Benign and Malignant Renal Disease

11

Lejla Aganovic and Dominik Nörenberg

Learning Objectives

- To learn when very small renal masses can be ignored and when they should be followed.
- To learn about imaging features of AMLs and non-macroscopic fat-containing solid renal masses.
- To be familiar with the updated Bosniak cystic renal mass classification (version 2019).
- To be familiar with renal cancer staging including the use of the RENAL nephrometry score.
- To be knowledgeable of the emerging role of advanced imaging and multidisciplinary approaches for the management of RCC including renal mass biopsy, surgery, local ablation, active surveillance, SABR, and the imaging appearance of patients after treatment of RCC (including immunotherapy).

11.1 Introduction

Over the last decades, there have been several exciting developments in imaging assessment of renal masses, utilizing a multimodality imaging approach for the differential diagnosis and risk stratification of renal masses. The value of imaging for differential diagnosis of renal masses, local staging, risk stratification, and subsequent renal mass management will be discussed in the following paragraphs.

L. Aganovic
Department of Radiology, University of California, San Diego Medical Center, San Diego, CA, USA

D. Nörenberg (✉)
Department of Radiology and Nuclear Medicine, University Medical Center Mannheim, Heidelberg University, Mannheim, Baden-Württemberg, Germany
e-mail: Dominik.Noerenberg@medma.uni-heidelberg.de

11.2 Modalities for Imaging Renal Masses

11.2.1 Ultrasound (US) and Contrast-Enhanced US (CEUS)

Although non-contrast US 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 non-contrast US to be diagnostically definitive only when it identifies a renal mass as a simple cyst. On the other hand, CEUS using intravenous microbubbles as contrast agent allows a dynamic assessment of the microvasculature of renal masses [1]. Similarly to CT and MRI, CEUS can differentiate between cystic and solid renal lesions and is also beneficial for the characterization of complex cystic lesions. Therefore, CEUS is increasingly used as a diagnostic tool for secondary correlation of indeterminate renal lesions or in patients with contraindications to CT or MRI contrast agents [2].

11.2.2 Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)

Multidetector CT can provide high spatial resolution images of the kidneys and renal vessels, respectively. MRI provides a higher signal-to-noise ratio and higher spatial as well as temporal resolution with a large spectrum of imaging sequences for a more detailed characterization of renal lesions. MRI is often considered as a "problem solver" in renal mass imaging, lesion classification, and staging (e.g., for the assessment of venous extension). The usage of contrast agents for renal MRI can now also be considered in patients with chronic and/or end-stage kidney disease according to the latest AUA guidelines [3, 4]. With the increasing use of cross-sectional imaging, the rate of incidentally detected indeterminate renal masses continues to increase [5]. On CT, it is quite common for only contrast-

J. Hodler et al. (eds.), *Diseases of the Abdomen and Pelvis 2023-2026*, IDKD Springer Series,
https://doi.org/10.1007/978-3-031-27355-1_11

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 cell cancers (RCCs) are unlikely to measure >70 HU on unenhanced CT and <40 HU on contrast-enhanced CT [6].

Key Point
Multiphase renal CT or MRI in patients with normal renal function is the most appropriate imaging modality for renal mass characterization. Patients 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).

11.3 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 [7]. Many very small renal masses detected with CT and MRI cannot be sufficiently characterized due to their size. In general, one in five detected small renal masses is histologically benign and may not benefit from aggressive treatment regimes. Accurate attenuation measurements in these very small lesions are problematic, due to volume averaging and "pseudoenhancement." Fortunately, the likelihood of any one of these lesions being malignant is exceedingly low [6, 8, 9].

Key Point
Follow-up imaging of very small 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 (associated with clear cell RCC), hereditary papillary renal cell cancer (associated with type I papillary RCC), Birt–Hogg–Dube (associated with chromophobe RCC and oncocytoma) or hereditary leiomyomatosis-renal cancer syndrome (associated with type II papillary RCC) [10]. Over the last years, there has been increasing knowledge of hereditary renal cancers, which account for approximately 8% of RCCs due to improved genotyping. 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 small cysts have characteristic high T2 signal intensity. MRI is also much more sensitive to contrast enhancement than CT and not compromised by "pseudoenhancement" [9].

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 [11]. 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, increasing heterogeneity, or progression of other complicating features [9].

11.4 Cystic Renal Masses

To date, cystic renal lesions are classified using the Bosniak classification system, which was first proposed in 1986 [12] and was last revised in 2019 [8]. This system classifies cystic renal masses into five categories based upon their likelihood of being malignant. It is important to emphasize that the initial Bosniak classification system was designed for use with dedicated renal mass CT and not for ultrasound or MRI, respectively. The updated Bosniak classification (2019) includes clear definitions for several imaging terms (e.g., definition of cystic lesions, enhancement, thin vs. thick septa, etc.) to improve the clarity of radiology reporting and incorporates newly defined MRI criteria for the classification of cystic renal lesions. Because the updated Bosniak classification has been adopted for the use of CT, MRI, and CEUS, the presence and thickness of calcifications is neglected for lesion classification. Enhancement is defined as either clearly visible on cross-sectional imaging or non-visible based on established quantitative criteria. This includes an increase of 20 HU (or more) on contrast-enhanced CT in comparison to the native scan. On MRI, a signal intensity increase of 15% (or more) in comparison to non-contrast imaging is considered as an enhancement. The five updated Bosniak categories of cystic renal masses are as follows [8]:

- *Bosniak category I lesions* are simple cysts that constitute most cystic renal masses. They are homogeneous fluid-filled cystic lesions, anechoic on ultrasound and of water attenuation on CT or water signal intensity on MRI. They have smooth, thin walls (less or equal to 2 mm) that may enhance, but they do not contain nodules, septa, solid components, or calcifications. They do not enhance when contrast material is administered. Bosniak category I lesions are always benign; no follow-up is needed.
- *Bosniak category II lesions* are either "minimally complicated" cysts or "benign hyperattenuating" cysts and do not enhance on (multiphase) renal mass imaging. They may contain few (less or equal to 3) and thin (less or equal to 2 mm) septations with or without any type of calcifications. On CT, hyperdense renal cysts smaller than 3 cm in diameter with >70 HU or between −9 and 20 HU (on unenhanced CT) or between 21 and 30 HU (on portal venous phase) are also classified as category II lesions. The attenuation threshold signifying the need for additional imaging was recently changed from >20 HU to >30 HU [6, 8]. On MRI, incompletely characterized cystic renal lesions with T2 signal intensities of CSF or hyperintense lesions on unenhanced T1 images which are with approximately 2.5 times renal parenchymal signal intensity fall into the category of Bosniak II lesions. Additionally, hypoattenuating lesions that are too small to characterize are also classified as Bosniak category II lesions. All of them are considered as (likely) benign (chance of malignancy less than 1%); no follow-up is needed.

Key Point
Incidental detection of small homogeneous renal masses measuring 21–30 HU at portal venous phase CT imaging as well as the detection of incompletely characterized hypoattenuating lesions that are too small to characterize are classified as Bosniak II cystic renal masses. They do not require further imaging evaluation and no follow-up is needed.

- **Bosniak category IIF lesions** are well-defined renal masses and contain more than a few (greater than four) septa or septa with "minimal thickening" (3 mm or less). The wall or septa of Bosniak IIF cysts must enhance. On MRI, cystic masses which are heterogeneously hyperintense on fat-saturated T1-weighted imaging without contrast enhancement—a feature of pRCCs—also fall into the category Bosniak IIF lesions. On CT, heterogeneous masses without enhancement are considered as "incompletely characterized" and require further evaluation (e.g., with MRI or CEUS).

Key Point
Most Bosniak IIF cystic renal masses are benign, only 5–11% have been found to represent cancers or progress to become cancers and if, they are all indolent without locally recurrent or metastatic disease. For this reason, Bosniak IIF cystic renal masses must be followed, with repeated imaging studies performed at 6 months and 12 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.

- **Bosniak category III lesions** include cystic renal masses with thickened (greater than 4 mm) walls or septa and irregular enhancing walls or septa (focal or diffuse convex protrusion measuring 3 mm or less with obtuse margins with the walls or septa). Bosniak III cystic renal masses have a likelihood of malignancy in about 50–60% of the time and require treatment. When malignant, they tend to be less aggressive than other (predominantly solid) renal cancers (Fig. 11.1).
- **Bosniak category IV lesions** include cystic renal masses with enhancing nodules. "Nodules" are defined as "focal or diffuse convex protrusion of any size that has acute margins with the wall or septa, or a convex protrusion that is 4 mm or greater and has obtuse margins with the wall or septa lesions that have irregular enhancing walls or enhancing nodules." Bosniak IV cystic renal masses are nearly always (>90%) malignant, so treatment is warranted.

