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Review

Contemporary update on imaging of cystic renal masses with histopathological correlation and emphasis on patient management

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This article presents an updated review of cystic renal mass imaging. Most cystic renal masses encountered incidentally are benign and can be diagnosed confidently on imaging and require no follow-up. Hyperattenuating masses discovered at unenhanced or single-phase enhanced computed tomography (CT) measuring between 20–70 HU are indeterminate and can be further investigated first by using ultrasound and, then with multi-phase CT or magnetic resonance imaging (MRI); as the majority represent haemorrhagic/proteinaceous cysts (HPCs). Dual-energy CT may improve differentiation between HPCs and masses by suppressing unwanted pseudo-enhancement observed with conventional CT. HPCs can be diagnosed confidently when measuring >70 HU at unenhanced CT or showing markedly increased signal on T1-weighted imaging. Although the Bosniak criteria remains the reference standard for diagnosis and classification of cystic renal masses, histopathological classification and current management has evolved: multilocular cystic renal cell carcinoma (RCC) has been reclassified as a cystic renal neoplasm of low malignant potential, few Bosniak 2F cystic masses progress radiologically during follow-up; RCC with predominantly cystic components are less aggressive than solid RCC; and Bosniak III cystic masses behave non-aggressively. These advances have led to an increase in non-radical management or surveillance of cystic renal masses including Bosniak 3 lesions. Tubulocystic RCC is a newly described entity with distinct imaging characteristics, resembling a pancreatic serous microcystadenoma. Other benign cystic masses including: mixed epithelial stromal tumours (MEST) are now considered in the spectrum of cystic nephroma and angiomyolipoma (AML) with epithelial cysts (AMLEC) resemble a fat-poor AML with cystic components.

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Introduction

It has been over 30 years since the cystic renal mass classification system proposed by Morton Bosniak was published,[1] yet the Bosniak criteria have stood the test of time as radiologists and urologists still primarily rely on these guidelines for cystic renal mass evaluation in clinical practice. The Bosniak Criteria (Table 1) represent a scale of increasing probability of cancer at histopathological analysis based upon imaging features.[1,2] Although the reported rates of expected malignancy in the various Bosniak criteria lesions vary slightly, a recent meta-analysis on the topic revealed that the likelihood of cancer at histopathological analysis of a cystic renal mass that is category 2F or below is low; whereas, a cancer diagnosis in a category 3 or above mass is high.[3] Nevertheless, the present understanding of cystic renal masses has evolved since the time of the original, and subsequently updated, Bosniak criteria were published; for example, multilocular cystic renal cell carcinoma (RCC) has been reclassified in the updated World Health Organization (WHO) classification of renal tumours as a cystic renal neoplasm of low malignant potential,[4] only approximately 10% of Bosniak 2F cystic masses have been shown to progress radiologically during follow-up in well-designed cohort studies[5] and only approximately 10% of 2F lesions will be malignant at histopathology[3]; RCC with predominantly cystic components are less aggressive than solid RCC[6–8]; and Bosniak III cystic masses behave non-aggressively.[9,10] These changes have led to an increase in non-radical management or surveillance of cystic renal masses, which would previously have been treated with partial or radical nephrectomy. Moreover, recent updates to cystic renal mass WHO classification may be unfamiliar to radiologists including: reclassification of mixed epithelial stromal tumours (MEST) within the spectrum of cystic nephroma; description of angiomyolipomas (AMLs) with epithelial cysts (AMLEC); and introduction of tubulocystic RCC (which has recently described distinct radiological appearances).[11–13] Advances in imaging techniques (e.g., dual-energy computed tomography [CT], contrast-enhanced ultrasound [CEUS]) and studies evaluating interpretation of imaging findings and technical factors in cystic masses (e.g., improved classification of haemorrhagic/proteinaceous cysts [HPCs]) have enhanced our ability to diagnose and classify renal cystic masses more efficiently. These important radiological, histopathological, and clinical advances should be incorporated into clinical practice to reduce unnecessary follow-up examinations and optimise treatment. The purpose of this review is to present an update regarding imaging of cystic renal masses with an emphasis on management decisions.

Technique

CT (including dual-energy CT)

CT remains the first-line imaging test at most institutions and according to the American College of Radiology for the evaluation of indeterminate renal masses[14] and, it should be emphasised that the Bosniak criteria were first described and are intended for use primarily with CT.[1] The details of a dedicated renal mass protocol multi-phase CT have been described elsewhere,[15,16] but briefly should include unenhanced, corticomedullary, and nephrographic phase enhanced CT images performed using the same peak voltage to enable accurate comparison of attenuation values (measured in Hounsfield units) between phases.[16]

At unenhanced CT, a homogeneous, well-circumscribed mass with a smooth and imperceptible wall measuring between −10 and 20 HU can be diagnosed confidently as a simple cyst (Bosniak 1) requiring no further follow-up imaging.[2,17] RCC, mainly clear cell subtype, can also measure in the −10 to 20 HU range[18] and caution should be taken to ensure that a low-attenuation renal mass fulfils the other subjective imaging criteria before a diagnosis of a simple cyst is made. Low-attenuation RCCs at unenhanced CT are usually heterogeneous and may show areas of increased attenuation when smaller region of interest (ROI) measurements are performed.[18] When a cyst shows fine septal or wall calcifications, it is considered minimally complicated but benign and not requiring any follow-up (Bosniak 2).[2] Coarse, nodular, or inhomogeneous calcifications should be considered separately and may require further characterisation with multiphase CT or magnetic resonance imaging (MRI). A homogeneously hyperattenuating renal lesion measuring >70 HU can be confidently diagnosed as a benign HPC and is characterised as a Bosniak 2 lesion,[2,15] requiring no further imaging follow-up. Although Bosniak initially considered hyperattenuating lesions measuring >3 cm separately, if homogeneous and measuring >70 HU, a diagnosis of HPC can probably still be made even when the mass measures >3 cm in size, as in the study by Jonisch *et al.*, HPCs were diagnosed using these criteria measuring up to 6.1 cm.[19]

After administration of contrast medium, a cyst showing a few thin (<1 mm) enhancing septa should still be

Table 1
Bosniak classification of renal cysts.

Bosniak 1	Simple cyst with water attenuation and pencil thin wall. No soft tissue, septa, or calcifications. No enhancement
Bosniak 2	Benign simple cyst with pencil thin septa with perceived, but not measurable, enhancement. Thin calcifications or short segments of thick calcifications may be present. Uniform high attenuation lesions with no enhancement and <3 cm in size
Bosniak 2F	Cysts with multiple thin septa or minimal smooth wall thickening. Thick and nodular calcifications may be present. Again perceived enhancement of the wall and/or may be seen, but there must not be any measurable enhancement or soft tissue. This category also includes totally intrarenal high-attenuation lesions >3 cm in size with no enhancement
Bosniak 3	Complex cysts with thickened wall and/or septa with measurable enhancement. The thickening can be smooth or irregular
Bosniak 4	Clearly malignant cystic masses that can have all of the criteria in category 3, but also contain distinct soft-tissue component separate from the wall or septa

considered benign (Bosniak 2).[1,2,15] Septa may also be seen at unenhanced CT, but are generally better depicted after they enhance. An increased number or minimally thickened septa with perceived, but non-measurable, enhancement in a cyst are categorised as Bosniak Type 2F cystic lesions.[2,5,15] Only when a cyst shows thick and nodular septa or walls with measurable enhancement, should it be considered a Bosniak 3 lesion,[2,5,15] which portends a higher risk (approximately 50%) of a malignant diagnosis at histopathology.[3] A Bosniak 4 cystic lesion is effectively a cystic or necrotic mass that is easily differentiated from the other categories and should be considered malignant until proven otherwise.[1–3,15] Effectively then, the Bosniak criteria differentiates between potentially malignant and malignant cystic masses by the presence of measurable (not simply perceived) thick nodular enhancing internal areas.

