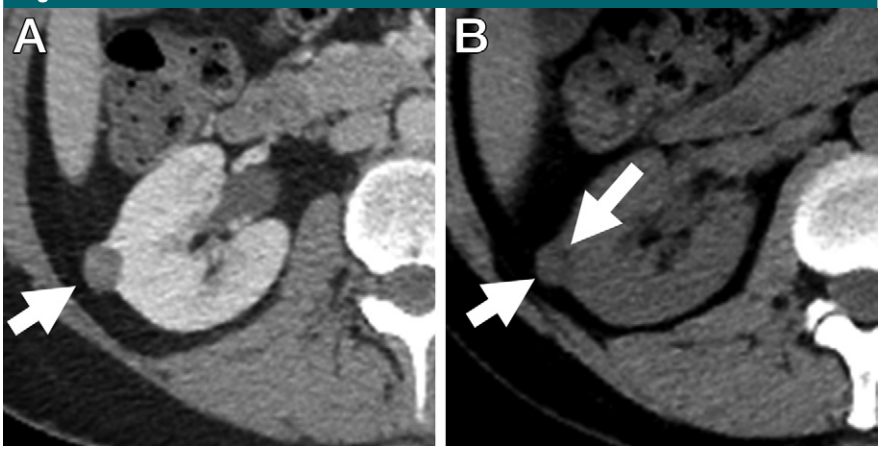

Figure 5: *A,* Axial 5-mm-thick contrast-enhanced CT image demonstrates an incompletely characterized incidental 1.6-cm right renal mass (arrow) in a 55-year-old woman. The slightly heterogeneous hyperattenuating (63-HU) mass could represent a proteinaceous cyst or an enhancing neoplasm. *B,* Axial 5-mm-thick unenhanced CT image demonstrates that the mass (short arrow) enhanced and also shows a region of low (−20 HU) attenuation (long arrow), which is diagnostic of angiomyolipoma. The fatty attenuation was not detected, and the mass was removed at partial nephrectomy; at pathologic examination, an angiomyolipoma with a small focal collection of fat cells was diagnosed. This patient demonstrates the importance of performing unenhanced CT when encountering hyperattenuating masses at contrast-enhanced CT to demonstrate fat that could be masked by intravenous contrast material.

Figure 6

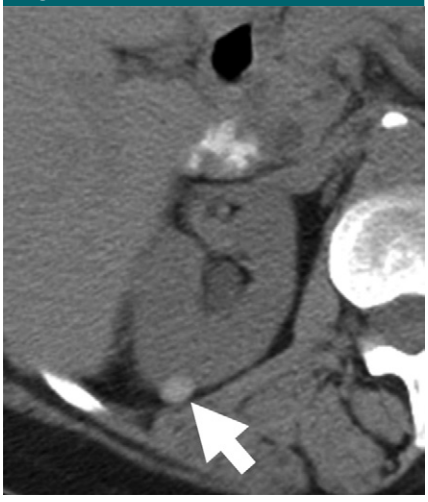

Figure 6: Axial unenhanced CT image in a 76-year-old man demonstrates an incompletely characterized incidental 1-cm homogeneously hyperattenuating (96-HU) right renal mass (arrow) that was proven to be a benign proteinaceous cyst with a renal mass protocol MR imaging examination 6 years after detection.

Figure 7

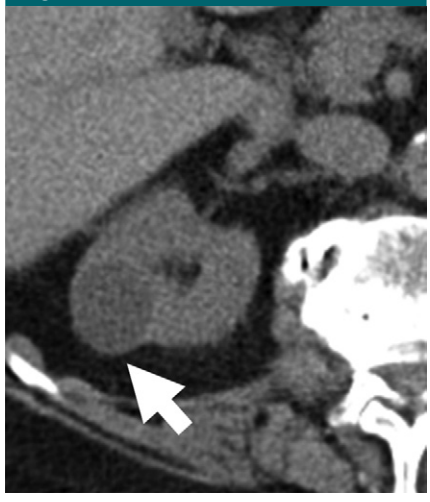

Figure 7: Axial unenhanced CT image obtained in a 70-year-old man demonstrates an incompletely characterized incidental right-sided 3-cm simple cyst–appearing renal mass (arrow) that has homogeneous low attenuation (9 HU) and was proven to be a benign simple cyst with follow-up US 6 years after detection.