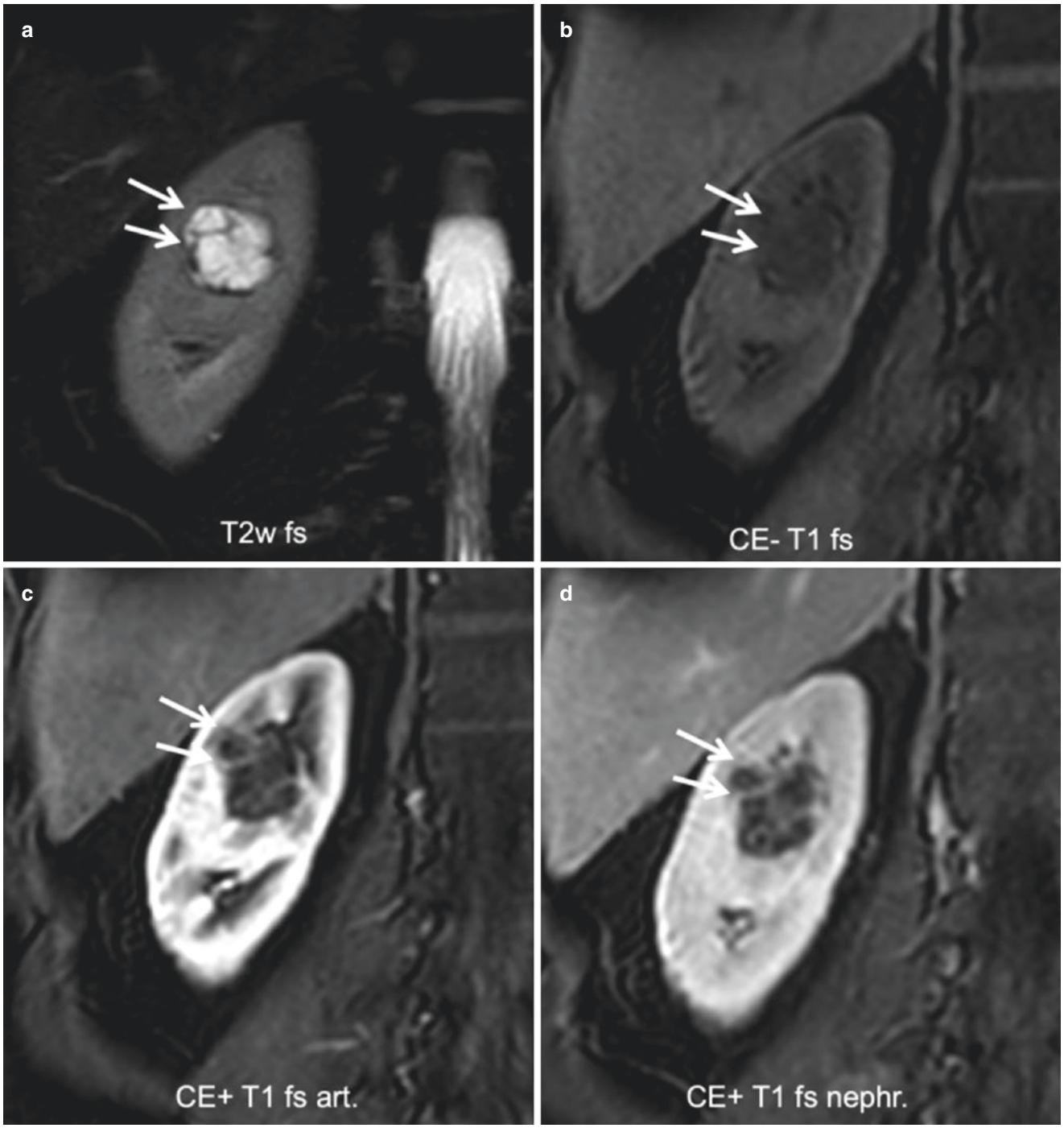

Fig. 11.1 Bosniak III cystic renal mass of the right kidney. (**a**) Coronal fs T2-weighted MR image shows a small hyperintense cystic mass (2.1 cm) in the upper pole of the right kidney with more than a few (>4) septa. (**b**) Coronal unenhanced fs T1-weighted MR image shows T1 hypointensity of the mass without hemorrhagic components. (**c**, **d**) Coronal contrast-enhanced fs T1-weighted MR images confirm enhancement of the lesion wall as well as septal enhancement both with "minimal thickening" (less or equal than 3 mm), no solid "nodules" are noted. Imaging findings are consistent with Bosniak III category of cystic renal masses. Postoperative histopathology confirmed the presence of a cystic ccRCC

11.5 Angiomyolipoma (AML)

AMLs are the most common benign solid renal neoplasms. Eighty percent of AMLs occur sporadically, are most diagnosed in middle-aged females, and are often associated with hereditary syndromes (tuberous sclerosis or lymphangioleiomyomatosis) [13]. AMLs are composed of angiomatous, myomatous, and fatty elements. While nearly all AMLs are echogenic on ultrasound, so are some small renal cancers. 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 as an AML (with only case reportable exceptions).

Key Point
On CT, visualization of at least some small areas of macroscopic fat within a renal mass (measuring 10 HU or less, predominantly with negative HU values) is considered diagnostic of macroscopic fat and thus, of an AML [14]. In contrast, the co-existence of macroscopic fat and calcifications within a lesion points toward malignancy (chromophobe or clear cell renal cancer) and requires further clarification.

Key Point
On MRI, such fat typically has high T1 and T2 signals 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. 11.2).

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 [13]. 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 [13, 15]. Results have been mixed. For example, some fpAMLs have higher unenhanced attenuation than normal renal parenchyma, but papillary renal cancers can also demonstrate

