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Seminars in ULTRASOUND CT and MRI

Multimodality Assessment of Cystic Renal Masses

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Renal cysts are a common imaging finding, often incidental. Ultrasound, CT and MRI are the main modalities responsible for renal cyst detection and characterization. These modalities often play a complementary role in modern radiological practice, each of them with strengths and limitations. In view of a recently proposed 'multimodality' update to the historical Bosniak classification, this article provides a general overview of the current imaging approach to renal cysts, and outlines some of the diverse pathologic entities responsible for renal cyst formation.
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Introduction

Renal cysts increase in incidence with age, being present in over 50% of patients older than 50 years.[1] In a large retrospective study of abdominal CT scans, 32.1% of patients (n = 2371/7365) had at least 1 renal cyst.[2] Cysts can be isolated findings or belong to the family of renal cystic diseases. They account for a broad spectrum of benign and malignant pathology. Biopsy of cystic lesions is seldom indicated; it carries a risk of spillage of cyst contents and is associated with sampling error, as only a small proportion of cells within a cyst may contain malignancy.[3] Imaging is therefore pivotal in identifying and classifying cysts non-invasively, before considering surgical resection or follow-up.

This article aims to: highlight the merits and limitations of different imaging modalities in the assessment of renal cysts; describe the imaging features that can aid cyst characterization; summarize traditional and novel classifications systems; briefly outline the pathologic entities associated with renal cysts.

Imaging Modalities

Ultrasound

Ultrasound (US) is cost effective, readily accessible, and does not use ionizing radiation. It can reliably distinguish between solid and cystic abnormalities, and has excellent contrast, temporal and spatial resolution. Image quality decreases at increased depth, which limits assessment in deeper regions of the body. Colour Doppler can be used to show vascularized areas.

Contrast-enhanced ultrasound (CEUS) is gaining ground in the evaluation of complex renal cysts and indeterminate masses. Contrast material composed of gas-filled lipid microspheres (microbubbles), measuring approximately 3-5 μm in diameter, is injected intravenously. When exposed to low mechanical index ultrasound waves, microbubbles resonate, reflecting acoustic signal that allows dynamic real-time visualisation of vasculature and enhancement characteristics.[4] CEUS contrast does not carry risk of nephrotoxicity and it can be safely administered in patients with renal dysfunction, including renal transplant recipients.[4]

Computed Tomography

Triple-phase contrast computed tomography (CT) is considered the mainstay for assessing indeterminate renal masses, including complex cysts. Unenhanced CT is performed to look for intrinsically hyperdense components such as calcification, and to act as a comparator when measuring enhancement. Contrast imaging is acquired in at least 2 phases: a corticomedullary phase, approximately 40-70 seconds after iodine contrast administration; and a nephrographic phase, around 100 seconds after injection. A 'dynamic' triple-phase acquisition allows assessment of enhancement kinetics. CT provides images with high spatial resolution, but lower soft tissue contrast compared to US and MRI. Ionizing radiation should be taken into account, and dose minimized in

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younger patients. Key benefits of CT are that full staging of the chest and pelvis can be performed quickly and simultaneously in case of malignancy, and that the relevant vascular anatomy can be adequately assessed ahead of surgery. Where iodinated contrast is contraindicated, non-contrast CT is of limited benefit.

MRI

MRI has excellent soft tissue contrast resolution and can easily depict septa and areas of wall thickening within a cyst, even when performed without contrast.[5] Either 1.5 tesla (T) or 3 T scanners can be used: 3 T systems offer increased signal-to-noise ratio, but suffer from greater chemical shift artefact and field inhomogeneity in the abdomen.[6] A combination of T1-weighted (T1w), T2-weighted (T2w), diffusion (DWI) and dynamic contrast-enhanced sequences provide complementary information and are performed as standard at our institution. Contrast administration allows assessment of vascularity and perfusion. Contrast is not usually administered in patients with renal failure, due to the risk of nephrogenic systemic fibrosis. Unenhanced MRI is a valuable cross-sectional method for the characterization of large complex cysts when intravenous contrast is contraindicated.