Dual-energy CT (DECT) is becoming more prevalent in the clinical evaluation of renal masses.[20,21] Advantages of DECT compared to conventional CT are: better correction of beam-hardening effects[22] and the ability to extract iodine overlay images with quantitative iodine concentration values to determine the presence or absence of enhancement.[23] Pseudo-enhancement is the artificial increase in attenuation of a cyst on enhanced CT due to inadequate correction of beam-hardening effects[24] and occurs more commonly in smaller cysts, which are endophytic in location.[25] To differentiate true enhancement from pseudo-enhancement, MRI is generally required or follow-up CT is performed.[16,25] With DECT, unwanted effects from pseudo-enhancement are potentially mitigated by better correction of beam hardening and the absence of iodine within a cyst can be confirmed by analysing virtual monochromatic image sets at optimal energy and iodine overlay images either quantitatively or subjectively[16,22] (Fig 1). Nevertheless, further investigation is required to validate DECT for diagnosis of benign cysts that show pseudo-enhancement from low enhancing homogeneous renal masses due to potential overlap in attenuation values and iodine concentration values. To our knowledge, DECT has not been evaluated specifically in complex cystic renal masses; however, in our experience may have several advantages compared to conventional CT and MRI. For suspected HPCs that are >3 cm or are mostly intrarenal (where enhancement cannot be accurately assessed with conventional CT and internal contents difficult to evaluate because of increased attenuation), a Bosniak 2F category should be typically assigned.[2] For these lesions, gadolinium-enhanced subtraction MRI images can confirm the absence of enhancement and a diagnosis of HPC, downgrading the Bosniak category to 2.[15,25] DECT may offer similar diagnostic information as the iodine overlay image reveals iodine-containing internal contents and minimises the effects of pseudo-enhancement (Fig 1). A limitation of DECT, and a previously described imaging pitfall, occurs in HPC where haemorrhagic or proteinaceous contents result in increased signal on iodine overlay images. This pitfall can be avoided by comparing the iodine overlay image to the true unenhanced CT image, which shows the baseline increased attenuation value.[26] Another theoretical advantage of DECT is sub-second acquisition speed compared to the longer breath-holds required for MRI, which may result in better image quality when a patient is not able to suspend respiration adequately to obtain high-quality pre- and post-gadolinium subtraction images (Fig 2). In summary, DECT is an exciting advance in the CT evaluation of renal masses; however, it still requires acquisition of a conventional unenhanced CT phase (to reliably compare pre- and post-contrast attenuation values) and requires further validation of iodine concentration values, which may differentiate benign cysts from solid masses.

Ultrasound (including CEUS)

Ultrasound is an attractive imaging method for the assessment of cystic renal masses, particularly Bosniak Type 2F lesions, due to low cost, increased accessibility, and that because the modality is non-ionising. Although the Bosniak criteria have been applied successively to some extent using ultrasound[27,28] important limitations should be acknowledged, and Bosniak himself, in a commentary published in

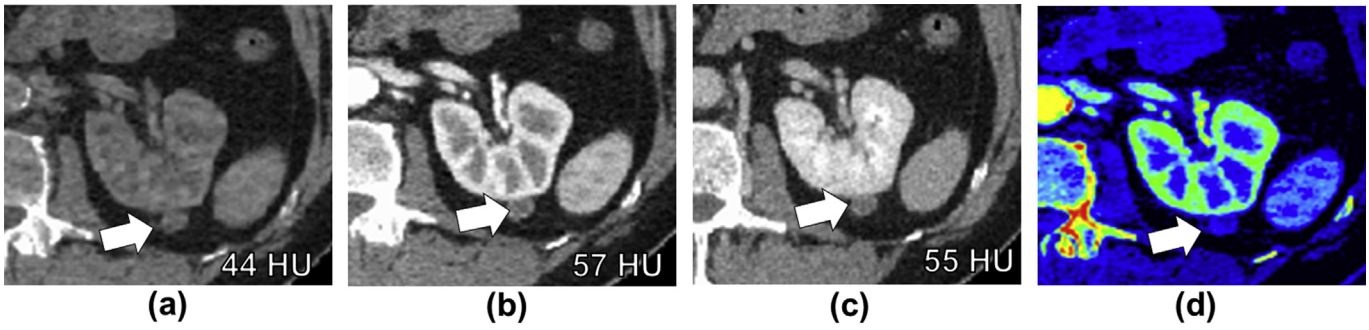

Figure 1 A 41-year-old woman with incidentally detected indeterminate small left renal mass on enhanced CT performed to assess for causes of abdominal pain. A DECT protocol for renal mass assessment was performed to further characterise. (a) Axial virtual unenhanced and enhanced CT images during the (b) corticomedullary and (c) nephrographic phases of enhancement depict the nodule (white arrows), which shows an increase in attenuation in the indeterminate range (between 10–20 HU difference). The nodule could be a hypo-enhancing papillary RCC or hyperattenuating cyst. (d) Colour iodine map image shows the absence of iodine within the nodule (arrow), which quantitatively measured below the previously described 2 mg/cm^3 threshold for enhancement at rapid peak voltage switching DECT. The imaging findings are compatible with a hyperattenuating cyst, which was later confirmed on ultrasound (not shown).