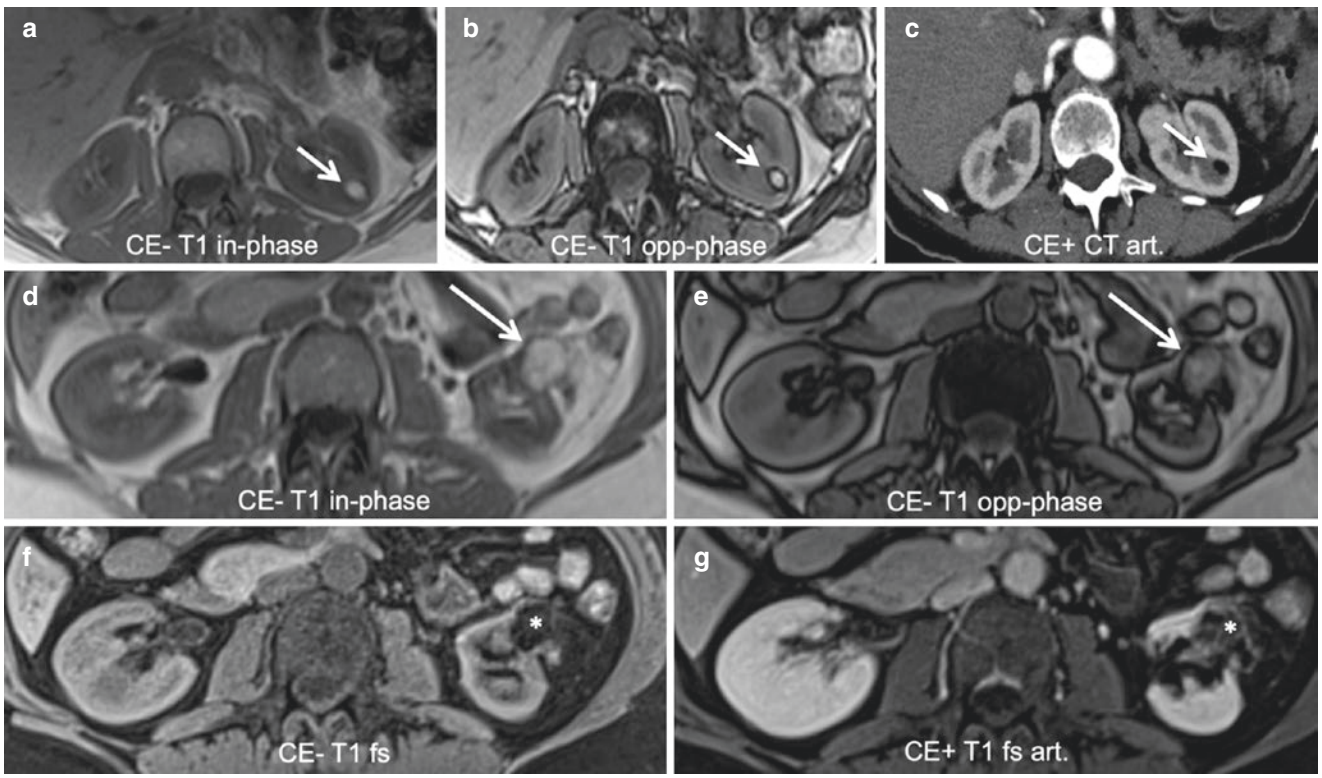

Fig. 11.2 Two solid renal masses with macroscopic fat consistent with AML (arrows) in two different patients (**a**–**c** and **d**–**g**). (**a**) axial in-phase T1-weighted MR image of the first patient shows a very small hyperintense mass (1 cm) of the left kidney. (**b**) opposed-phase MR image demonstrates "India ink" artifact at the interface of the renal mass with the kidney. (**c**) axial CT confirms intralesional macroscopic fat, confirming the diagnosis. (**d**–**g**) 2.5 cm AML of the left kidney in another patient with macroscopic fat (hyperintensity) on T1-weighted in-phase images without contrast (**d**), signal loss on T1-weighted opposed-phase images and (**e**) heterogenous, hypervascular enhancement on arterial phase imaging in comparison to non-contrast fs T1 imaging (*) (**f**, **g**)

this feature [16]. 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 or low-T2 signal intensity on MRI is most likely to be an AML.

11.6 Other Solid Renal Masses and Cancer Mimics

Other solid renal masses without macroscopic fat include oncocytomas, renal cell cancers, lymphoproliferative neoplasms, and metastases. Many studies attempted to distinguish among the various non-fat or minimal fat-containing solid renal masses on CT and MRI and have met with limited success; however, a few occasionally suggestive imaging features have been described.

11.6.1 Oncocytomas

Oncocytomas are benign solid renal tumors. They may contain central scars that can be detected on imaging studies. However, necrosis in renal cancers is indistinguishable from scars in oncocytomas [17, 18]. In fact, differentiating oncocytomas from RCCs on imaging is not possible which is further supported by overlapping histopathological features [19].

11.6.2 Renal Cell Cancers (RCCs)

Chromosomal analysis has demonstrated that there are at least 13 distinct types of renal cancer of which the most common are clear cell (about 70–80%), papillary (10–15%), and chromophobe (less than 10%) renal cell cancer. 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 with infiltrative behavior on imaging.

11.6.2.1 Clear Cell Renal Cell Cancer (ccRCC)

Clear cell renal cancers account for 70% of RCCs and have the highest metastatic potential and poorest survival of the major histologic RCC subtypes. They are usually heterogeneous renal cortical masses, and high-grade tumors may already present with renal vein invasion or perinephric fat infiltration on diagnosis. On unenhanced MRI, most ccRCCs demonstrate hyperintensity on T2-weighted images (Fig. 11.3) and a rather low amount of diffusion restriction. Due to abundant intracellular fat, clear cell cancers can lose signal on opposed-phase gradient echo T1-weighted images. Macroscopic fat within ccRCCs is very rare; however, this tends to occur with accompanying calcifications. Clear cell RCCs are hypervascular lesions and usually demonstrate heterogeneous enhancement, with peak enhancement occurring early on CMP images (Fig. 11.3):

11.6.2.2 Papillary Renal Cell Cancer (pRCC)

Papillary RCC accounts for 10–15% of RCCs and is the most common multifocal renal cancer subtype in up to 20–25% of the cases and bilaterally in up to 10% of the cases [20]. Papillary RCCs behave less aggressively than ccRCCs and are often less than 3 cm in size, rarely contain fat, are predominantly peripherally located, and show only indeterminate enhancement (between 10 and 20 HU). In these cases, further examination with CEUS or MRI is recommended [17]. On contrast-enhanced CT or MRI, papillary cancers tend to be homogeneous. On unenhanced CT, they may have higher attenuation than adjacent renal parenchyma and may be misdiagnosed as hemorrhagic cysts. A key feature on unenhanced MRI is low T2 signal intensity although this characteristic is unspecific and may be displayed as well by fat-poor AML or cysts with hemorrhagic components. In

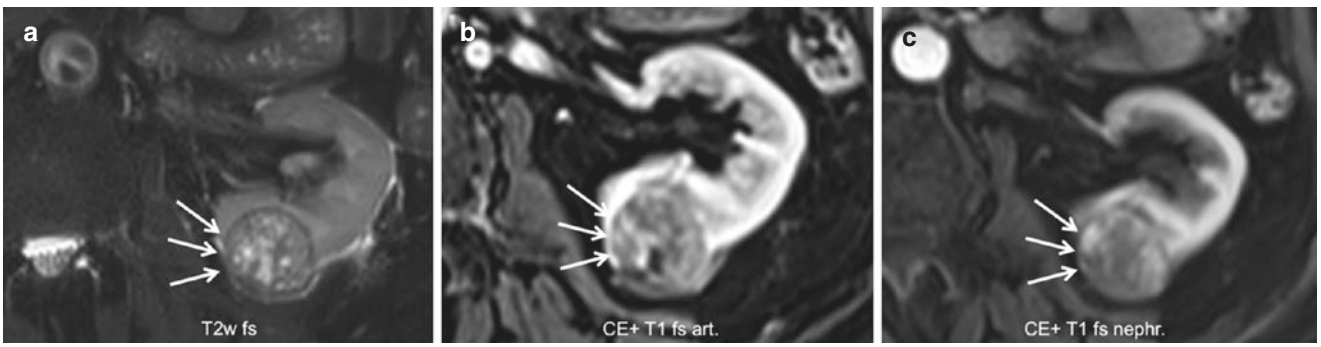

Fig. 11.3 Organ-confined clear cell renal cell carcinoma of the left kidney (arrows). (**a**) Axial fs T2-weighted image shows a lesion with smooth margins and moderate, heterogenous signal hyperintensity. (**b**, **c**) Axial fs T1-weighted arterial and nephrographic phase images show a hypervascular renal mass with heterogenous enhancement, subsequently confirmed to be ccRCC

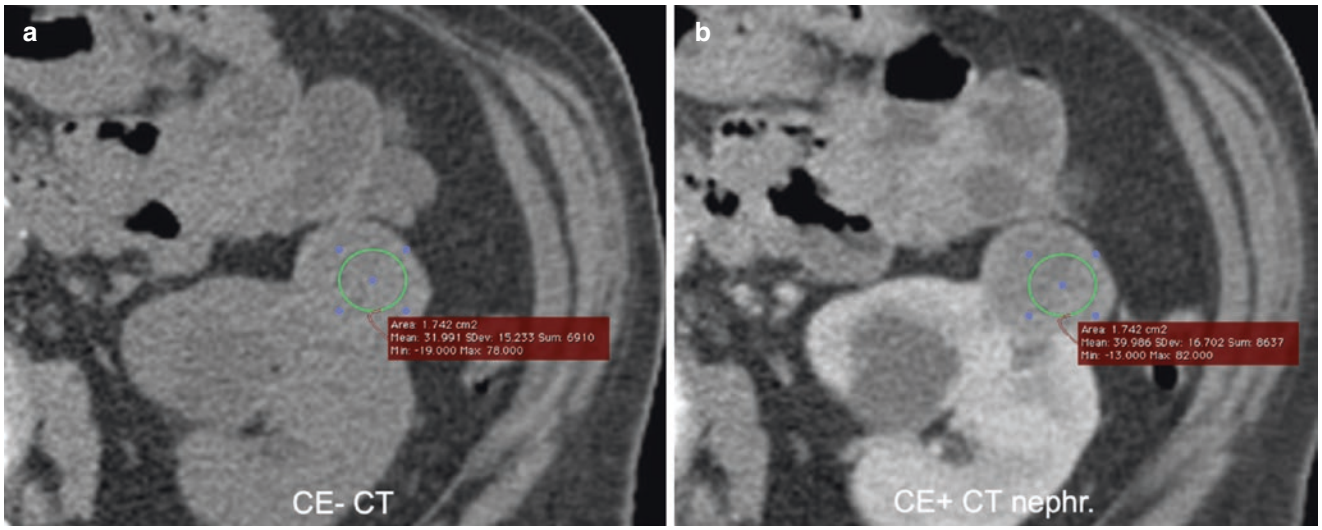

Fig. 11.4 Papillary renal cell carcinoma of the left kidney. Axial unenhanced CT (**a**) and contrast-enhanced CT (nephrographic phase) (**b**) demonstrate a homogenous hypoenhancing mass (ROI) measuring 2.4 cm in size in the anterior aspect of the mid-left kidney. Increase in HU density from 31 to 39 HU classifies this lesion as indeterminate. Subsequent CEUS and postoperative histopathology confirmed the presence of a pRCC

addition, they can lose signal on in-phase relative to out-of-phase T1 images due to hemosiderin content. They usually enhance homogeneously, more slowly, and to a lesser extent in comparison to other renal cancers, with peak enhancement not occurring until the NP or even the EP (Fig. 11.4):

11.6.2.3 Chromophobe Renal Cell Cancer (chRCC)

Chromophobe renal cell cancers account for 5% of renal malignancies and are less malignant than ccRCCs (with 5-year survival rates of 80–90%) [20]. chRCCs are generally well-differentiated cancers and, if they do not have sarcomatoid differentiation, are slow growing, show moderate, relatively uniform enhancement on CT- and MR imaging and may show areas of focal calcification. Even though some chRCCs may show "spoke-wheel enhancement" comparable to oncocytoma, they also do not have a definite characteristic appearance on imaging studies and cannot be reliably distinguished from other solid renal masses that do not contain macroscopic fat.

