Renal Tumors

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Learning Objectives

- To be familiar with the Bosniak cystic renal mass classification system
- To learn when very small renal masses can be ignored and when they should be followed
- To be aware of ultrasound, CT, and MRI appearance of angiomyolipomas
- To learn about imaging features of non-macroscopic fat containing renal masses
- To be familiar with renal cancer staging and use of RENAL nephrometry
- To be knowledgeable of the normal imaging appearance of patients after treatment of renal cancer and the appearance of treated and untreated metastatic disease
- To be aware of unique features related to treatment of metastatic renal cancer with targeted chemotherapeutic agents, including immunotherapy

1.1 Introduction

In recent years, there have been dramatic developments in imaging assessment of renal tumors and their treatment, some of which will be provided in the paragraphs that follow.

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1.2 Modalities for Imaging Renal Masses

1.2.1 Ultrasound

Although noncontrast ultrasound evaluates the internal morphology of cystic lesions with more detail than CT, it is not as sensitive in detecting or accurate in characterizing renal masses as CT or MRI. Most consider ultrasound to be diagnostically definitive only when it identifies a renal mass as a simple cyst.

1.2.2 CT and MRI

Renal tumors may be detected incidentally on CT or MRI examinations. On CT, it is quite common for only contrast-enhanced images to have been obtained, in which case assessment of mass enhancement is limited. When only contrast-enhanced CT images are available, it may be difficult to distinguish hyperdense cysts from solid hypoenhancing renal lesions. Renal cancers are unlikely to measure >70 HU on unenhanced CT and <40 HU on contrast-enhanced CT [1].

Key Point

- Patients referred to CT or MRI with known or suspected renal masses should be evaluated with unenhanced and at least one contrast-enhanced series (with the unenhanced MRI sequences including T1-weighted, fat-suppressed, T2-weighted, in- and out-of-phase gradient-echo, diffusion-weighted images).

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Key Point

- Renal mass detection and characterization are maximized when delayed rather than early contrast-enhanced images are obtained (either in the nephrographic phase [NP], which begins 90–100 s after initiation of a contrast injection, or the excretory phase [EP], which begins when excreted contrast material is first detected in the renal collecting system, usually 120 s or more after initiation of contrast injection) [2].

Key Point

- Most benign and malignant very small renal masses grow at comparable slow rates, with many of these masses enlarging at a rate of no more than 3–5 mm in maximal diameter per year [6]. As a result, interval enlargement of a renal mass cannot be used to predict that the mass being followed is malignant. Instead, masses should be assessed for changes in morphology. These changes include increasing heterogeneity or the progression of the other aforementioned complicating features [5].

1.3 Very Small Renal Masses (<1–1.5 cm)

Very small renal masses (<1.0–1.5 cm in maximal diameter) are detected on nearly half of all adult patients undergoing CT scans [3]. Many such renal masses detected with CT and MRI cannot be characterized due to their size. Accurate attenuation measurements in these lesions are problematic, due to volume averaging and pseudoenhancement. Fortunately, the likelihood of any one of these lesions being malignant is exceedingly low [3]. The overwhelming majority of these lesions will be benign renal cysts.

Because very small renal masses are so common, further assessment of all of these lesions is not feasible, even though a few will be cancers.

Key Point

- Follow-up imaging of tiny renal masses should be performed only when they subjectively appear to be complex with evidence of heterogeneity, internal septations, mural nodules, wall thickening, or heterogeneity.

Some homogeneous low attenuation lesions can be considered suspicious if they appear in high-risk patients, such as those with known or suspected hereditary cancer syndromes (such as von Hippel-Lindau, hereditary papillary renal cell cancer, Birt-Hogg-Dubé, or hereditary leiomyomatosis-renal cancer syndrome) [4]. When a very small renal mass is deemed suspicious, further evaluation should be performed within 6–12 months. Suspicious masses should be followed for at least 5 years. While follow-up can be obtained with CT or MRI, MRI is more accurate. Even tiny cysts have characteristic high T2 signal intensity. MRI is also much more sensitive to contrast enhancement than is CT, and it is not compromised by pseudoenhancement [5].

1.4 Cystic Renal Masses

Many radiologists and urologists classify cystic renal lesions using the Bosniak classification system, which was first proposed in 1986 [7] and revised several times, including in 2005 [8]. This system classifies renal cystic masses into five categories, based upon their likelihood of being malignant. It is important to emphasize that the Bosniak system was designed for use with dedicated renal mass CT and not for ultrasound or MRI.

Category I lesions, which constitute the overwhelming majority of cystic renal masses, are simple renal cysts. They are homogeneous masses. They are anechoic on ultrasound and of water attenuation on CT or water signal intensity on MRI. They have imperceptible walls and do not contain nodules or calcifications. They do not enhance when contrast material is administered. Category I lesions are always benign and no follow-up is needed. *Category II lesions* are minimally complex. They may contain one to three septations or thin peripheral calcifications. Hyperdense renal cysts <3 cm in diameter are also Category II lesions. Category II lesions are essentially always benign and no follow-up is needed. *Category IIF lesions* contain multiple or thickened septa, thickened walls, or coarse calcifications. Hyperdense cysts measuring >3 cm in diameter are also Category IIF lesions.