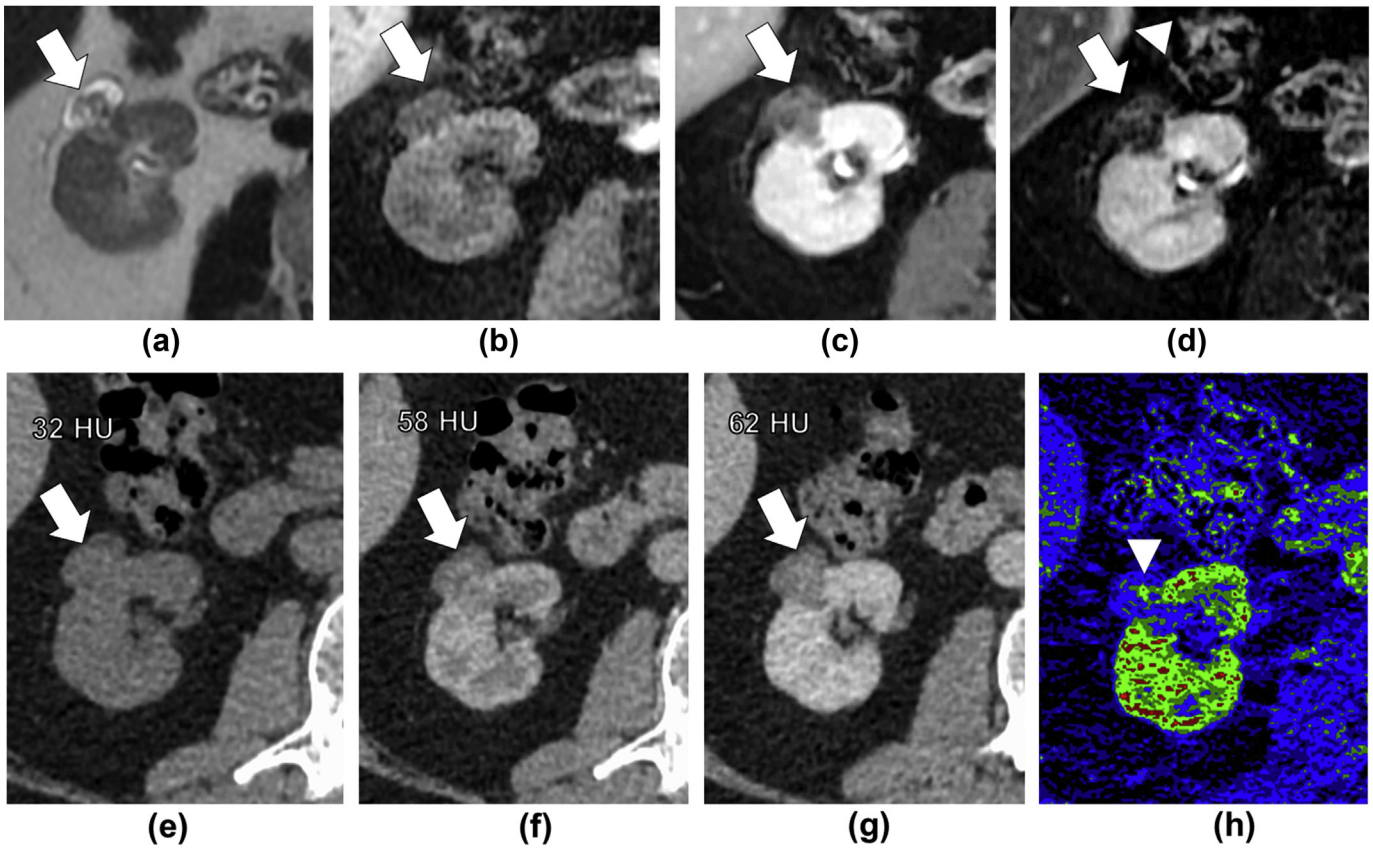

Figure 2 A 47-year-old woman with incidentally detected complex cystic right renal mass on ultrasound performed for left upper quadrant pain. MRI was performed to further characterise. (a) Axial T2-weighted single-shot fast spin echo (ssFSE) image shows a complex cystic mass in the right kidney (white arrow). Axial T1-weighted fat-suppressed images before (b) and after (c) gadolinium injection during the nephrographic phase of enhancement are degraded by motion artefacts. (d) The subtraction image was also degraded by motion (edge [ringing]) artefacts at the liver edge (arrowhead) and enhancement was deemed indeterminate. Follow-up CT was suggested. DECT was performed showing definite internal enhancement of the thick septa comparing pre-contrast axial (e), corticomedullary (f), and nephrographic (g) phase images (attenuation change >20 HU). (h) Colour iodine overlay image shows definite enhancement of septal components (arrowhead) to a better extent than both conventional CT images and MRI. A Bosniak Type III cyst was diagnosed confidently with CT.

2012, suggested that the criteria could not be readily applied using ultrasound.[29] The main disadvantages of ultrasound, aside from limitations in image quality related to patient size, compared to CT and MRI, are an inability to reliably demonstrate enhancement of internal septa using colour or power Doppler techniques compared to intravenous contrast media, and that cysts may appear more complex on grey-scale ultrasound (for example, show internal low-level echoes or fine septa) compared to CT, which may result in an increase in Bosniak categorisation[30] (Fig 3). Despite these limitations, ultrasound is useful for the initial characterisation of hyperattenuating renal lesions detected on unenhanced CT or single-phase conventional CT examinations. In a recent study by Mahadevaswamy *et al.*, ultrasound was used to confidently diagnose HPC among indeterminate hyperattenuating lesions detected on CT in the majority of cases with an extremely low false-positive risk (Fig 4).[31] Although ultrasound did upgrade a proportion of HPCs, which were eventually classified correctly on multi-phase CT or MRI examinations in that study, it remains useful as an intermediate step to multi-phase CT or MRI because it can potentially reduce the number of costly follow-up examinations in many lesions. When using DECT, discussed above, indeterminate hyperattenuating lesions encountered on single-phase enhanced CT may be further characterised using iodine overlay images and quantitative iodine concentration.[16,32] Through the use of CEUS, more lesions that would otherwise be indeterminate or incorrectly classified using conventional grey-scale and colour/power Doppler techniques can be accurately diagnosed.[28] CEUS remains limited by patient body habitus, operator experience, and has yet to gain widespread acceptance for use in renal imaging, so requires further study.

MRI

MRI offers several advantages over CT for the evaluation of cystic renal masses. MRI provides higher contrast resolution than CT, is able to better evaluate the internal contents and enhancement of hyperattenuating lesions, and is non-ionising and so well suited for surveillance in patients who require repeat examinations.[33] Disadvantages of MRI primarily relate to cost, limited accessibility, and poor

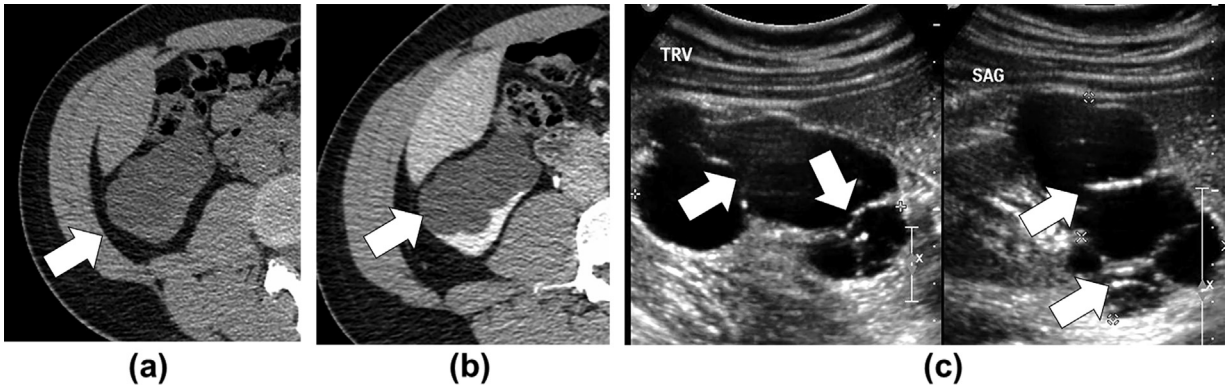

Figure 3 A 46-year-old man with incidentally detected complex renal cyst on ultrasound. CT was performed for further characterisation. (a) Unenhanced and (b) contrast-enhanced axial CT images show a water attenuation lesion in the lower pole of the right kidney (arrows) without any solid component, septa, or measurable enhancement. This lesion was classified as a Bosniak I cyst. (c) Transverse and sagittal grey-scale ultrasound images retrieved from the patient's electronic file revealed multiple complex thick septa (arrow), which were not perceptible on CT. In this example, ultrasound upgrades the Bosniak category compared to CT from Bosniak 1 to 2F or 3.