11.6.2.4 Uncommon Renal Cancer Cell Types

Many of the uncommon renal cancers do not have suggestive imaging appearances. 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 [21]. The (rare) combination of an infiltrative renal lesion, African American race, sickle cell trait and metastases at baseline presentation points toward renal medullary cancer [22].

11.6.3 Urothelial Neoplasms and Lymphoma

It can occasionally be difficult to distinguish centrally located infiltrative RCC from urothelial cancers [23]. However, the correct etiology may be predicted in many instances, especially an additional lesion within the upper urinary tract or bladder points toward urothelial cancer. Upper tract urothelial cancer (UTUC) represents about 15% of all renal tumors, whereas simultaneous cancer of the bladder is present in 15–20% of UTUCs. Most UTUCs are low-grade tumors, only approximately 15% show infiltrative behavior. Unlike RCCs, UTUCs 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 or necrotic areas seen in many, but not all, RCCs. Renal mass biopsy (RMB) is recommended when imaging findings are indeterminate. Another often centrally located and infiltrative renal mass that can be encountered and that can occasionally mimic infiltrative RCC (or UTUC) includes renal lymphoma.

In lymphomas, kidney involvement is rare and occurs most often in advanced disease stages with an established diagnosis at the time of imaging (typically for B-cell NHL subtypes). In addition, primary renal lymphoma is an extremely rare condition that accounts for less than 1% of the cases. On imaging, renal lymphomas present as hypovascular masses, and the renal veins/arteries remain patent despite extensive encasement. In parallel, there is often the presence of lymphadenopathy and splenomegaly. RMB may be recommended due to unspecific findings.

11.6.4 Other Non-neoplastic and Vascular Lesions

Other non-neoplastic lesions for the differential diagnosis of RCC include infective, inflammatory, and vascular entities such as renal artery aneurysms, xanthogranulomatous pyelonephritis (XGP) and post-transplant lymphoproliferative disease (PTLD).

Renal artery aneurysms are an extremely rare condition with a prevalence of <1% [24]. Risk factors include fibromuscular dysplasia and atherosclerosis and only 10% of renal artery aneurysms occur intraparenchymal, thereby mimicking solid or cystic renal lesions on US. CT- or MR-imaging should support definitive diagnostic characterization.

In the context of inflammatory cancer mimics, XGP is considered as a chronic inflammatory, destructive granulomatous kidney disease (accounting for 0.5–1% of histologically documented cases of pyelonephritis) [25]. XGP has a female predominance and is associated on imaging with renal calculi (either calyceal or staghorn), marked dilatation of the calyces, cortical thinning as well as reniform enlargement of the kidney. XGP can display features of (inflammatory) soft tissue proliferation that may extend into the perinephric space potentially mimicking infiltrative malignancy and/or lymphoproliferative disease.

Regarding lymphoproliferative cancer mimics, PTLD develops after solid organ or stem cell transplantation [26]. PTLD ranges from benign lymphoid hyperplasia to lymphoid hyperplasia with malignant potential and may mimic UTUC, lymphoma or solid renal cell cancer. Of note, PTLD occurs most frequently within 12 months after transplantation with a predominance in pediatric patients (or allograft PTLD in patients with renal transplants). On imaging, PTLD presents as heterogenous hilar mass and may encase vessels; additionally, it can present with multiple hypovascular lesions. RMB is required to confirm definitive diagnosis.

11.7 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. It has been suggested that a small solid mass that has an average growth rate of <3 mm per 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 (>5 mm in 12 months) may indicate aggressiveness and/or malignant potential [27].

11.8 Radiomics

In recent years, there has been increasing interest in the utility of computer-assisted diagnosis (CAD) systems and advanced deep/machine-learning techniques such as "radiomics" 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 solid and cystic renal masses [28–30]. 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 [31]. 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 [32]. Renal mass perfusion parameters have been employed to distinguish some renal cancers of higher Fuhrman grade from those of lower grade [33]. These results are promising, but preliminary and currently still subjected to academic research.

11.9 Use of Imaging for Solid Renal Mass Differentiation

Over the past decades, there have been significant paradigm shifts in the treatment of renal masses, including active surveillance (AS), minimal-invasive ablations, and improvements in RMB accuracy. Additionally, the effects of neoadjuvant therapy for patients with advanced localized disease are under investigation [34]. Many of incidentally detected renal masses will remain indolent with either no or very slow growth and require no therapeutic intervention. Accordingly, the US and European guidelines for the management of clinical stage 1 renal masses include active surveillance (AS) as a valid option for patients with comorbidities and T1a (≤4 cm) or T1b (4–7 cm) tumors [35]. The reported metastatic risk is very low even for larger tumors (cT1b/T2, >4 cm) in patients undergoing AS, but varies significantly by histologic subtype whereas ccRCC has the worst prognosis and a higher risk of metastatic disease [36]. To date, there is no clear beneficial effect on reducing renal cancer-specific mortality after aggressive treatment of small renal tumors. This may suggest that many renal cancers have indolent oncologic behavior. Although active surveillance is increasingly recognized as a treatment option for some patients, the lack of reliable predictive biomarkers limits its use in clinical practice. The multiparametric MRI-derived clear cell likelihood score (ccLS), based on a Likert scale, is useful for identifying clear cell renal carcinoma as the most common and aggressive subtype that can be used in clinical practice [37].

The ccLS provides a framework for standardized multiparametric MRI evaluation of small solid renal masses with moderate diagnostic accuracy for ccRCC classification. The ccLS was shown to be associated with lesion growth of small renal masses and may be considered as useful tool for therapy guidance (e.g., AS selection for lesions with a low ccLS or early treatment for lesions with a high ccLS) [38].

Key Point
The MRI-derived clear cell likelihood score (ccLS) may provide useful information for identifying aggressive small renal masses such as ccRCC and is positively correlated with lesion growth; however, the ccLS is not intended to classify tumors as malignant versus benign.

11.10 Renal Mass Biopsy (RMB)

RMB can be performed accurately and safely, and the risk of needle tract seeding is minimal [39, 40]. The updated AUA guideline defines indications for RMBs more clearly following a "utility-based" approach whenever it may influence patient management [3, 41]. Given the substantial overlap in the imaging features of many renal lesions, percutaneous renal mass biopsy can be necessary for determining the nature of renal masses prior to treatment. Thus, RMB has an emerging role to guide the management of renal masses, to limit invasiveness and overtreatment as well as to support patient risk stratification (e.g., in cases prior ablation, prior active surveillance, with infiltrative or metastatic renal disease to allow subtyping for potential systemic therapy or to detect an underlying hereditary condition).

11.11 Pretreatment Assessment of Renal Cancer

11.11.1 Staging and Diagnostic Workup

CT and MRI (obtained during the portal venous phase of enhancement) are at least 90% accurate in renal cancer staging, with the AJCC TNM staging system for renal cancer as follows [42] (Table 11.1):

The most substantial limitation of imaging for renal cancer staging results from the fact that both CT and MRI have difficulties in determining whether renal cancer has invaded the renal capsule and spread into the perirenal or renal sinus fat (differentiating T2 from T3 cancers). Perinephric soft tissue stranding can be produced by tumor, edema, or blood vessels.