Key Point

- Category IIF cysts have been found to represent cancers or progress to become cancers about 11% of the time [9] and, for this reason, must be followed, with repeat imaging studies performed at 6 months and then annually for at least 5 years. Cancer should be suspected, not when these lesions grow over time, but instead if they become increasingly complex.

Studies have indicated that such follow-up can be performed safely. In the series reported by Hindman et al. [9], none of 17 Category IIF renal cystic masses that were ultimately diagnosed as cancers developed locally recurrent or metastatic disease during the follow-up period. *Category III lesions* contain thickened irregular enhancing septa or walls. They are malignant about 50–60% of the time. When malignant, they tend to be less aggressive than other renal cancers. Treatment of these lesions is usually recommended due to the high risk of malignancy. *Category IV lesions* are cystic lesions that have irregular enhancing walls or enhancing nodules. These lesions are nearly always malignant, so treatment is warranted.

The Bosniak system has been adopted for use with ultrasound and MRI; however, the percentages of lesions of different categories that are malignant with these modalities are not well known. For example, on MRI, about 20% of cystic renal masses appear more complex and are assigned to higher categories than they would have been if imaged with CT [10]. This is largely due to MRI's ability to detect internal cyst features not visible with CT.

1.5 Angiomyolipomas (AMLs)

AMLs are the most common benign solid renal neoplasms. They are composed of angiomatous, myomatous, and fatty elements, in varying relative distribution. Eighty percent occur sporadically. The remainder are associated with syndromes (tuberous sclerosis or lymphangioleiomyomatosis) [11].

While nearly all AMLs are echogenic on ultrasound, so are some small renal cancers. It has been found, however, that the likelihood of a small echogenic renal case being a cancer is exceedingly low. In one recent study, only 1 of 161 small renal masses (measuring 1 cm or smaller) were subsequently found to be renal cancers [12]. Acoustic shadowing has been identified posterior to some echogenic AMLs, but not posterior to any echogenic renal cancers [13]. An echoic rim or intratumoral cysts have been observed around or in some renal cancers, but not any AMLs.

Echogenic masses detected on US are often further evaluated with CT or MRI to determine if macroscopic fat is present in the mass. If macroscopic fat is identified on CT or MRI, then the mass can be diagnosed definitely as an AML (with only case reportable exceptions).

Key Point

- On CT, visualization of at least some small areas within a renal mass measuring–(negative) 10 HU or less is considered diagnostic of macroscopic fat and of an AML [14].

Key Point

- On MRI, fat typically has high T1 and T2 signal and loses signal with fat suppression. On opposed-phase chemical shift imaging, there is a characteristic "India ink" artifact at fat-water interfaces in the AML and between the AML and adjacent renal tissue (Fig. 1.1) [15].

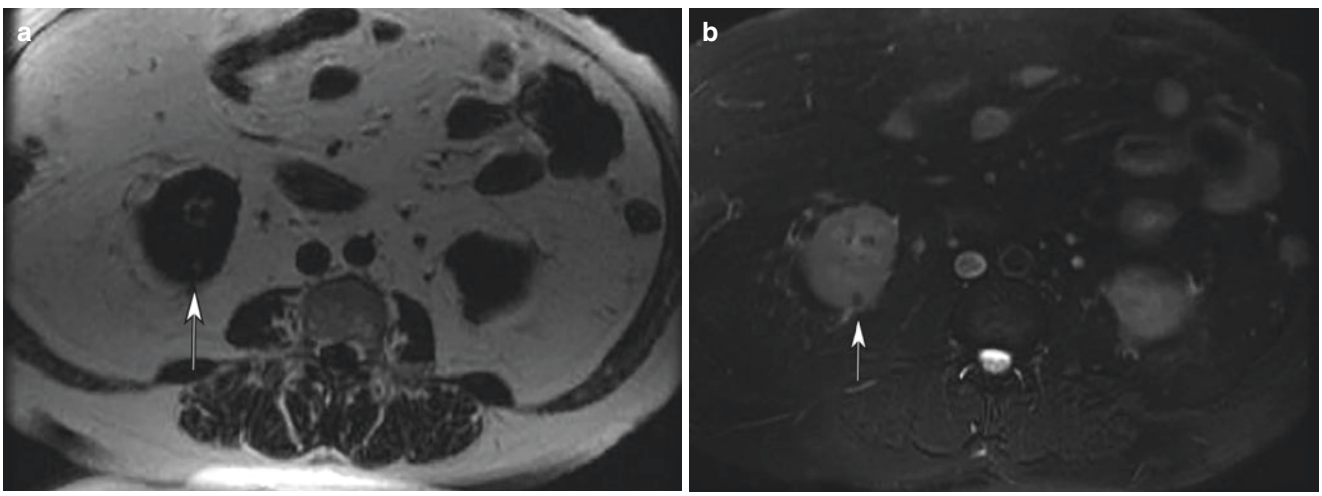

Fig. 1.1 MRI of an AML. (**a**) Axial T1-weighted MR image shows a tiny hyperintense mass in the lower pole of the right kidney (arrow). (**b**) Axial T2-weighted MR image with fat suppression shows that the lesion has lost signal (arrow), confirming the diagnosis. (**c**) Opposed-phase MR image demonstrates India ink artifact at the interface of the renal mass with the kidney (arrow)