with attenuation less than 20 HU, or they were hyperattenuating with attenuation higher than 70 HU, except for 53 masses (12.2%) that had attenuation between 20 and 70 HU, 15 masses (3.5%) that contained calcifications, and five masses (1.2%) that had one or more septa. After a mean follow-up period of 3.3 years, only four RCCs were diagnosed; all had attenuation between 20 and 70 HU. None of the simple cyst–appearing or hyperattenuating (>70 HU) renal masses was found to be cancer (93) (Figs 6, 7). However, of the four cancers that were found, none were cystic, and, therefore, these results may not have addressed the likelihood of missing a cystic renal cancer. Thus, a larger study was needed to define better the true risk of ignoring a simple cyst–appearing renal mass (94). Of 15 695 patients examined with unenhanced abdominal CT, no cancers were found among 2669 simple cyst–appearing renal masses, 1159 of which were followed up for a mean of 8 years and a minimum of 5 years (95% confidence interval: 0%, 0.4%) (Fig 6). Among the cohort, six patients received a diagnosis of renal cancers, but all cancers were located elsewhere in the kidneys. Patients who did not develop renal cancers were followed up for 5–12 years (median, 8 years). Although retrospective, data from this large cohort of patients with long-term follow-up provided additional support for foregoing further evaluation of simple cyst–appearing renal masses (Table 2). Furthermore, since cystic renal cancers are thought to be less aggressive than solid cancers, it is possible that a rare initially "missed" cystic renal cancer ultimately would be diagnosed at a curable stage (33,34,36). In another study, analysis of the unenhanced CT scans of 193 RCCs showed that all cancers had attenuation between 20 and 70 HU, and all were heterogeneous except for 9%, which were homogeneous and had attenuation between 20 and 70 HU (95). Stated another way, of 193 RCCs, none was homogeneous or had attenuation less than 20 HU or higher than 70 HU. Thus, all the data to date suggest that at unenhanced CT, simple cyst–appearing renal masses—that is, those with water attenuation values (−10 to +20 HU), a hairline-thin smooth wall, and no calcifications,

septa, or mural nodules (3,6,7)—and homogeneously hyperattenuating (70 HU and higher) renal masses are reliably considered benign cysts (Table 2). The most recent American College of Radiology appropriateness criteria include these data and concur (2). However, when encountering a non–fat-containing renal mass at unenhanced CT that is heterogeneous, the mass could be RCC (Fig 8) (Table 2). The differential diagnosis would also include a hemorrhagic or benign complicated cyst, and a renal mass protocol CT or MR imaging examination would be needed to characterize such masses completely.

Unenhanced MR Imaging

There is a paucity of data on the management of incompletely characterized renal masses detected with unenhanced MR imaging. A renal mass that is homogeneous and as hyperintense as cerebrospinal fluid on T2-weighted images is almost certainly a benign simple cyst (96). Angiomyolipomas that contain fat can be diagnosed in most cases by using sequences that can be used to identify fat cells (14). However, for virtually all other masses, a renal mass protocol CT or MR imaging examination is generally recommended (Fig 9). Although there are no specific data, akin to the approach taken with CT, it may be reasonable to forego evaluating simple cyst–appearing renal masses that are smaller than 1 cm at MR imaging—that is, those masses that are homogeneously hypointense on T1-weighted images and homogeneously hyperintense on T2-weighted images. However, the appearance on T1- and T2-weighted images should be