image quality in patients who are not able to suspend their respiration or in patients who perform inconsistent breath-holds limiting image quality in pre- and post-gadolinium enhanced subtraction images due to poor registration. Fears over nephrogenic systemic fibrosis when gadolinium is used in patients with compromised renal function have largely been tempered when gadolinium does not exceeding standard dosing and newer linear or macrocyclic agents are used.[34] Performing breath-holding in the end expiratory phase improves registration of pre- and post-gadolinium enhanced images[35]; however, the expiratory phase of respiration is shorter than the inspiratory phase, which means a patient is more likely to breathe during the expiratory phase compared to inspiratory phase potentially creating increased motion artefacts. Breath-hold imaging acquisition times can be shortened through the use of parallel imaging techniques (without the traditional loss of spatial resolution obtained through decreasing phase encoding or section thickness). Scan time decreases directly proportional to r (the parallel imaging or acceleration factor) and although signal-to-noise ratio (SNR) decrease proportional to $\sqrt{r}$, there is typically no compromise in image quality due to the higher signal afforded through gadolinium enhancement.[35] Breath-hold acquisition times of $<$10 seconds are now commonly available through most of the MRI vendors when parallel imaging is optimised. High-quality free-breathing post-gadolinium enhanced MRI images can also currently be acquired on most commercial MRI systems through the use of navigator sequences or radial sampling schemes. In our own experience, free-breathing gadolinium-enhanced subtraction imaging can be performed and represents an alternative in patients who are not able to adequately breath-hold.[36] The use of 3 T MRI is particularly advantageous when parallel imaging is employed (due to higher baseline SNR); however, caution should be exercised when comparing cystic masses on follow-up at 1.5 and 3 T as a study by Rosenkrantz *et al.* demonstrated a tendency for readers to upgrade cyst

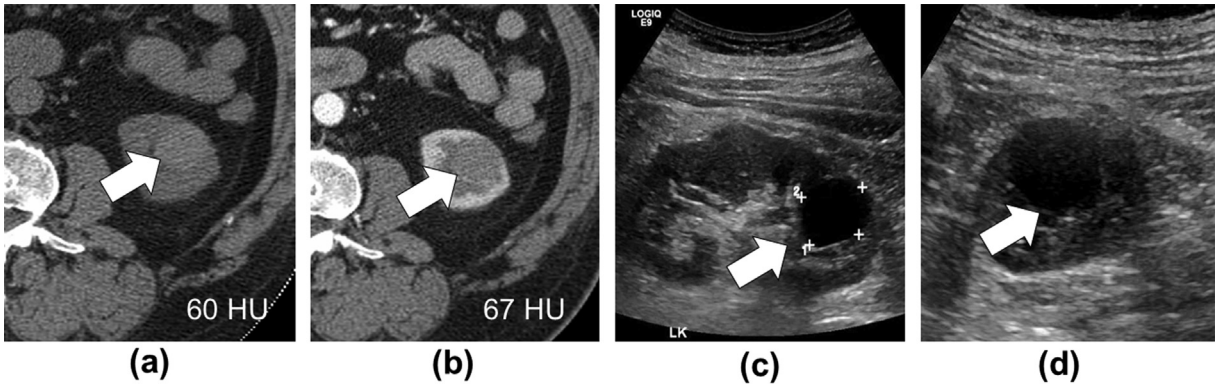

Figure 4 A 76-year-old woman with incidentally detected right renal mass on unenhanced CT performed for renal colic. (a) Axial unenhanced CT image shows a homogeneously hyperattenuating nodule with an attenuation value of 60 HU. A dedicated renal protocol CT was suggested to further characterise. (b) Axial contrast-enhanced CT image obtained during the nephrographic phase shows no enhancement (increase to 67 HU). (c) Sagittal and (d) transverse grey-scale ultrasound images performed prior to CT, but not reviewed at the time of the CT recommendation or protocolling, confirm the hyperattenuating nodule as an anechoic simple cyst with an imperceptible wall and increased through transmission features, which are diagnostic of a Bosniak type I cyst requiring no further management or imaging follow-up (white arrows).

complexity at 3 T and suggested that follow-up of renal cysts be performed at similar field strength.[37]

The Bosniak criteria have been validated for use on MRI; however, it is acknowledged that MRI will show more septa and internal complexity of cysts compared to CT,[29,33] which can result in an upward migration of the Bosniak category for a particular lesion (Fig 5). MRI can better diagnose HPC compared to CT, and this was traditionally through the use of gadolinium-enhanced subtraction images; however, more recently it has been described that a homogeneously markedly T1-weighted hyperintense renal mass is most likely a HPC and may not necessarily require gadolinium administration to confirm diagnosis.[38,39] Diffusion-weighted imaging (DWI) has been applied successively in renal masses; however, its usefulness in cystic masses is not established and a well-known pitfall of DWI is that benign HPC may show restricted diffusion.[16]

Benign or low malignant potential cystic masses

Simple (Bosniak 1) and minimally complex (Bosniak 2) cysts are almost always benign with a pooled rate of malignancy of much less than 10%[3] and accordingly do not require any further management including no further radiological follow-up. Simple non-neoplastic renal cysts are commonly encountered in the adult kidney and are characterised pathologically by a single layer of cuboidal, flattened or atrophied epithelial cells which may have thickened walls and septae.[4] A diagnosis of simple and minimally complex (Bosniak 1 and 2) cysts can be made reliably with US, CT and MRI, as discussed above. The majority of Bosniak 2F and approximately half of Bosniak 3 cystic masses will be proven to be benign after resection.[3] In addition to complex cysts with chronic hemorrhage and inflammatory changes, distinct benign cystic masses are described in the WHO classification of renal tumours. The following section describes the most commonly encountered benign cystic masses at histopathology and imaging and their current WHO classification. In addition to benign cystic masses, two distinct cystic masses, multilocular cystic renal neoplasm of low malignant potential and tubulocystic RCC, which have excellent prognosis with no or rare cases of local recurrence or metastatic disease[40,41] are included in this section. A diagnosis which is not included in the WHO classification of renal tumours but which occasionally simulates a complex cystic mass on imaging is localised cystic disease of the kidney. In this condition, multiple cysts (resembling autosomal dominant polycystic kidney disease at histopathology) involve a segment of or even an entire kidney but without (or to a much lesser extent) involvement of the contralateral kidney. The imaging differentiation of localised cystic disease of the kidney from a complex cystic renal mass is made by noting the absence of a well defined surrounding capsule.[42]

Cystic nephroma and MEST (Figs 6 and 7)