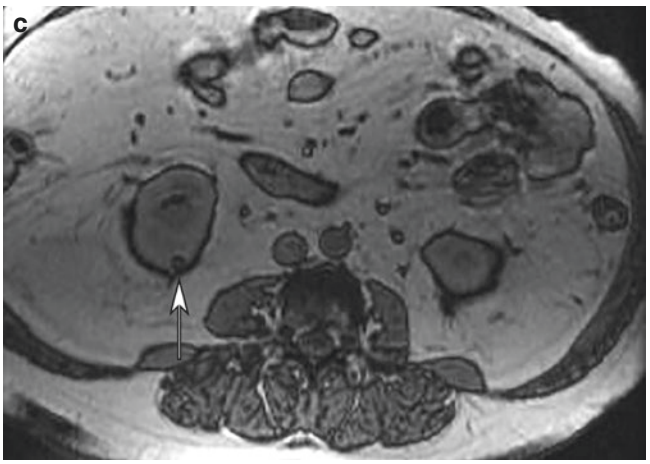

Fig. 1.1 (continued)

Occasionally, exophytic AMLs can be difficult to differentiate from perinephric liposarcomas. Some imaging features can be used to facilitate differentiation. AMLs are more likely to invaginate into the kidneys and produce a focal parenchymal defect. Liposarcomas, in comparison, merely compress the kidney, without having an associated defect. AMLs are more likely to contain large vessels that extend to the renal cortex than are liposarcomas [16].

Some AMLs do not contain easily identifiable macroscopic fat. These AMLs are referred to as fat-poor AMLs (fpAMLs) and include fpAMLs that have the same or higher attenuation than normal renal parenchyma on unenhanced CT and AMLs with epithelial cysts (AMLEC), which can appear as solid masses with small cystic areas or multilocular cystic lesions [11].

Many studies have attempted to identify small foci of fat or other imaging features that might permit fpAMLs to be correctly distinguished from other solid renal neoplasms. These features have included assessing unenhanced CT mass attenuation, CT histograms, quantitatively assessed fat on MRI, and the degree and homogeneity of mass of enhancement [11, 17–19]. Results have been mixed. For example, some fpAMLs have higher unenhanced attenuation than normal renal parenchyma, but papillary renal cancers can also demonstrate this feature [20]. Some fpAMLs have low signal intensity on T2-weighted MR images, but papillary renal cancers may also demonstrate this behavior. Fortunately, fpAMLs usually demonstrate more MR contrast enhancement than do papillary renal neoplasms, so a hypervascular lesion that demonstrates a combination of high attenuation on unenhanced CT and/or low-T2 signal intensity on MRI is most likely to be an AML.

A rare type of AML is the epithelioid AML (eAML). Some epithelioid AMLs behave aggressively. They can spread locally to invade the renal vein or IVC, involve regional lymph nodes, or even metastasize distantly [11]. Epithelioid AMLs do not demonstrate imaging features that allow them to be differentiated from other AMLs. While many epithelioid AMLs do not contain identifiable macroscopic fat on imaging studies, some do [21]. Because this subtype of AML is so rare, AMLs that have a classic appearance on imaging studies should all be treated as benign lesions anyway. Exceptions should be considered to be case reportable.

1.6 Other Solid Renal Masses

Many solid renal masses do not contain identifiable fat. This includes oncocytomas and renal cancers. A large number of studies attempting to distinguish among the various nonfat- or minimal-fat-containing solid renal masses on CT and MRI have met with limited success; however, a few occasionally suggestive imaging features have been described.

1.6.1 Oncocytomas

Oncocytomas are benign renal tumors. They may contain central scars that can be detected on imaging studies; however, this feature is not diagnostic. Necrosis in renal cancers is indistinguishable from scars in oncocytomas. Further, most oncocytomas evaluated on CT do not contain visible central scars [22]. One feature that has been used by some to differentiate oncocytomas from renal cancers is segmental enhancement inversion, in which two differently enhancing components identified on CMP images reverse their attenuation on EP images, with the initially higher attenuation and briskly enhancing component becoming lower in attenuation than the initially lower attenuation and less intensely enhancing component [23]. This feature is not consistently detected in oncocytomas and is, therefore, frequently not helpful [24].

1.6.2 Renal Cancers

In the past, it was believed that there were only a few types of cancer; however, chromosomal analysis has demonstrated that there are at least 13 distinct types of renal cancer, with most being very rare. This includes clear cell (about 70–80%), papillary (10–15%), chromophobe (less than 10%), acquired renal cystic disease-associated, clear cell and papillary combined, collecting duct, renal medullary, mucinous tubular and spindle cell, succinate dehydrogenase-deficient, tubulocystic, and unclassified cancers, multilocular cystic neoplasms of low malignant potential, and MiT translocation cancers including Xp11.2 [25]. Sarcomatoid renal cancer is no longer believed to be a distinct cell type. Instead, any type of primary renal neoplasm can dedifferentiate and develop sarcomatoid features. While again imaging differentiation among most renal cancers is not possible, some cell types tend to demonstrate certain imaging features, as summarized below.