Table 11.1 AJCC TNM staging system for renal cancer [42]

Category	Definition
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1a	≤4 cm in greatest diameter and limited to the kidney
T1b	>4 but ≤7 cm and limited to the kidney
T2a	>7 but ≤10 cm and limited to the kidney
T2b	>10 cm and limited to the kidney
T3a	Extension into renal vein or its branches or invading perirenal or renal sinus fat
T3b	Extension into IVC below diaphragm
T3c	Extension into IVC above the diaphragm or invading the IVC wall
T4	Invasion beyond perinephric (Gerota) fascia or into ipsilateral adrenal gland
Nx	Lymph nodes cannot be assessed
N0	No regional (retroperitoneal) lymph node involvement
N1	Regional (retroperitoneal) lymph node involvement
Mx	Distant metastatic status cannot be determined
M0	No distant metastasis
M1	Distant lymph node or other metastasis, including non-continuous adrenal involvement

Key Point
It is recommended that T3 disease is diagnosed on CT or MRI only when nodular tissue is identified in the perinephric space. Non-continuous adrenal gland invasion is regarded as M1 stage.

Figure 11.5 gives an overview about the diagnostic workup for renal cancer staging:

11.11.2 RENAL Nephrometry Score

Many urologists prefer that RENAL nephrometry scoring of suspected or known renal cancers also be obtained prior to surgery. According to the AUA and EAU guidelines, small T1a renal lesions should be treated with partial nephrectomy (PN) whenever technically feasible [3, 44]. Renal nephrometry scoring provides standard metrics to assess the tumor complexity, allowing the urologist to predict the likelihood that partial nephrectomy can be performed effectively and safely with a reduced risk of complications (39). For RENAL nephrometry scoring, a renal mass receives a score of 1–3 points for each of the five features: **R**enal mass size, **E**xophyticity, **N**earness to the renal collecting system or sinus, **A**nterior or posterior location, and **L**ocation with respect to the upper and lower polar lines (Table 11.2) [45]. Tumors that have composite nephrometry scores of 4–6 are very amenable to PN, while those that have scores of 10–12 are poor candidates for PN. Radical nephrectomy should be considered in the latter group.

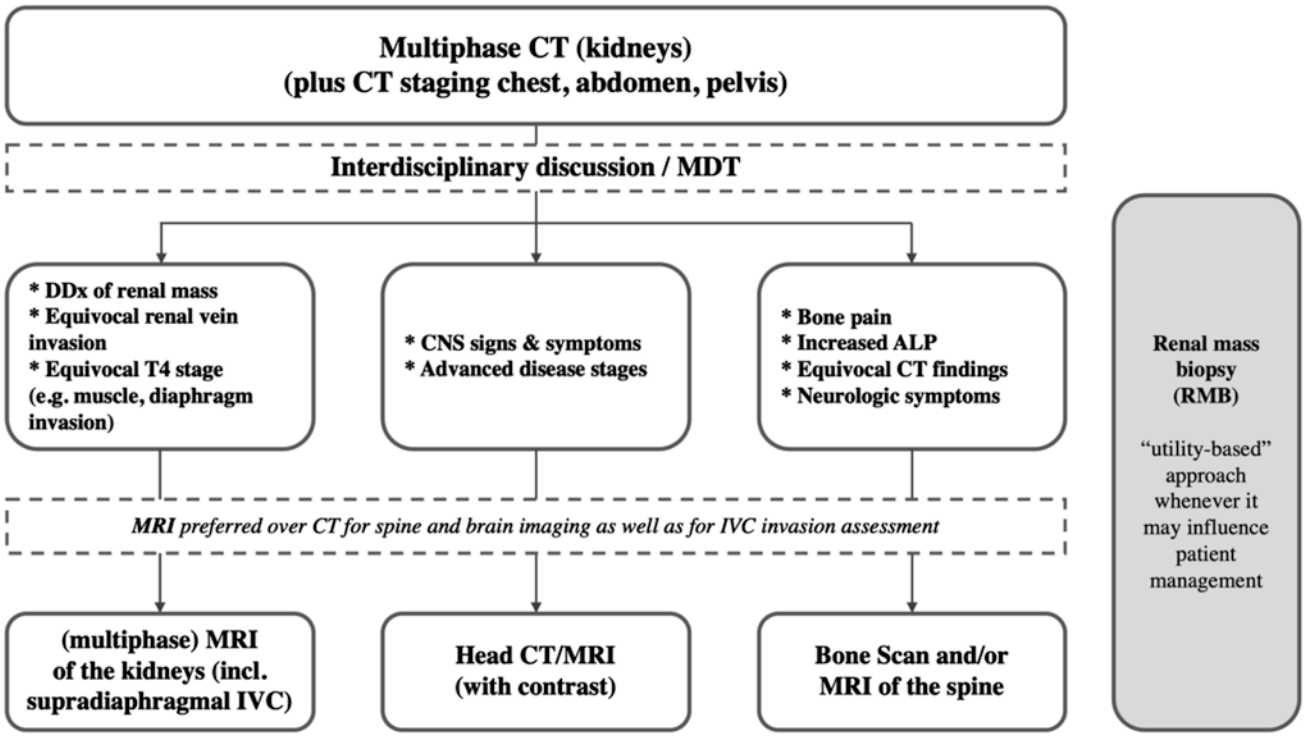

Fig. 11.5 Diagnostic workup for renal cancer staging [43]

Table 11.2 RENAL nephrometry score [45]

Feature	1 point	2 points	3 points
R = renal mass size	≤4 cm	>4–<7 cm	≥7 cm
E = Exophyticity/Endophyticity	≥50%	<50%	Entirely endophytic
N = nearness to collecting system or renal sinus	≥7 mm	>4–<7 mm	≤4 mm
A = anterior or posterior location	No points given. Mass is listed as a, p, or neither (x)		
L = location relative to upper and lower polar lines Add "**h**" if it 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

11.12 Management of Local or Locoregional Renal Cancer

Management of renal cancers that have not metastasized regionally or distantly now ranges from AS (for small (<4 cm) indolent (low Fuhrman grade) tumors in elderly patients with significant comorbidities) to local and/or thermal ablation (TA), partial nephrectomy (PN), or radical nephrectomy (RN) (32, 37). Over the last decades, there has been an increasing paradigm shift toward nephron-sparing treatments for small renal lesions (<4 cm) as well as an increasing role of AS as a management alternative to immediate treatment options. For patients with a solid renal mass <3 cm, or masses that are complex but predominantly cystic, not infiltrating on imaging, and a tumor growth of less than 5 mm per year, AS may be selected [4]. For patients with solid renal masses or complex Bosniak 3 (or 4) cystic renal masses who prefer AS, clinicians should consider RMB for oncologic risk stratification (if the risk-benefit analysis for AS vs. treatment is inconclusive). Patients on AS should undergo subsequent imaging every 3–6 months for a year to assess interval growth, 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 [46, 47]. For small cT1a solid renal masses, there is growing evidence for the effectiveness of TA and/or local ablation as an alternative to PN, especially in patients who elect ablation [4]. The EAU guideline recommends performing an RMB before (ideally not concomitantly with) ablative therapy [44]. AS and/or TA is especially relevant for frail or comorbid patients with small renal masses who are not eligible for surgery. For advanced locoregional disease, the need for adjuvant therapy after surgery has been recently addressed [4, 48]. Furthermore, adjuvant pembrolizumab (a type of

immunotherapy) can be considered as an alternative surgical MDT consideration for patients with locally advanced ccRCC following surgery with curative intent. Adjuvant pembrolizumab has been shown to be beneficial for intermediate- and high-risk ccRCC patients with a risk of recurrence (shown for pT2 G4 OR pT3 any G OR pT4 any G OR pN+ any G cancers) [48].

11.13 Management of (Oligo-)Metastatic Renal Cancer

For synchronous or early oligometastatic disease, the ESMO guideline 2019 does not usually recommend metastasectomy as an alternative to systemic therapy in patients with synchronous or early oligometastatic disease [35]. Oligometastatic disease may be observed without immediate treatment for up to 16 months before systemic therapy is required due to progression [44]. Furthermore, the role of stereotactic ablative radiotherapy (SABR) was recently investigated within the SABR-COMET trial for oligometastatic renal cancer disease in patients with one to five metastatic lesions, in comparison to standard-of-care palliative treatment [49]. Within the SABR-COMET trial, SABR was associated with an overall survival benefit and increased progression-free survival in oligometastatic patients in comparison to patients undergoing standard-of-care treatment. Overall, there is emerging evidence that SABR can be considered as a novel treatment reserved for patients with T1-T3a tumors (as well as for oligometastatic lesions) who are not medically or surgically operable [50].