Cystic nephroma, also referred to as multilocular cystic nephroma, is a rare benign tumour with bimodal age and sex distribution. It occurs in boys <5 years of age and in perimenopausal women.[43] The presenting symptoms vary with age. Children present with an enlarging flank mass, while adults are usually asymptomatic or present with abdominal pain or urinary tract infection.[44] Grossly, these tumours are usually large, solitary, and consist of multiple fluid filled non-communicating cysts surrounded by a thick capsule. Microscopically, these cysts are lined by flat or cuboidal cells separated by fibrous septa, and may have an ovarian stroma-like appearance.[45] On imaging, cystic nephroma appear as a lobulate multicystic mass with enhancing septa.[46] Contents of the mass have described to have a higher attenuation at CT and higher T1-weighted signal intensity compared to simple fluid. The septa and the capsule demonstrate low signal on T2-weighted imaging due to presence of fibrotic elements.[47] Herniation of the mass into the renal pelvis is a characteristic, but not specific, imaging finding.[48] There may be significant mass effect and obstruction on the ureter and the renal collecting system. No risk of malignant transformation has been reported. Childhood cystic nephroma must be

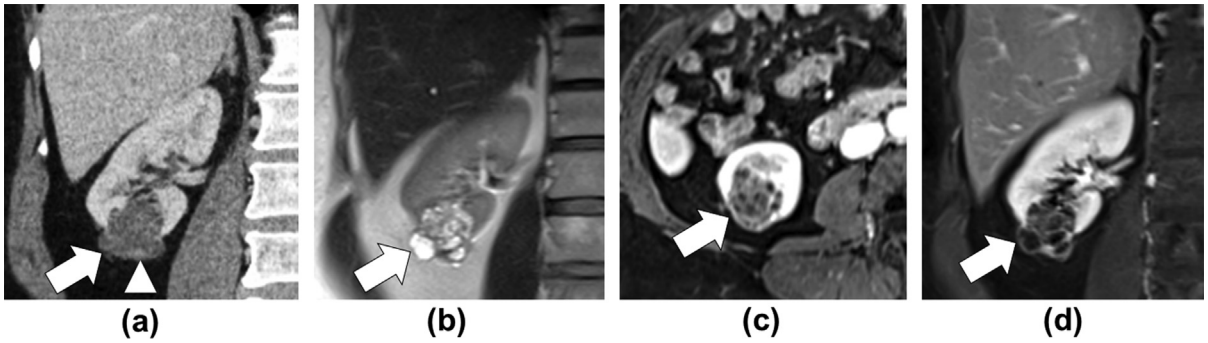

Figure 5 A 54-year-old woman with right lower pole cystic mass detected incidentally on CT. (a) Coronal enhanced CT image shows irregular cystic lesion in the lower pole of the right kidney (arrow) with a single, thin enhancing septa (arrowhead). The lesion was characterised as a Bosniak 2F cyst on CT. MRI was performed during next follow-up. (b) Coronal T2-weighted ssFSE, (c) axial, and (d) coronal T1-weighted post-gadolinium-enhanced images reveal substantially more numerous and thicker septa, some with measurable and nodular enhancement (arrows). In this instance, MRI upgrades the Bosniak category from Bosniak 2F to Bosniak 3.

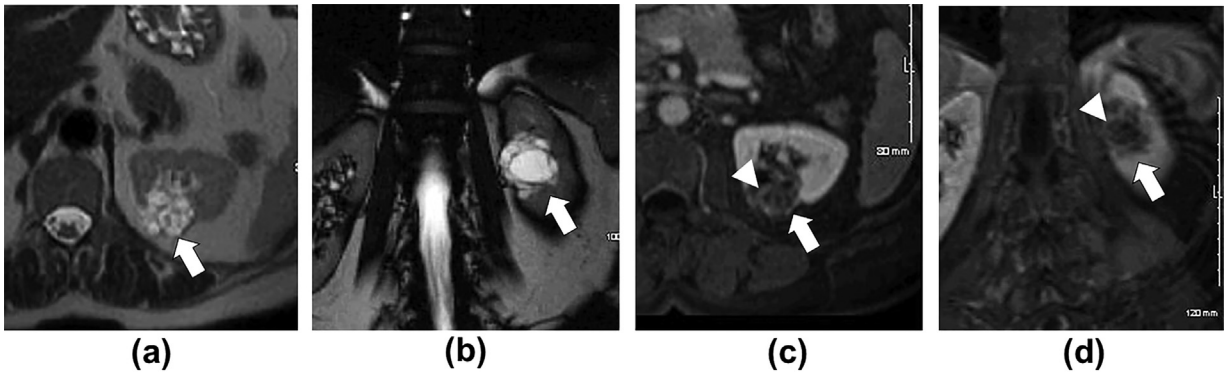

Figure 6 A 60-year-old female patient with cystic nephroma. (a) Axial and (b) coronal FS T2-weighted images show a predominantly cystic mass in the interpolar region of the left kidney (arrows). The mass shows several thin internal septa (arrowheads) on the (c) axial and (d) coronal T1-weighted FS gadolinium-enhanced images. The mass was characterised as a Bosniak Type 3 cyst. Diagnosis of cystic nephroma was confirmed after total nephrectomy.

differentiated from a necrotic Wilm's tumour and the presence of any solid component essentially excludes a cystic nephroma.

MEST is a recently described entity with <100 cases reported in literature. MEST occur most commonly in perimenopausal women[49] on exogenous hormones. Pathologically MEST is characterised by cystic and solid growth of benign mesenchymal and epithelial elements in an ovarian type stroma.[49] Cystic nephroma and MEST are considered lesions in the same spectrum with cystic nephroma containing greater proportion of fluid and MEST containing a greater proportion of ovarian stromal tissue.[13] Typical imaging appearance is a complex multiloculate Bosniak 3 or 4 cyst herniating into the renal hilum with variable proportion of cystic and solid elements.[50] Enhancing septa, mural nodules, and calcifications may be present. Delayed contrast enhancement has been reported. MEST does not recur or metastasise after treatment.[43]