1.6.2.1 Clear Cell Renal Cancer

Clear cell renal cancers have the highest metastatic potential and poorest survival of the major histologic RCC subtypes. They are usually heterogeneous renal cortical masses. On unenhanced MRI, most clear cell cancers demonstrate hyperintensity on T2-weighted images. Due to abundant intracellular fat, clear cell cancers can lose signal on opposed-phase gradient-echo T1-weighted images. Clear cell carcinomas usually demonstrate heterogeneous enhancement, with peak enhancement occurring early, on CMP images [26] (Fig. 1.2).

1.6.2.2 Papillary Renal Cancer

Most papillary cancers behave less aggressively than do clear cell cancers. On contrast-enhanced CT or MRI, papillary cancers tend to be homogeneous. On unenhanced CT, they may have higher attenuation than adjacent renal parenchyma. On unenhanced MRI, they often are hypointense on T2-weighted images and can lose signal on in-phase T1-weighted images due to presence of hemosiderin [27]. They usually enhance homogeneously, more slowly, and to a lesser extent than do other renal cancers, with peak enhancement not occurring until the NP or even the EP [28] (Fig. 1.3).

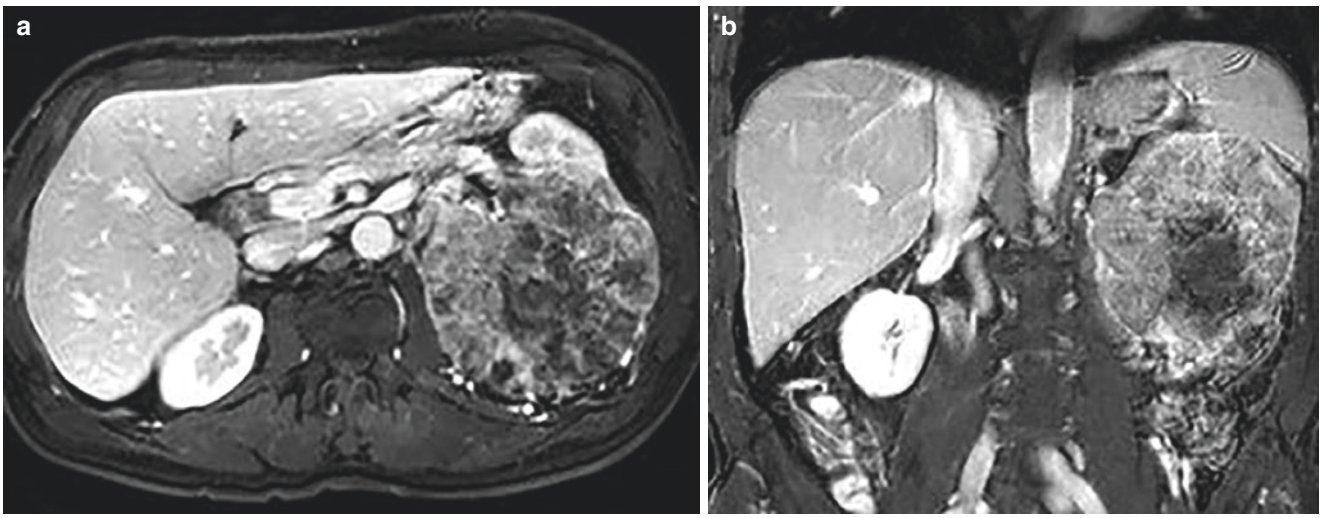

Fig. 1.2 Clear cell renal cell carcinoma. Contrast-enhanced axial **(a)** and coronal **(b)** images obtained during the CMP demonstrate a heterogeneously and briskly enhancing left renal mass, subsequently confirmed to be a clear cell RCC