Figure 8

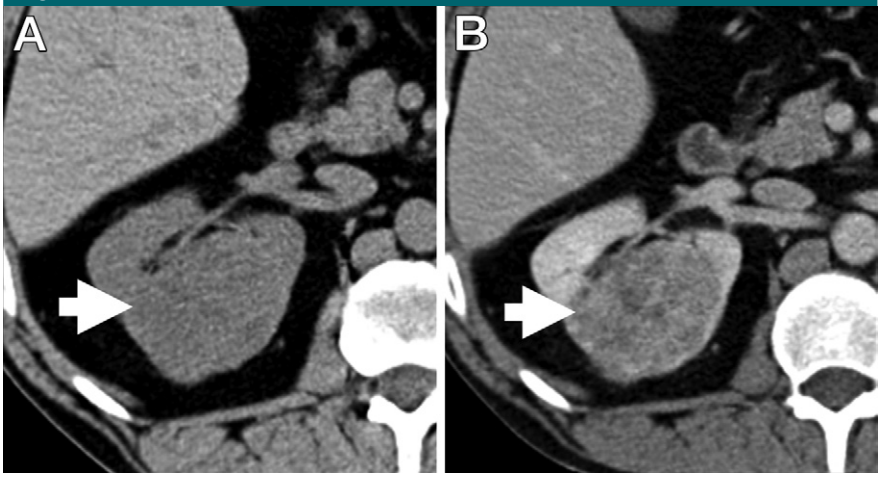

Figure 8: *A,* Axial unenhanced CT image obtained in a 44-year-old man demonstrates an incompletely characterized incidental 5.6-cm right renal mass (arrow) that is heterogeneous; attenuation values ranged from 25 to 44 HU. Diagnoses of proteinaceous cyst and solid neoplasm were considered. *B,* Axial enhanced image acquired with renal mass protocol CT shows that the mass enhanced (arrow); attenuation values ranged from 36 to 90 HU. Clear cell RCC was removed at nephrectomy.

Figure 9

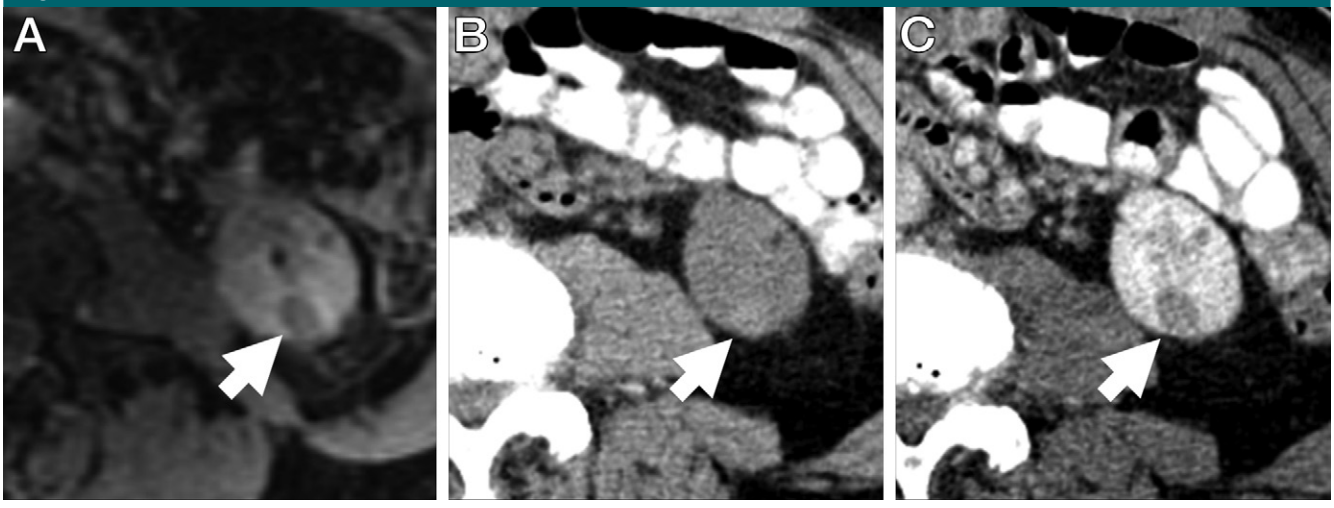

Figure 9: *A,* Axial 5-mm-thick contrast-enhanced fat-suppressed T1-weighted MR image obtained in a 67-year-old man examined with MR imaging of the prostate gland to stage prostate cancer demonstrates an incompletely characterized incidental 1.3-cm left renal mass (arrow). The signal intensity of the mass was higher than expected for a simple cyst; there are no other images of the mass. A differential diagnosis of proteinaceous cyst and solid neoplasm was considered. *B,* Axial unenhanced and, *C,* enhanced images obtained with renal mass protocol CT show that the mass (arrow) is hyperattenuating (45 HU) and enhanced (77 HU), which is diagnostic of a solid benign or malignant neoplasm. Percutaneous biopsy demonstrated a fat-poor angiomyolipoma.

similar to other simple fluid-containing structures (eg, cerebrospinal fluid).