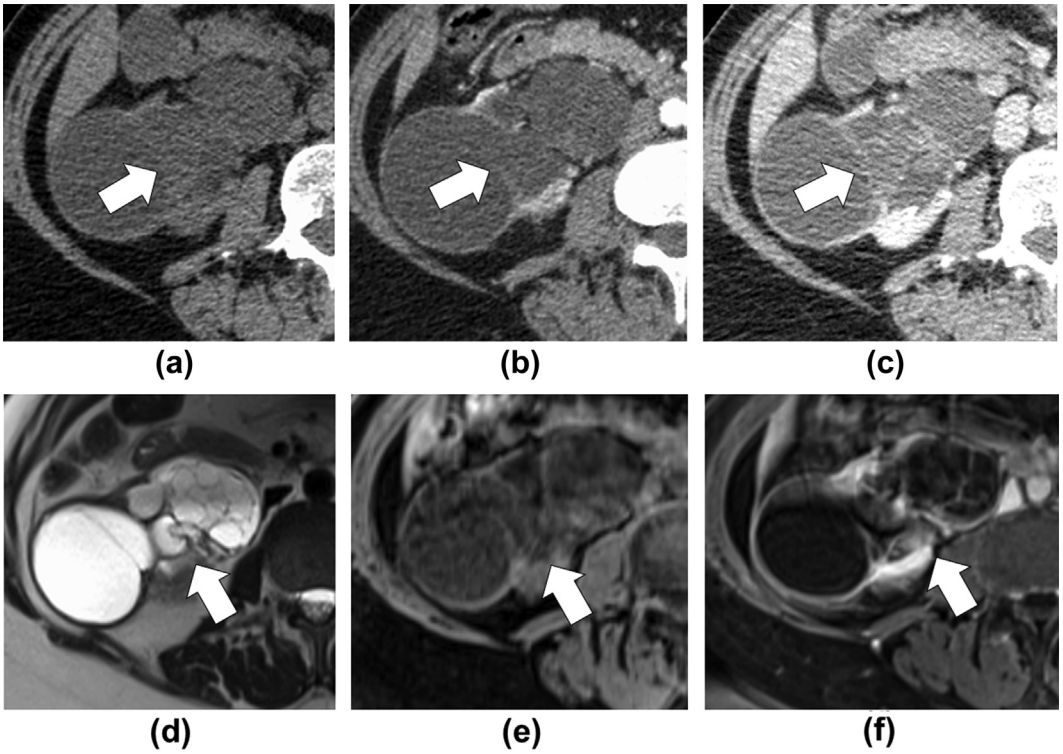

Figure 7 A 63-year-old woman with incidentally detected complex cystic right renal mass on ultrasound. Renal mass protocol CT was performed. (a) Axial unenhanced, (b) corticomedullary phase, and (c) nephrographic phase CT images show a complex renal mass with thick solid septa progressively enhancing components (white arrows). MRI was also performed in the same patient. (d) Axial T2-weighted ssFSE image shows a complex cystic mass in the right kidney (white arrow). Axial T1-weighted FS images before (e) and after (f) gadolinium injection shows septal and solid internal enhancement (arrows). A total nephrectomy was performed and final diagnosis was compatible with MEST.

AMLEC

AMLEC is a more recently described variant of fat-poor AML that mimics a cystic RCC.[51] AMLEC are very rare and only a handful of cases have been reported since their initial description by Fine *et al.* in 2006.[52,53] These lesions are benign and are more common in women.

AMLs are commonly solid lesions and can be classified into classic or fat-rich and fat-poor AMLs. AMLEC are a cystic subtype of fat-poor AML and contains little to no fat on histology. Histopathologically they are composed of cystic spaces lined by cuboidal or "hobnail" epithelium, a smooth muscle component that stains positive for muscle actin and desmin, and a subepithelial endometroid stroma that stains positive for oestrogen and progesterone receptors.[52,54] In addition, AMLEC may also express melanocytic markers such as HMB-45 and Melan-A.[54]

Imaging features have been described elsewhere[51,52,54]; usually AMLEC appear as a mixed solid–cystic tumour on CT and MRI. The solid components of the lesion are hyperattenuating on CT and have a low T2-weighted signal on MRI with homogeneous enhancement (similar to fat-poor AMLs).[53,55] AMLECs are very difficult to diagnose preoperatively and other renal cystic masses, including RCC, must be included in an imaging differential. An imaging diagnosis can be suspected when a solid–cystic mass shows hyperattenuating areas on unenhanced CT and corresponding low signal intensity on T2-weighted imaging with homogeneous enhancement.[55]

Multilocular cystic renal neoplasm of low malignant potential (Fig 8)

This tumour is a rare low-grade multicystic renal neoplasm with an excellent prognosis.[56] Some authors consider it to be a distinct subtype of clear-cell RCC. The tumour is most commonly seen in middle-aged adults with a mean age of 46 years.[57] Previously called "benign behaving multilocular cystic renal cell carcinoma", the terminology has been revised in the new WHO[11] to multilocular cystic renal neoplasm of low malignant potential. The tumour is nearly entirely cystic. Grossly the tumour is composed of multiple variable-sized cysts filled with clear or serous fluid. Microscopically, the septa are lined by single or groups of clear cells without any expansile component.[40] Some of these tumours may show vascularised septa. These tumours must be differentiated from clear-cell RCCs with cystic degeneration. RCCs with cystic degeneration are more aggressive with a poorer prognosis and often show haemorrhage or necrosis and solid areas of expansile clear cells. Presence of any expansile nodules of clear cells within the septa at histology excludes the diagnosis of multilocular cystic renal neoplasm of low malignant potential.

The reported imaging features are highly variable and can range in appearance from a Bosniak category 2 to Bosniak category 4 lesions.[58,59] There are no classical imaging features to differentiate these tumours from RCC or other multilocular cystic renal neoplasms including cystic nephromas. Hence, a preoperative diagnosis is not possible and these lesions are commonly resected. Post-resection, these tumours almost never recur or metastasize.[40] In the largest series of 76 cases reported to date,[57] none of the lesions demonstrated recurrence or metastatic disease.

Tubulocystic RCC (Fig 9)

Tubulocystic carcinomas are a group of recently described low-grade variants of collecting duct carcinomas[56] and are also termed as low-grade collecting duct carcinomas and Bellini duct carcinomas. These tumours were not included in the WHO classification of renal tumours (2004)[60] as the first case was described in 2005.[61] They are extremely rare and <70 cases have been reported in literature.[56] There is a very strong male predominance with a male: female ratio of 7:1.[62,63] In the series by Cornelis *et al.*, patients ranged in age from 26 to 76 years with a mean age of 56 years.[12] Coexistence with papillary RCC has been reported.[62]

Grossly, the tumours are usually greyish white solid–cystic masses with very small cystic spaces giving a "bubble-wrap" appearance.[64] The tumours are surrounded by a rim of fibrous tissue. Microscopically, they consist of closely packed tubules and cysts lined by cuboidal epithelium and separated by fibrous stroma.[41,62] There is absent to minimal haemorrhage, necrosis, desmoplasia, or tissue invasion.

The imaging features are not well known; however, they may be diagnostic and are similar in appearance to the microcystic serous cystadenoma of the pancreas except for their location in the kidney. Due to multicystic nature, they appear solid and hyperechoic on ultrasound with some tumours showing posterior acoustic enhancement.[12] On CT, they have been variably described as both cystic and solid,[12,64] and these tumours are usually hypovascular; however, about half of tumours did not demonstrate any significant enhancement on post-contrast imaging. MRI is very useful to demonstrate the micro-cystic nature of these tumours due to its superior contrast resolution.[12] These tumours have a favourable prognosis and are rarely associated with distant metastases or recurrence.[41]

Malignant cystic masses

Bosniak 4 cystic masses are effectively malignant RCC until proven otherwise and just over half of Bosniak 3 cysts are also malignant after surgical resection.[3] A commonly misused or misunderstood radiological term is that of a "cystic RCC", which has no pathological correlation in the WHO classification of renal tumours. In our opinion, a better term, which is more representative of histological findings and classification, would be "RCC with cystic changes". All of the conventional subtypes of RCC (e.g., clear cell, papillary, and chromophobe) may show cystic change; however, cystic changes are most commonly observed in clear cell tumours. Pathologists may report extensive cystic changes in an RCC; however, they are not obligated to do so and the diagnosis of cystic changes is often inferred from preoperative CT or MRI. Pathologists do report the presence of necrosis, which is an adverse histological feature in RCC,[65] and