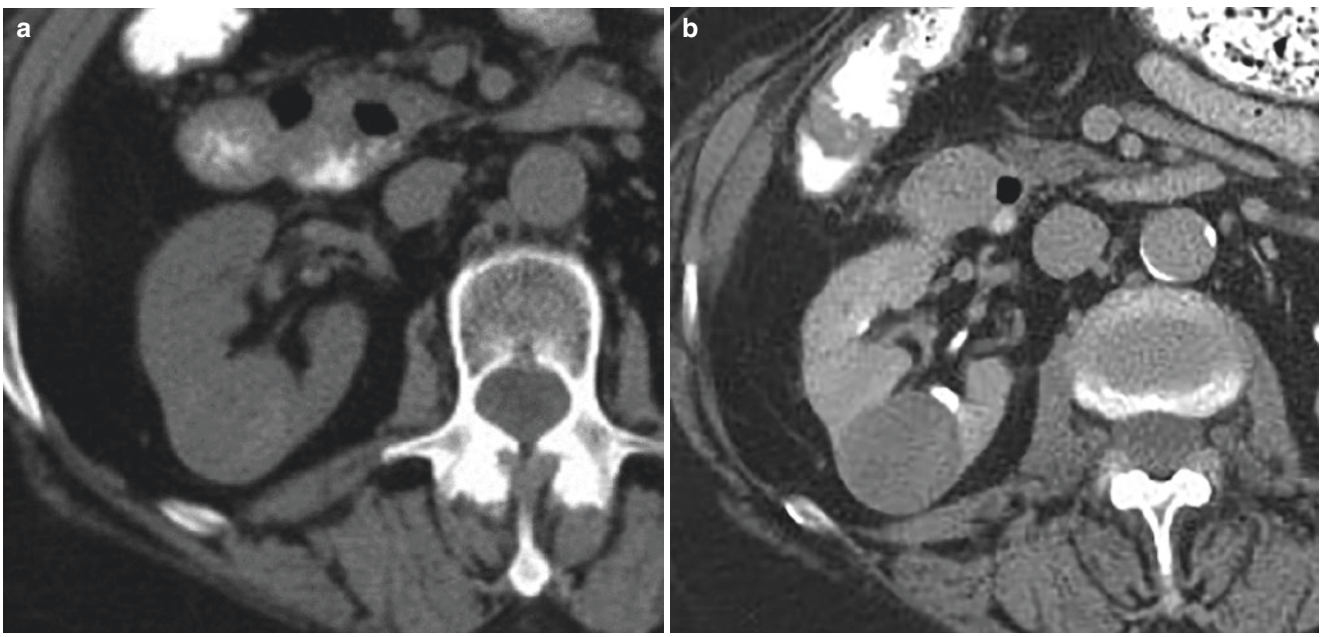

Fig. 1.3 Papillary renal cell carcinoma. Unenhanced **(a)** and excretory phase (EP) contrast-enhanced **(b)** axial CT images demonstrate a mildly heterogeneous hypoenhancing papillary cancer in the posterior aspect of the mid right kidney

1.6.2.3 Chromophobe Renal Cancer

Chromophobe renal cancers are generally well-differentiated cancers and, provided that they do not have sarcomatoid degeneration, are slow growing and have an excellent prognosis. They do not have a unique appearance on imaging studies and cannot be reliably distinguished from other solid renal masses that do not contain macroscopic fat.

1.6.2.4 Uncommon Renal Cancer Cell Types

Many of the uncommon renal cancers do not have suggestive imaging appearances. A few specific comments about some of these cancers can be made, however. Renal medullary, collecting duct, and XP11.2 translocation cancers generally arise in the renal medulla. Collecting duct cancers frequently occur in older adults; renal medullary and XP11.2 cancers are usually encountered in young patients [25]. Renal medullary cancers typically develop in patients with sickle cell trait [29].

1.6.3 Urothelial Neoplasms, Lymphoma, and Renal Artery Aneurysms

It can occasionally be difficult to distinguish centrally located RCC from urothelial cancers; however, the correct etiology may be predicted in many instances. Unlike RCC, urothelial cancers have an epicenter in the renal collecting system, can produce renal pelvic filling defects, and tend to preserve the normal renal contour. They also rarely contain cystic/necrotic areas seen in many, but not all, RCCs [30]. Other centrally located renal masses that can be encountered and that can occasionally mimic urothelial cancers of RCC include renal lymphoma and renal artery aneurysms.

1.7 Solid Renal Mass Growth Rates

Both benign and malignant solid renal masses can remain stable in size or enlarge over time, with growth rates of both types of lesions usually being similarly slow [31]. It has been suggested that a small solid mass that has an average growth rate of <3 mm/year over at least a 5-year period and that has not changed in morphology should be considered stable. Such a lesion, even if malignant, is exceedingly unlikely to metastasize. Conversely, rapid growth of a mass (by more than 5 mm in 12 months) may indicate aggressiveness/malignancy [32].

1.8 Radiomics

In recent years, there has been increasing interest in the utility of computer-assisted diagnosis (CAD) in detecting and characterizing genitourinary abnormalities. With respect to renal masses, this has centered on the ability of computer-assisted techniques to differentiate among different types of renal masses. For example, studies using computer-assisted diagnosis have demonstrated clear cell renal cancers to have greater objective heterogeneity (pixel standard deviation, entropy, and uniformity) than papillary renal cancers or AMLs [33]. CAD detection of differences in peak lesion attenuation has also been used to differentiate clear cell renal cancers from other renal neoplasms with some success [34]. Renal mass perfusion parameters have been employed to distinguish some renal cancers of higher Fuhrman grade from those of lower grade [35]. These results are promising but preliminary.

1.9 Use of Imaging for Solid Renal Mass Differentiation

Key Point

- Due to overlap of many imaging findings detected subjectively and using CAD, at the present time, imaging differentiation of many malignant from benign nonfat-containing solid renal masses (or among the various types of malignant solid renal masses) is not possible.

1.10 Percutaneous Biopsy of Renal Masses

Given the substantial overlap in the imaging features of many renal lesions, percutaneous biopsy is necessary for determining the nature of many renal masses prior to treatment. Biopsy can be performed accurately and safely [36]. The risk of needle tract seeding of tumor is minimal. There are only isolated case reports of renal cancer seeding [37]. One potential pitfall of biopsy relates to the fact that only a few portions of a renal mass are sampled. Areas containing higher-grade cancer may not be sampled, leading to underestimation of tumor aggressiveness.