Caveats, Perspectives, and Future Challenges

This article provides management recommendations that could be applied to patients in general; however, as with all guidelines and recommendations in the medical literature, the care of an individual patient can differ. For example, the management of a renal mass could be conservative in patients with limited life expectancy or major comorbidities (7). Also, a separate active surveillance renal mass CT or MR imaging protocol may not be needed in patients already undergoing surveillance for other conditions. For example, an incompletely characterized renal mass suspicious for cancer in a patient who is already undergoing imaging surveillance for a malignancy could be evaluated with the same protocol used to follow up the malignancy.

Referring physicians, particularly general practitioners who may not be familiar with renal masses, can be informed by radiology reports that include management recommendations. Since incompletely characterized renal masses by definition cannot be diagnosed, it is helpful for the radiology report to include management recommendations so that "critical" findings, or those that generally prompt treatment or additional imaging, are addressed, and so that unnecessary imaging is not performed for those findings that are not critical. In a recent retrospective study of abdominal CT images, renal mass findings considered "critical," such as solid renal masses and Bosniak category IIF, III, and IV masses, were interpreted according to published guidelines and led to an additional separate, closed-loop form of communication to be sure the results were communicated (97).

In this article, we review our current understanding of the incompletely characterized renal mass. The studies described herein add to our ability to evaluate renal masses, including those that are incompletely characterized, largely because the investigators relate imaging findings to outcomes, rather than to a diagnosis based on pathologic findings alone. As indicated throughout this review, further studies will be needed to uphold and refine the management recommendations described here. Although not comprehensive, the recommendations may help reduce the number of unnecessary imaging examinations that follow the detection of an incompletely characterized renal mass, while also leading to additional imaging of masses that have a reasonable chance of being cancerous. The recommendations could be added to future guidelines on the management of the incidental renal mass.

Central to the "incidentaloma conundrum" is the acceptance of diagnostic uncertainty. Management of diagnostic uncertainty is an important challenge that faces healthcare providers today (98). Historically, the goal has been to evaluate every potentially important radiologic finding as fully as possible, thus leading to a diagnosis (99). As more incompletely characterized renal masses are detected incidentally, there is a need to accept the fact that it is not always possible to differentiate those that are clinically important from those that are not. Nevertheless, in addition to being able to diagnose renal masses that are completely characterized, there are emerging data about managing many of the remainder, thus reserving additional imaging for a limited number of renal masses.

The problem of "overdiagnosis" occurs when tumors that are detected, if left untreated, would not become clinically manifest or cause death; this has been cited for many tumors, particularly those discovered with screening programs (100–102). Data suggest that RCC and renal masses suspected of being cancerous may be overdiagnosed and, hence, overtreated (103). The current problems facing physicians as to how to manage incidental renal masses are also found in other organ systems (101). As a result, there has been a general call for *(a)* molecular diagnostic tools that can be used to identify indolent or low-risk lesions and *(b)* a reclassification of such cancers as indolent lesions of epithelial origin (100). There is no question that renal indolent lesions of epithelial origin exist; hence, there is a need to continually assess how incompletely characterized renal masses are managed.

As the field of renal mass imaging matures, the definition of a "completely characterized" mass will change. Ideally, a completely characterized renal mass in the future will be one in which imaging can be used to diagnose fully the condition, and, if cancerous, predict its biological behavior and direct appropriate therapy. The heterogeneity of renal neoplasms is established (104) and, under the rubric of personalized medicine, the goal will be to develop noninvasive means, perhaps with imaging, to reach these goals for individual patients. Regardless of what constitutes a completely characterized renal mass, for the foreseeable future, it is likely that there will always be incompletely characterized renal masses that will be detected incidentally in imaging examinations that are not designed for complete evaluation of renal masses. Thus, there is a need to adopt management recommendations that are evidenced based, medically appropriate, and practical.

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