11.14 Imaging after Renal Cancer Treatment

11.14.1 After Renal Mass Ablation

After successful renal mass radiofrequency ablation or cryoablation, there is an 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. 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 perilesional halo, changes that create an appearance that can be confused with an AML. Ablation bed expansion is not typically seen after microwave ablation.

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 [51].

Persistent or recurrent tumors 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 [51].

11.14.2 Imaging after Partial or Total Nephrectomy

After PN or RN, it is common to see post-operative inflammatory or fibrotic changes in the surgical bed, along with deformity of the renal contour at the site of partial nephrectomy. Post-ablation surgical findings may also include fat invagination between the surgical bed and normal renal parenchyma. Ablation bed expansion is not typically seen after microwave ablation. 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 it contains 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 renal artery pseudoaneurysm (RAP), arteriovenous (AV) fistula, urinoma, or abscess. If urinoma is a concern, delayed imaging >1–2 h after contrast administration might prove useful to document the urinary leak. Although RAPs or AV fistulas after PN are rare conditions (in 1–5% of the cases after PN [52]) both represent a potentially life-threatening complication. Patients typically present 7–12 days after PN with hematuria and/or clinical signs of blood loss. Emergency treatment of choice is selective transarterial embolization as an effective minimally invasive treatment option for the management of hemodynamically unstable patients with RAP (or AV fistula) with minimal impact on renal function [52].

After PN or RN, recurrent tumor recurrence may develop in the surgical bed, regionally within the retroperitoneum or distantly. Surgical bed recurrences may initially be difficult to differentiate from post-operative scarring or fibrosis, although tumor recurrence often demonstrates detectable (hyper-)enhancement and enlarges over time (Fig. 11.6).

Renal cancer usually metastasizes to regional lymph nodes, liver, adrenal glands, lungs, and bones. Adrenal cancer metastases from ccRCC can be problematic, since they may contain large amounts of intracellular fat. As a result,

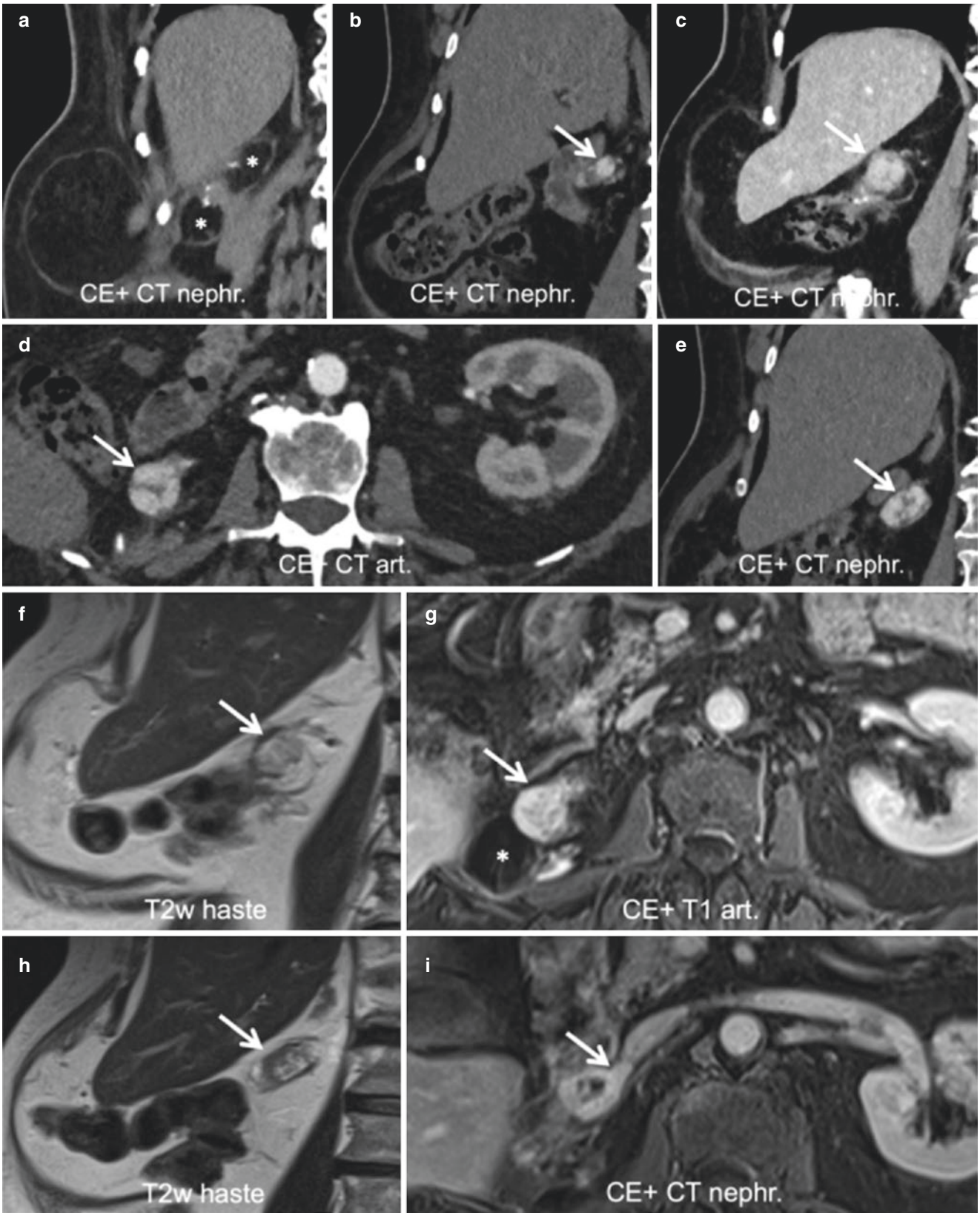

Fig. 11.6 Post-surgical appearance of the tumor bed on CT- (**a**–**e**) and MR-imaging (**f**–**i**) >3 years after PN of a ccRCC in the upper pole of the right kidney. (**a**, **g**) appearance of the post-surgical tumor bed (*) with fat invagination between the surgical bed and normal renal parenchyma on coronal CT (**a**) and coronal T2w haste images (**f**). (**b**–**i**) Surgical bed cancer recurrence (arrows) on CT- and MR imaging with a hypervascular soft tissue mass including renal vein invasion (**b**, **e**, **h**, **i**). Of note, tumor recurrence/tumor thrombus demonstrates T2 hyperintensity on MR imaging (**f**, **h**) as well as hypervascularity (**d**, **e**, **g**) consistent with ccRCC recurrence and venous invasion

like 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 [53].

11.14.3 Imaging After Treatment of Metastatic Disease

11.14.3.1 RECIST

Metastatic disease occurs approximately in 17% of patients at diagnosis of RCC. Patients who present with or develop metastatic disease must receive systemic treatment. Follow-up imaging is then performed regularly to determine whether (or not) patients are responding to adjuvant chemotherapy. 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 according to the newest version 1.1 [54]. RECIST 1.1 involves measurements of up to five metastatic lesions (no more than two reference lesions 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 between a 30% decrease and a 20% increase is considered a stable disease.

11.14.3.2 Multikinase Inhibitors

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 multi-kinase inhibitors. This is because multi-kinase inhibitors may produce necrosis (and resulting diminished attenuation on contrast-enhanced CT) in responding to 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 1.1 is used.

Several alternative measuring systems have been devised, which consider changes in lesion attenuation in addition to changes in size. This includes the Choi, modified Choi, and the "Morphology, Attenuation, Size, and Structure" (MASS) systems [55, 56]. With the Choi criteria, 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 features must be present at the same time.

11.14.3.3 Immunotherapy

Recently, patients with metastatic RCC have been increasingly 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, PDL2) (47).

Key Point

A unique feature of RCC 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 as unconfirmed progressive disease (UPD). UPD must be confirmed by another follow-up imaging study in no less than 4 weeks [57]. 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." The system for assessing metastatic tumor in immunotherapy patients has been modified to take these issues into account (iRECIST criteria) [57]. 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.

11.14.3.4 Complications of Multikinase Inhibitor Treatment and Immunotherapy

Complications encountered in patients undergoing new systemic treatments include hepatic steatosis, cholecystitis, pancreatitis, bowel perforation, arterial thrombosis (after multikinase therapy) and segmental or diffuse colitis, pneumonitis, dermatitis, and, less commonly, thyroiditis, hypophysitis, pancreatitis, and adrenal dysfunction [57].