1.11 Pretreatment Assessment of Renal Cancer

1.11.1 Staging

CT and MRI (obtained during the portal venous phase of enhancement) are at least 90% accurate in renal cancer staging, with the TNM staging system as follows:

Stage	Feature
T1a	≤4 cm in greatest diameter and limited to the kidney
T1b	>4–7 cm and limited to the kidney
T2a	7–10 cm and limited to the kidney
T2b	>10 cm and limited to the kidney

Stage	Feature
T3a	Extension into the renal vein or its branches or invading perirenal or renal sinus fat
T3b	Extension into the IVC below the diaphragm
T3c	Extension into the IVC above the diaphragm or invading the IVC wall
T4	Invasion beyond perinephric fascia or into ipsilateral adrenal gland
N0	No lymph node involvement
N1	Regional lymph node involvement
M0	No distant metastases
M1	Distant metastases
Mx	Distant metastatic status not determined

The most substantial limitation of imaging in stage renal cancers results from the fact that both CT and MRI have difficulty in determining whether a renal cancer has invaded the renal capsule and spread into the perirenal or renal sinus fat (differentiating T2 from T3 cancer). Perinephric soft tissue stranding can be produced by tumor, edema, or blood vessels [38]. It is recommended that T3 disease be diagnosed on CT or MRI only when nodular tissue is identified in the perinephric space.

1.11.2 RENAL Nephrometry

Many urologists prefer that RENAL nephrometry scoring of suspected or known renal cancers also be obtained prior to surgery. Nephrometry scoring allows the urologist to predict the likelihood that partial nephrectomy can be performed effectively and safely [39]. With this system, a renal mass receives a score of 1–3 points for each of five features (**R**enal mass size, **E**xophyticity, **N**earness to the renal collecting system, **A**nterior or posterior location, and **L**ocation with respect to the upper and lower polar lines (see table immediately below). Tumors that have composite nephrometry scores of 4–6 are considered to be very amenable to partial nephrectomy, while those that have scores of 10–12 are poor candidates for partial nephrectomy. Complete nephrectomy should be considered in the latter group.

Feature	1 point	2 points	3 points
R = diameter	≤4 cm	>4 to <7 cm	≥7 cm
E = exophyticity	≥50%	<50%	Entirely endophytic
N = nearness to collecting system or renal sinus	≥7 mm	>4 to <7 mm	≤4 mm
A = anterior or posterior	No points given. Mass is listed as a, p, or neither (x)		
L = location relative to polar lines Add "h" if touches renal artery or vein	Above upper or lower pole line	Crosses polar line	>50% of mass crosses polar line or crosses midline or entirely interlobar

From Ref. [39]

1.12 Renal Cancer Management

Management of renal cancers that have not metastasized regionally or distantly now ranges from active surveillance (for small [<4 cm] indolent (low Fuhrman grade) tumors in elderly patients with significant comorbidities) to thermal ablation, partial nephrectomy, or complete nephrectomy [32, 37]. Patients on active surveillance should undergo subsequent imaging every 6 months for a year, followed by annual imaging for at least 5 years. Intervention in these patients is only considered when masses exceed 4 cm in size or grow by >5 mm per year [32].

1.13 Imaging After Renal Cancer Treatment

1.13.1 After Renal Mass Ablation or Resection

After successful renal mass radiofrequency or cryoablation, there is initial expansion of the ablation site. Initially, some enhancement may be detected normally in the ablation bed, particularly on MRI exams. This normal enhancement resolves over time [40]. In the months following ablation, the ablation bed typically decreases but rarely disappears completely. Other normal post-ablation findings include fat invagination between the ablation bed and normal renal parenchyma and a peri-lesional halo, changes that create an appearance that can be confused with an AML (Fig. 1.4). Ablation bed expansion is not typically seen after microwave ablation.

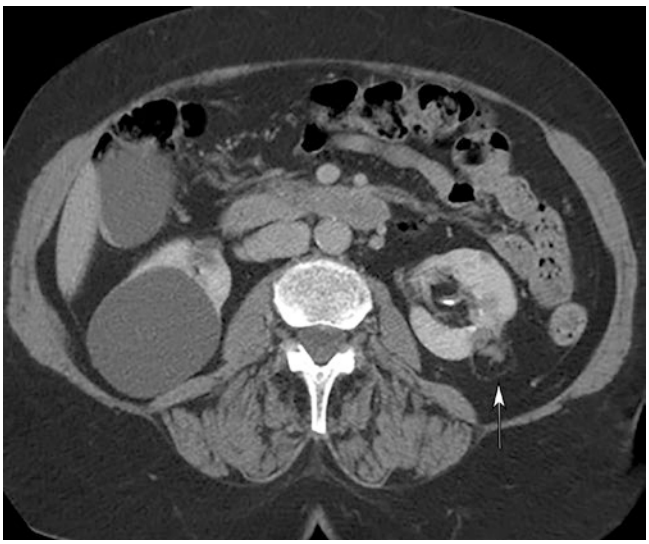

Fig. 1.4 Normal post-thermal ablation appearance. An EP contrast-enhanced CT image on a patient, who had a left renal radiofrequency ablation 7 months earlier, demonstrates a normal post-ablation appearance. Soft tissue attenuation material is surrounded by invaginated perinephric fat, an appearance that can be confused with an AML

Key Point

- Frequent imaging should be performed after ablation (e.g., at 1, 3, 6, and 12 months). This is because residual or recurrent tumor is usually detectable within the first few months of ablation [41].