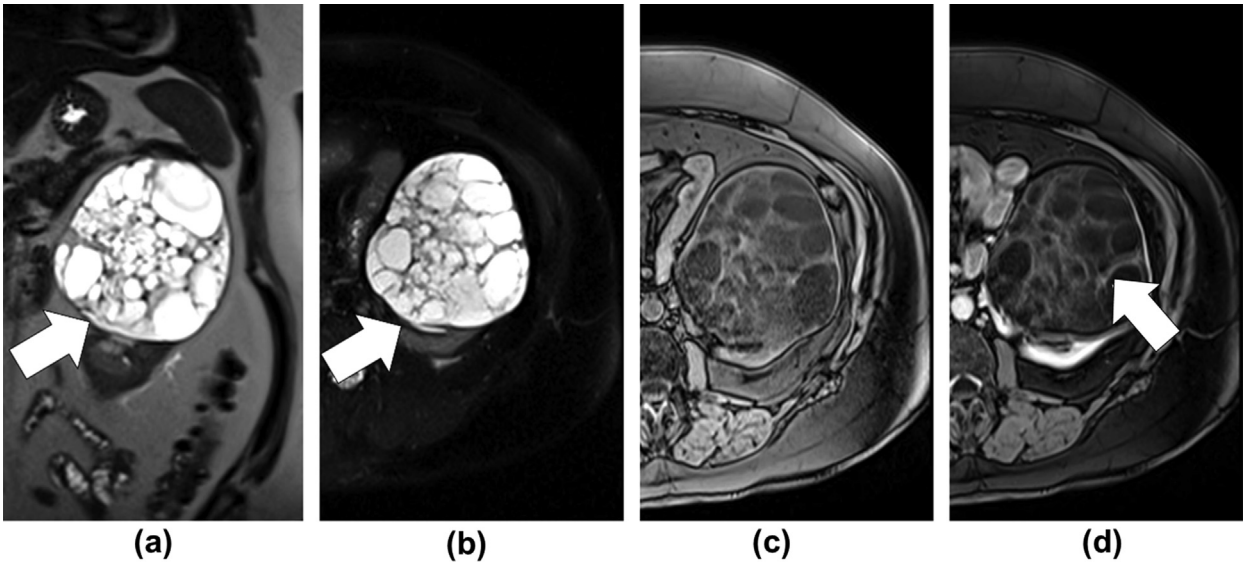

Figure 8 A 59-year-old female imaged with MRI to evaluate fullness in her left flank. (a) Coronal and (b) axial T2-weighted ssFSE images without and with FS demonstrate a large multiloculate cystic mass in the interpolar region of the left kidney (white arrows) with internal variably thick septa. (c) Axial unenhanced and (d) post-gadolinium-enhanced T1weighted FS images show enhancement within the septa (arrow). The mass was characterised as Bosniak 3 cystic lesion and total nephrectomy was performed. Final diagnosis of "cystic renal neoplasm of low malignant potential" was confirmed at histopathology.

it may be very difficult (if not impossible) to differentiate necrosis from cystic changes on imaging (Fig 10).[58]

RCCs with a majority of intratumoural cystic spaces account for <5% of all RCCs. These are characterised by a tumour composed of numerous cysts, the septa of which contain groups of cells that are indistinguishable from solid RCC. The patients with these tumours tend to be younger, female patients who present with lower-stage disease and lower histopathology grade.[66] Patients with RCCs showing cystic changes on imaging without necrosis at histopathology have a better long-term prognosis when compared to solid RCC[66]; which has been speculated to be related to a lower amount of tumour within the mass. In the study by Winters *et al.*, using the Surveillance, Epidemiology and End Results (SEER) population-based database, RCC with cystic changes had lower rates of local recurrence and metastases compared to solid tumours.[66] Other authors have also demonstrated better long-term prognosis with lower rates of local recurrence and metastatic disease in RCC, which are cystic compared to reported rates of solid RCC with similar histological subtype.[10,67,68] As the reported rate of malignancy in Bosniak 2F cystic masses is low (approximately 10%),[3] just under half of Bosniak 3 cystic masses are benign[3] and the remaining masses may have a favourable long-term outcome with lower rates of metastases and local recurrence, imaging surveillance rather than surgery is becoming an increasingly popular option in urological

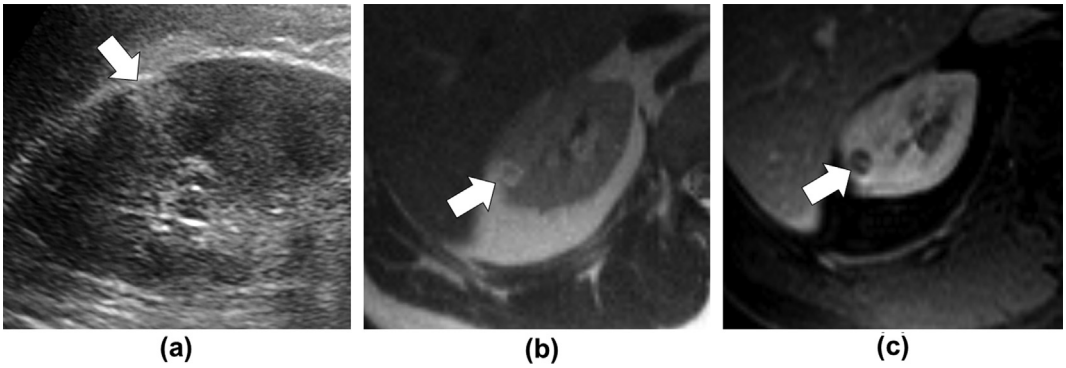

Figure 9 A 51-year-old man with an incidentally detected renal nodule on ultrasound. (a) Sagittal grey-scale ultrasound image shows that the nodule is homogeneously echogenic (arrow). MRI was performed for further characterisation. (b) Axial T2-weighted ssFSE and (c) axial T1-weighted FS post-gadolinium-enhanced images demonstrate a discordance between the ultrasound (where the mass appears solid) and MRI (where the true cystic nature of the mass is confirmed). The cystic lesion shows several faint thin internal enhancing septa. The imaging features are highly suggestive of a tubulocystic carcinoma, which resembles a serous microcystic pancreatic tumour. The lesion was biopsied and tubulocystic carcinoma was confirmed at histopathology.