11.15 Concluding Remarks

Over the last years, there have been several exciting developments with respect to imaging, diagnosis, treatment, and management of cystic and solid renal masses. This has included the identification of imaging features that can differentiate among some of the many cystic and solid renal masses. In 2019, an updated Bosniak classification has been introduced also incorporating MR-based assessment of cystic renal masses and clear terms for radiology reporting. Unfortunately, in many patients, overlapping features still prevent the distinction of renal cancers from benign renal lesions or non-neoplastic cancer mimics. Therefore, RMB, which can be performed safely and without concern for tumor tract seeding, has an emerging role for definitive diagnosis and risk stratification. Imaging remains crucial for differential diagnosis, staging, and management of renal masses, as it is very accurate. In patients with organ-confined disease, imaging can be used to determine which patients are candidates for PN versus RN. It has become increasingly clear that some patients with small malignant renal masses may not undergo immediate treatment and that AS should be increasingly considered for selected patients. Novel chemotherapeutic agents have greatly prolonged the survival of patients with regional or distant oligometastatic disease and immunotherapy is increasingly implemented in adjuvant settings.

Take Home Messages

- Most renal masses are incidentally detected.
- Most solid renal masses are malignant.
- CT is the most frequent imaging technique to detect renal masses.
- CT is the main imaging modality for RCC staging.
- MRI can be helpful to characterize solid renal masses and serves as problem solver.
- Renal mass biopsy is an integral part of clinical staging.
- Multidisciplinary approach is key, and treatment should be tailored to each patient.

References

1. Herms E, Weirich G, Maurer T, Wagenpfeil S, Preuss S, Sauter A, et al. Ultrasound-based "CEUS-Bosniak"classification for cystic renal lesions: an 8-year clinical experience. World J Urol. 2022; https://doi.org/10.1007/s00345-022-04094-0.
2. Expert Panel on Urologic Imaging, Wang ZJ, Nikolaidis P, Khatri G, Dogra VS, Ganeshan D, et al. ACR appropriateness criteria(R) indeterminate renal mass. J Am Coll Radiol. 2020;17(11S):S415–S28. https://doi.org/10.1016/j.jacr.2020.09.010.
3. Campbell SC, Clark PE, Chang SS, Karam JA, Souter L, Uzzo RG. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: part I. J Urol. 2021;206(2):199–208. https://doi.org/10.1097/JU.0000000000001911.
4. Campbell SC, Uzzo RG, Karam JA, Chang SS, Clark PE, Souter L. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: part II. J Urol. 2021;206(2):209–18. https://doi.org/10.1097/JU.0000000000001912.
5. Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F. International variations and trends in renal cell carcinoma incidence and mortality. Eur Urol. 2015;67(3):519–30. https://doi.org/10.1016/j.eururo.2014.10.002.
6. Corwin MT, Altinmakas E, Asch D, Bishop KA, Boge M, Curci NE, et al. Clinical importance of incidental homogeneous renal masses that measure 10-40 mm and 21-39 HU at portal venous phase CT: a 12-institution retrospective cohort study. AJR Am J Roentgenol. 2021;217(1):135–40. https://doi.org/10.2214/AJR.20.24245.
7. Hindman NM. Approach to very small (<1.5 cm) cystic renal lesions: ignore, observe, or treat? AJR Am J Roentgenol. 2015;204(6):1182–9. https://doi.org/10.2214/AJR.15.14357.
8. Silverman SG, Pedrosa I, Ellis JH, Hindman NM, Schieda N, Smith AD, et al. Bosniak classification of cystic renal masses, version 2019: an update proposal and needs assessment. Radiology. 2019;292(2):475–88. https://doi.org/10.1148/radiol.2019182646.
9. Herts BR, Silverman SG, Hindman NM, Uzzo RG, Hartman RP, Israel GM, et al. Management of the Incidental Renal Mass on CT: a white paper of the ACR incidental findings committee. J Am Coll Radiol. 2018;15(2):264–73. https://doi.org/10.1016/j.jacr.2017.04.028.
10. Walker SM, Gautam R, Turkbey B, Malayeri A, Choyke PL. Update on hereditary renal cancer and imaging implications. Radiol Clin N Am. 2020;58(5):951–63. https://doi.org/10.1016/j.rcl.2020.04.003.
11. Bosniak MA, Birnbaum BA, Krinsky GA, Waisman J. Small renal parenchymal neoplasms: further observations on growth. Radiology. 1995;197(3):589–97. https://doi.org/10.1148/radiology.197.3.7480724.
12. Bosniak MA. The current radiological approach to renal cysts. Radiology. 1986;158(1):1–10. https://doi.org/10.1148/radiology.158.1.3510019.
13. Jinzaki M, Silverman SG, Akita H, Mikami S, Oya M. Diagnosis of renal Angiomyolipomas: classic, fat-poor, and epithelioid types. Semin Ultrasound CT MR. 2017;38(1):37–46. https://doi.org/10.1053/j.sult.2016.11.001.
14. Davenport MS, Neville AM, Ellis JH, Cohan RH, Chaudhry HS, Leder RA. Diagnosis of renal angiomyolipoma with hounsfield unit thresholds: effect of size of region of interest and nephrographic phase imaging. Radiology. 2011;260(1):158–65. https://doi.org/10.1148/radiol.11102476.
15. Catalano OA, Samir AE, Sahani DV, Hahn PF. Pixel distribution analysis: can it be used to distinguish clear cell carcinomas from angiomyolipomas with minimal fat? Radiology. 2008;247(3):738–46. https://doi.org/10.1148/radiol.2473070785.
16. Zhang YY, Luo S, Liu Y, Xu RT. Angiomyolipoma with minimal fat: differentiation from papillary renal cell carcinoma by helical CT. Clin Radiol. 2013;68(4):365–70. https://doi.org/10.1016/j.crad.2012.08.028.
17. Krishna S, Murray CA, McInnes MD, Chatelain R, Siddaiah M, Al-Dandan O, et al. CT imaging of solid renal masses: pitfalls and solutions. Clin Radiol. 2017;72(9):708–21. https://doi.org/10.1016/j.crad.2017.05.003.
18. Woo S, Cho JY, Kim SH, Kim SY, Lee HJ, Hwang SI, et al. Segmental enhancement inversion of small renal oncocytoma: differences in prevalence according to tumor size. AJR Am J Roentgenol. 2013;200(5):1054–9. https://doi.org/10.2214/AJR.12.9300.