Persistent or recurrent tumor should be suspected after ablation if the ablation bed progressively increases (rather than decreases) in size, when there is increased perinephric nodularity, or when persistent or new areas of nodular or crescentic enhancement are detected, with these areas usually located at the interface of the ablation bed with adjacent renal parenchyma [41].

1.13.2 Imaging After Partial or Total Nephrectomy

After partial or total nephrectomy, it is common to see postoperative inflammatory or fibrotic changes in the surgical bed, along with deformity of the renal contour at the site of partial nephrectomy [42]. Gore-Tex mesh along the nephrectomy site appears as a linear area of high attenuation along the renal margin.

Key Point

- Frequently used hemostatic material can be mistaken for infection or tumor, since an occasional gas within the material and its low attenuation components can persist for months after surgery.

Complication rates after partial nephrectomy are typically higher than after total nephrectomy, with complications including pseudoaneurysm, urinoma, or abscess. If urinoma is a concern, delayed imaging >1–2 h after contrast administration might prove useful to document the urinary leak.

After partial or total nephrectomy, recurrent tumor may develop in the surgical bed and/or regionally or distantly. Surgical bed recurrences may initially be difficult to differentiate from postoperative scarring/fibrosis, although tumor often demonstrates detectable enhancement and enlarges over time. Renal cancer usually metastasizes to regional lymph nodes, the liver, the adrenal glands, the lungs, and the bones. Adrenal cancer metastases from clear cell renal cancer can be problematic, since they may contain large amounts of intracellular fat. As a result, similar to adenomas, adrenal metastases can demonstrate low signal intensity on opposed-phase MR images and can also demonstrate pronounced (>60%) washout on delayed enhanced CT. Renal cancer metastasizes to the pancreas more commonly than do other neoplasms [43].

1.13.3 Imaging After Treatment of Metastatic Disease

1.13.3.1 RECIST

Patients who present with or develop metastatic renal cancer must receive systemic treatment. Imaging is then performed regularly to determine whether or not patients are responding to their chemotherapy. Metastatic foci are then measured and compared, from one imaging study to the next. The most commonly used measurement system for assessing tumor response to chemotherapy has been the **r**esponse **e**valuation **c**riteria **i**n **s**olid **t**umors (RECIST) system [44]. The RECIST 1.1 system involves measurements of up to five metastatic lesions (no more than two per organ, with each measured lesion being at least 10 mm in length). Most metastases are measured in maximal dimensions; however, lymph nodes are measured in short axis diameter. Complete response is diagnosed when all metastases resolve on follow-up imaging. A partial response is diagnosed when the sum of all target lesions decreases by ≥30% from one study to the next. Progressive disease is diagnosed when the sum of all target lesions increases by ≥20% or more. Any change in between a 30% decrease and a 20% increase is considered stable disease.

Key Point

- While RECIST 1.1 has worked well for following metastatic disease treated by prior standard chemotherapy, there are problems with its use in patients treated with anti-angiogenesis drugs, including multikinase inhibitors. This is because multikinase inhibitors may produce necrosis (and resulting diminished attenuation on contrast-enhanced CT) in responding metastatic lesions without these lesions decreasing significantly in size. As a result, a patient who is a partial responder can be misidentified as not having responded to treatment, if only RECIST is used.

1.13.3.2 Multikinase Inhibitors

A number of alternative measuring systems have been devised, which take into account changes in lesion attenua-

tion, as well as changes in size. This includes the Choi, modified Choi, and the morphology, attenuation, size, and structure (MASS) systems [45, 46]. With the Choi criteria, for example, a decrease in target lesion size of only 10% or more or a decrease in target attenuation of 15% or more indicates a partial response. With the modified Choi criteria, both of these features must be present at the same time.

1.13.3.3 Immunotherapy

In the last few years, patients with metastatic renal cancer have been treated with immunotherapy. These agents are antibodies targeted to attack receptors on lymphocytes or surface ligands on tumor cells. They work by interfering with a tumor's ability to inhibit an immune response. At the present time, the immune checkpoints which are being inhibited include those related to cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) and the program cell death protein 1 receptor on T-cells (PD-1) or its related ligands on tumor cells (PDL1 and PDL2) [47].