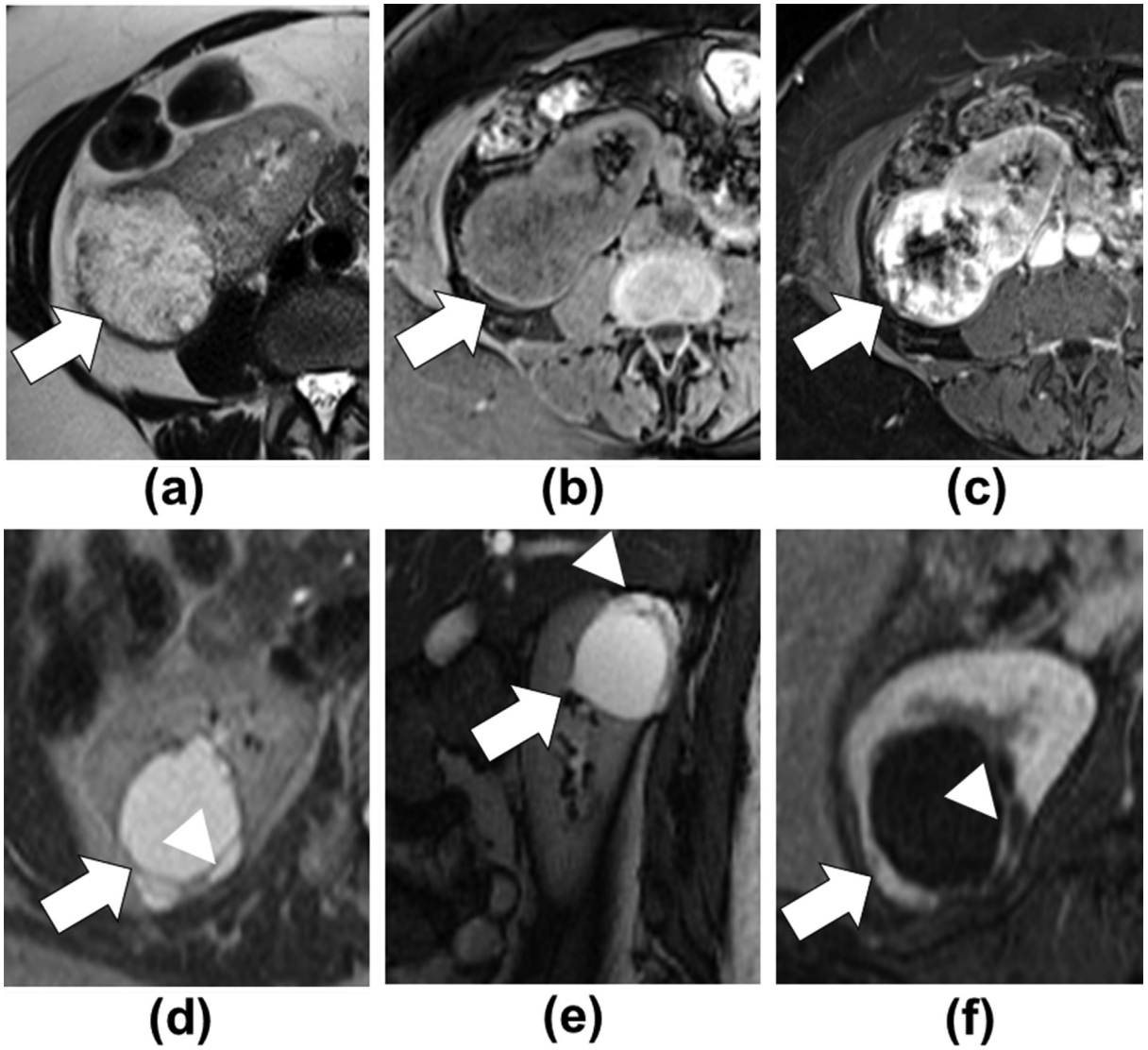

Figure 10 Top panel: A 50-year-old woman with a complex mass in the lower pole of right kidney. (a) Axial T2-weighted ssFSE, (b) axial unenhanced, and (c) post-gadolinium-enhanced T1-weighted FS images demonstrate an avidly enhancing renal mass with non-enhancing central components, which were reported prospectively as likely representing central necrosis (arrows). This mass was resected and a diagnosis of clear-cell RCC with necrosis was confirmed at histopathology. Bottom panel: A 59-year-old man with right interpolar region cystic mass. (d) Axial T2-weighted ssFSE and (e) sagittal bSSFP images show a predominantly cystic mass in the interpolar region of the right kidney extending up to the renal hilum (arrows). The mass shows several variably thick internal septa (arrowheads). Axial T1W FS gadolinium-enhanced image (f) shows enhancement in the septa. The mass was characterised as a Bosniak Type 3 cyst and was resected. Histopathology revealed a clear-cell RCC with extensive cystic changes. It is important to differentiate RCC with necrosis from RCC with cystic changes; however, differentiation may be difficult or indistinguishable using CT and MRI. The presence of necrosis is an aggressive feature and portends a worse prognosis compared to cystic changes.

practices,[7,10,69,70] particularly in older patients who are not fit for surgery or may require complete nephrectomy to appropriately manage the cystic mass.

Percutaneous biopsy of cystic renal masses has been described[71–73]; however, it is generally limited by the variable sampling of lower amounts of solid elements and potentially unreliable histological diagnosis. Routine use of biopsy in the evaluation of Bosniak 2F lesions is not recommended and in Bosniak 3 and 4 lesions is controversial.[73,74] Nevertheless, it may be of value in selected patients who are poor surgical candidates. Although thermal ablation and cryotherapy are accepted alternatives for management of Bosniak 3 and 4 cystic lesions in non-surgical candidates, they are not widely used.[75,76]

There is no established follow-up schedule in terms of timing or imaging methods for Bosniak 2F and Bosniak 3 cystic masses. In the original and revised Bosniak criteria, Bosniak 3 lesions are considered surgical lesions[1,2] and therefore, follow-up or surveillance is generally performed according to local or institutional urological practice. Although the present standard of care is surgery for Bosniak 3 cystic masses, there is an increasing body of evidence to support active surveillance instead of surgery in these lesions.[66,74,77,78] Follow-up every 6 months up to 2 years and

then yearly follow-up is considered appropriate.[74] An interval increased in size of the solid component to >3 cm and accelerated growth of lesion has been suggested as criteria for resection.[74] Some authors have even suggested that Bosniak 4 lesions with solid component <3 cm can be managed with active surveillance.[10]

Bosniak 2F lesions are generally followed yearly for signs of radiological progression to Bosniak 3 and the duration of imaging follow-up, although also subject to institutional variation and surgeon or patient preference, has been suggested to be 4 years in the study by Hindman *et al.*, which showed that approximately 10.9% (17 out of 156 lesions) of Bosniak 2F lesions progressed to malignancy (Bosniak 3 and Bosniak 4 categories) with time to progression between 6 months to 3.2 years.[5]

Conclusion

In conclusion, this article summarises recent developments regarding the imaging, histopathological classification, and most importantly, management of cystic renal masses. The Bosniak criteria remain the reference standard for imaging interpretation and classification of renal masses; however, important updates must be incorporated into clinical practice. Homogeneously hyperattenuating lesions detected at unenhanced CT measuring >70 HU can be confidently diagnosed as hyperattenuating cysts and other hyperattenuating lesions can be well classified using ultrasound first and DECT, not necessarily always requiring MRI for assessment. Both ultrasound and MRI may upgrade the Bosniak classification of a cystic mass due to improved depiction of internal complexity. Although Bosniak 3 cystic lesions are considered surgical, multilocular cystic RCC has now been reclassified as a cystic renal neoplasm of low malignant potential, few Bosniak 2F cystic masses radiologically progress during follow-up, RCC with predominantly cystic components are less aggressive than solid RCC, and Bosniak 3 cystic masses behave non-aggressively. These advances have led to an increase in non-radical management or surveillance of cystic renal masses. The term “cystic” RCC is confusing and in our opinion should not be used; rather, an RCC showing cystic changes on imaging should be reported in that manner. It is important to acknowledge that cystic change and necrosis may appear similar on imaging, although portending very different prognoses. Benign low-aggressive causes for Bosniak 3 cystic lesions including: cystic nephroma, AML with epithelial cysts, multilocular cystic neoplasm of low malignant potential, and tubulocystic RCC exist and are generally not possible to diagnose prospectively on imaging.

Conflicts of interest

The authors declare no conflict of interest.

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