19. O'Malley ME, Tran P, Hanbidge A, Rogalla P. Small renal oncocytomas: is segmental enhancement inversion a characteristic finding at biphasic MDCT? AJR Am J Roentgenol. 2012;199(6):1312–5. https://doi.org/10.2214/AJR.12.8616.
20. Low G, Huang G, Fu W, Moloo Z, Girgis S. Review of renal cell carcinoma and its common subtypes in radiology. World J Radiol. 2016;8(5):484–500. https://doi.org/10.4329/wjr.v8.i5.484.
21. Moch H, Cubilla AL, Humphrey PA, Reuter VE, Ulbright TM. The 2016 WHO classification of tumours of the urinary system and male genital organs-part a: renal, penile, and testicular tumours. Eur Urol. 2016;70(1):93–105. https://doi.org/10.1016/j.eururo.2016.02.029.
22. Zhu QQ, Wang ZQ, Zhu WR, Chen WX, Wu JT. The multislice CT findings of renal carcinoma associated with XP11.2 translocation/TFE gene fusion and collecting duct carcinoma. Acta Radiol. 2013;54(3):355–62. https://doi.org/10.1258/ar.2012.120255.
23. Roberts JL, Ghali F, Aganovic L, Bechis S, Healy K, Rivera-Sanfeliz G, et al. Diagnosis, management, and follow-up of upper tract urothelial carcinoma: an interdisciplinary collaboration between urology and radiology. Abdom Radiol (NY). 2019;44(12):3893–905. https://doi.org/10.1007/s00261-019-02293-9.
24. Osako Y, Tatarano S, Nishiyama K, Yamada Y, Yamagata T, Uchida Y, et al. Unusual presentation of intraparenchymal renal artery aneurysm mimicking cystic renal cell carcinoma: a case report. Int J Urol. 2011;18(7):533–5. https://doi.org/10.1111/j.1442-2042.2011.02775.x.
25. Dwivedi US, Goyal NK, Saxena V, Acharya RL, Trivedi S, Singh PB, et al. Xanthogranulomatous pyelonephritis: our experience with review of published reports. ANZ J Surg. 2006;76(11):1007–9. https://doi.org/10.1111/j.1445-2197.2006.03919.x.
26. Katabathina V, Menias CO, Pickhardt P, Lubner M, Prasad SR. Complications of immunosuppressive therapy in solid organ transplantation. Radiol Clin N Am. 2016;54(2):303–19. https://doi.org/10.1016/j.rcl.2015.09.009.
27. Pierorazio PM, Hyams ES, Mullins JK, Allaf ME. Active surveillance for small renal masses. Rev Urol. 2012;14(1–2):13–9.
28. Miskin N, Qin L, Matalon SA, Tirumani SH, Alessandrino F, Silverman SG, et al. Stratification of cystic renal masses into benign and potentially malignant: applying machine learning to the bosniak classification. Abdom Radiol (NY). 2021;46(1):311–8. https://doi.org/10.1007/s00261-020-02629-w.
29. Diaz de Leon A, Davenport MS, Silverman SG, Schieda N, Cadeddu JA, Pedrosa I. Role of virtual biopsy in the management of renal masses. AJR Am J Roentgenol. 2019:1–10. https://doi.org/10.2214/AJR.19.21172.
30. Kim NY, Lubner MG, Nystrom JT, Swietlik JF, Abel EJ, Havighurst TC, et al. Utility of CT texture analysis in differentiating Low-attenuation renal cell carcinoma from cysts: a bi-institutional retrospective study. AJR Am J Roentgenol. 2019;213(6):1259–66. https://doi.org/10.2214/AJR.19.21182.
31. Leng S, Takahashi N, Gomez Cardona D, Kitajima K, McCollough B, Li Z, et al. Subjective and objective heterogeneity scores for differentiating small renal masses using contrast-enhanced CT. Abdom Radiol (NY). 2017;42(5):1485–92. https://doi.org/10.1007/s00261-016-1014-2.
32. Coy H, Young JR, Douek ML, Brown MS, Sayre J, Raman SS. Quantitative computer-aided diagnostic algorithm for automated detection of peak lesion attenuation in differentiating clear cell from papillary and chromophobe renal cell carcinoma, oncocytoma, and fat-poor angiomyolipoma on multiphasic multidetector computed tomography. Abdom Radiol (NY). 2017;42(7):1919–28. https://doi.org/10.1007/s00261-017-1095-6.
33. Chen C, Kang Q, Wei Q, Xu B, Ye H, Wang T, et al. Correlation between CT perfusion parameters and Fuhrman grade in pTlb renal cell carcinoma. Abdom Radiol (NY). 2017;42(5):1464–71. https://doi.org/10.1007/s00261-016-1009-z.
34. Bindayi A, Hamilton ZA, McDonald ML, Yim K, Millard F, McKay RR, et al. Neoadjuvant therapy for localized and locally advanced renal cell carcinoma. Urol Oncol. 2018;36(1):31–7. https://doi.org/10.1016/j.urolonc.2017.07.015.
35. Escudier B, Porta C, Schmidinger M, Rioux-Leclercq N, Bex A, Khoo V, et al. Renal cell carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up dagger. Ann Oncol. 2019;30(5):706–20. https://doi.org/10.1093/annonc/mdz056.
36. Delahunt B, Cheville JC, Martignoni G, Humphrey PA, Magi-Galluzzi C, McKenney J, et al. The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. Am J Surg Pathol. 2013;37(10):1490–504. https://doi.org/10.1097/PAS.0b013e318299f0fb.
37. Pedrosa I, Cadeddu JA. How we do it: managing the indeterminate renal mass with the MRI clear cell likelihood score. Radiology. 2022;302(2):256–69. https://doi.org/10.1148/radiol.210034.
38. Rasmussen RG, Xi Y, Sibley RC 3rd, Lee CJ, Cadeddu JA, Pedrosa I. Association of clear cell likelihood score on MRI and growth kinetics of small solid renal masses on active surveillance. AJR Am J Roentgenol. 2022;218(1):101–10. https://doi.org/10.2214/AJR.21.25979.
39. Halverson SJ, Kunju LP, Bhalla R, Gadzinski AJ, Alderman M, Miller DC, et al. Accuracy of determining small renal mass management with risk stratified biopsies: confirmation by final pathology. J Urol. 2013;189(2):441–6. https://doi.org/10.1016/j.juro.2012.09.032.
40. Park SH, Oh YT, Jung DC, Cho NH, Choi YD, Park SY. Abdominal seeding of renal cell carcinoma: radiologic, pathologic, and prognostic features. Abdom Radiol (NY). 2017;42(5):1510–6. https://doi.org/10.1007/s00261-016-1029-8.
41. Ozambela M Jr, Wang Y, Leow JJ, Silverman SG, Chung BI, Chang SL. Contemporary trends in percutaneous renal mass biopsy utilization in the United States. Urol Oncol. 2020;38(11):835–43. https://doi.org/10.1016/j.urolonc.2020.07.022.
42. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The eighth edition AJCC cancer staging manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93–9. https://doi.org/10.3322/caac.21388.
43. Motzer RJ, Jonasch E, Boyle S, Carlo MI, Manley B, Agarwal N, et al. NCCN guidelines insights: kidney cancer, version 1.2021. J Natl Compr Cancer Netw. 2020;18(9):1160–70. https://doi.org/10.6004/jnccn.2020.0043.
44. Ljungberg B, Bensalah K, Canfield S, Dabestani S, Hofmann F, Hora M, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol. 2015;67(5):913–24. https://doi.org/10.1016/j.eururo.2015.01.005.
45. Kutikov A, Uzzo RG. The R.E.N.a.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol. 2009;182(3):844–53. https://doi.org/10.1016/j.juro.2009.05.035.
46. Sury K, Pierorazio PM. Definitive treatment vs. active surveillance for small renal masses: closing the preference gap. Can Urol Assoc J. 2022;16(4):102–3. https://doi.org/10.5489/cuaj.7841.
47. Schieda N, Krishna S, Pedrosa I, Kaffenberger SD, Davenport MS, Silverman SG. Active surveillance of renal masses: the role of radiology. Radiology. 2022;302(1):11–24. https://doi.org/10.1148/radiol.2021204227.
48. Choueiri TK, Tomczak P, Park SH, Venugopal B, Ferguson T, Chang YH, et al. Adjuvant Pembrolizumab after nephrectomy in renal-cell carcinoma. N Engl J Med. 2021;385(8):683–94. https://doi.org/10.1056/NEJMoa2106391.
49. Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic can-

cers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet. 2019;393(10185):2051–8. https://doi.org/10.1016/S0140-6736(18)32487-5.
50. Motzer RJ, Jonasch E, Agarwal N, Alva A, Baine M, Beckermann K, et al. Kidney cancer, version 3.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Cancer Netw. 2022;20(1):71–90. https://doi.org/10.6004/jnccn.2022.0001.
51. Kawamoto S, Solomon SB, Bluemke DA, Fishman EK. Computed tomography and magnetic resonance imaging appearance of renal neoplasms after radiofrequency ablation and cryoablation. Semin Ultrasound CT MR. 2009;30(2):67–77. https://doi.org/10.1053/j.sult.2008.12.005.
52. Chen J, Yang M, Wu P, Li T, Ning X, Peng S, et al. Renal arterial Pseudoaneurysm and renal arteriovenous fistula following partial nephrectomy. Urol Int. 2018;100(3):368–74. https://doi.org/10.1159/000443700.
53. Corwin MT, Lamba R, Wilson M, McGahan JP. Renal cell carcinoma metastases to the pancreas: value of arterial phase imaging at MDCT. Acta Radiol. 2013;54(3):349–54. https://doi.org/10.1258/ar.2012.120693.
54. Nishino M, Jagannathan JP, Ramaiya NH, Van den Abbeele AD. Revised RECIST guideline version 1.1: what oncologists want to know and what radiologists need to know. AJR Am J Roentgenol. 2010;195(2):281–9. https://doi.org/10.2214/AJR.09.4110.
55. Smith AD, Shah SN, Rini BI, Lieber ML, Remer EM. Morphology, attenuation, size, and structure (MASS) criteria: assessing response and predicting clinical outcome in metastatic renal cell carcinoma on antiangiogenic targeted therapy. AJR Am J Roentgenol. 2010;194(6):1470–8. https://doi.org/10.2214/AJR.09.3456.
56. Thian Y, Gutzeit A, Koh DM, Fisher R, Lote H, Larkin J, et al. Revised Choi imaging criteria correlate with clinical outcomes in patients with metastatic renal cell carcinoma treated with sunitinib. Radiology. 2014;273(2):452–61. https://doi.org/10.1148/radiol.14132702.
57. Seymour L, Bogaerts J, Perrone A, Ford R, Schwartz LH, Mandrekar S, et al. iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics. Lancet Oncol. 2017;18(3):e143–e52. https://doi.org/10.1016/S1470-2045(17)30074-8.