Key Point

- A unique feature of metastases treated by immunotherapy is that some responding lesions may initially appear stable or even enlarge to such an extent that progressive disease would be diagnosed if RECIST 1.1 were to be used. An apparent initial increase in size should be considered to be unconfirmed progressive disease (UPD). UPD must be confirmed by another follow-up imaging study in no less than 4 weeks [48]. If metastases continue to enlarge, then progressive disease can be diagnosed. In some instances, however, a subsequent study will indicate tumor response (consisting of decreased size and/or attenuation), confirming that the initial change in size was merely "pseudoprogression" (Fig. 1.5). The system for assessing metastatic tumor in immunotherapy patients has been modified to take this issue into account (iRECIST criteria) [48].

Initial studies on the efficacy of immunotherapy in treating patients with metastatic renal cancer have been promising. Many patients have had sustained responses, which have even persisted after therapy was discontinued.

1.13.3.4 Complications of Multikinase Inhibitor Treatment and Immunotherapy

Complications encountered in patients undergoing new systemic treatments include hepatic steatosis, cholecystitis, pancreatitis, bowel perforation, and arterial thrombosis

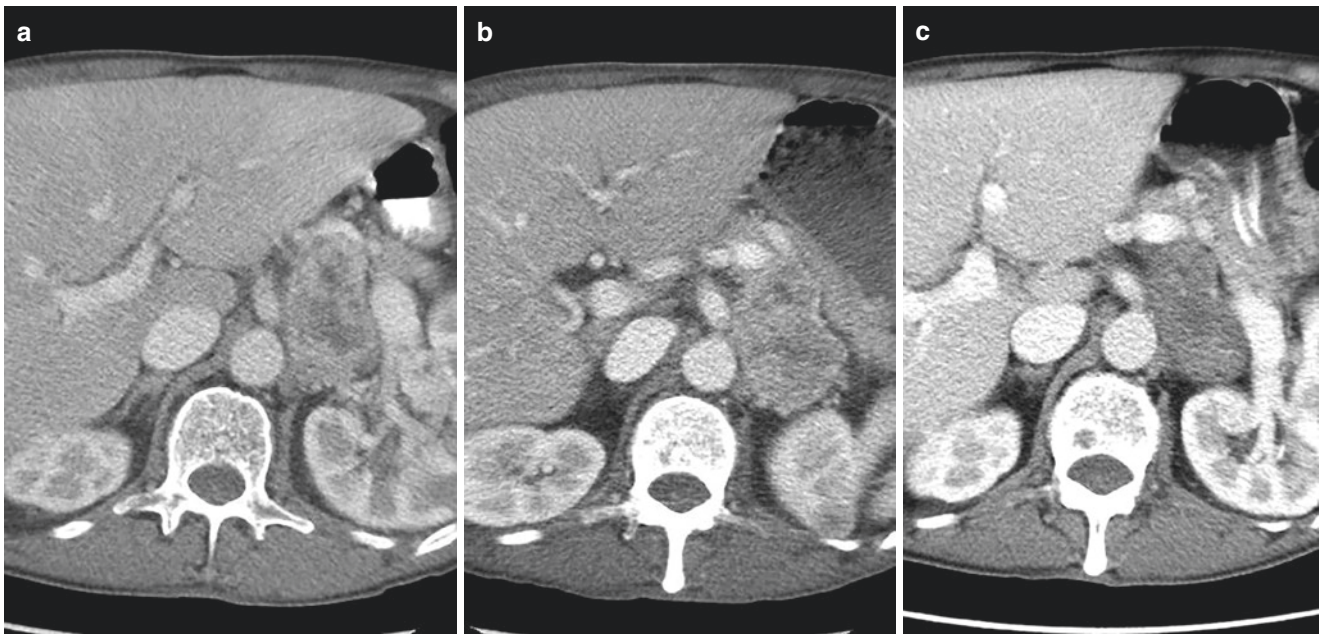

Fig. 1.5 Adrenal metastasis treated with immunotherapy. (**a**) Initial contrast-enhanced CT image demonstrates a large left adrenal mass. (**b**) The mass remains heterogeneous and is larger on a follow-up CT obtained 6 weeks later. (**c**) A follow-up study obtained after another 4 weeks now shows the mass to be necrotic and smaller

(after multikinase therapy) and colitis (segmental or diffuse), pneumonitis, and dermatitis and, less commonly, thyroiditis, hypophysitis, pancreatitis, and adrenal dysfunction (after immunotherapy) [49].

1.14 Concluding Remarks

There have been many exciting recent developments with respect to the imaging, diagnosis, and treatment of solid renal masses in the past few years. This has included the identification of imaging features that can differentiate among some of the many cystic and solid renal masses. Unfortunately, in many patients, overlapping features still prevent distinction of renal cancers from benign renal lesions. For this reason, biopsy, which can be performed safely and without concern for tumor tract seeding, is often used for diagnosis. Imaging remains crucial for staging of renal cancer, as it is very accurate. In patients with organ-confined disease, imaging can be used to determine which patients are candidates for partial versus total nephrectomy. It has become increasingly clear that some patients with small malignant renal masses may never need to have the masses treated. Novel chemotherapeutic agents have greatly prolonged survival of patients with regional or distant metastatic disease. Tumor response after treatment with the new targeted agents can be sustained but can sometimes be delayed. Tumor necrosis without size reduction can be seen occasionally and should not be confused with a lack of response.

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