The limitations of MRI include low sensitivity to calcification, long acquisition times (compared to CT), the requirement of good breath-holding abilities from patients, and reduced availability in certain geographical areas.

Characterization of Renal Cysts

Simple Cysts

The sonographic features of a simple cyst include a rounded shape with sharply defined borders, anechoic contents and posterior acoustic enhancement. On CT, a simple cyst is sharply defined with a smooth, thin or imperceptible wall; no complex features such as septations, calcifications or enhancement can be appreciated; its contents are of water density (−9 to 20 Hounsfield units [HU]). On MRI, the features are similar and the contents have water signal characteristics (hyperintense on T2w, hypointense on T1w). If the classical features of a simple renal cyst are shown, no further imaging or investigation is usually required.

Complex Cysts

Cysts displaying any of the following features are defined as complex.

Septations

Septations are frequently observed in renal cysts, particularly on US and MRI.[5] Their significance depends on number, thickness and morphology: thin ('hairline'), smooth septations are normally considered benign. Thick septations become suspicious and any septal nodularity is likely to be malignant.[7]

Calcification

Linear, peripheral calcification in a thin-walled cyst tends to be benign. Historically, thick or nodular calcification was deemed suspicious for malignancy, requiring follow-up[8]; more recent work has shown that nodular or thickened calcification can be present in both malignant and benign lesions, and that calcification alone has no predictive value.[9]

Dense/Haemorrhagic Contents

Cyst contents with density greater than 20 HU on CT should prompt further assessment with US or MRI, as dense fluid (due to proteinaceous fluid, haemorrhage or calcium) cannot be distinguished from soft tissue. Hyperdense cysts share features with simple cysts, being round, well circumscribed, homogenous and not enhancing. They usually measure 50-90 HU on unenhanced CT. They can be occult on contrast CT alone, due to similar density of the enhancing adjacent renal parenchyma. On US, dense cysts may correspond to simple cysts, or contain low-level echoes, or layering of reflective debris. On MRI, proteinaceous fluid is typically isointense to hyperintense on T1w and T2w. Haemorrhagic cysts vary in signal characteristics depending on the age of haemorrhage; they are usually hyperintense on T1w, with layering of contents ('shading') on T2w.

Wall Thickening

Thickening of the cyst wall is associated with malignancy, but can also be seen in infection and acute haemorrhage.[7] The degree of thickening, and any wall irregularity or nodularity, increase the risk of malignancy.[10,11]

Enhancement

Presence or absence of enhancement is a key indicator for distinguishing benign from malignant lesions.[12] On CT, Hounsfield units can be easily measured within a 'fixed' region of interest on unenhanced and contrast acquisitions, making it possible to trace a time/enhancement curve. Enhancement less than 10 HU is considered non-significant; greater than 20 HU is considered unequivocal; between these values, it is indeterminate. 'Pseudoenhancement', that is the spurious change in HU related to reconstruction algorithms in different contrast phases, can be mitigated using subtraction algorithms or dual-energy CT.[13] Similar principles for enhancement evaluation apply to MRI. An increase in signal intensity of >15% has been proposed as an appropriate cut-off for true enhancement.[14] CEUS is an alternative dynamic method for assessing enhancement. It is particularly useful in patients who cannot receive iodine or gadolinium-based contrast agents due to allergy or reduced renal function.

Classification Systems

Classification systems establish a standardized language that enables health professionals to group patients with similar conditions, establish correlations between groups and specific outcomes, and determine the most appropriate management for each group. An example is the TNM system used for cancer staging.

Bosniak Classification

The Bosniak classification (Table) has been the dominant system for characterizing renal cysts in terms of risk of malignancy, and is used internationally.[7] It was first proposed in 1986 and has been periodically updated since.[8] It is based on CT, as the mainstay for renal mass assessment at the time of development. The classification was proposed out of need: as CT was becoming more established in clinical practice, there was an increase in the number of incidental renal lesions. A robust way of determining which lesions needed surgical resection was required. The classification comprises 5 categories; it has been externally validated, such that the likelihood

Table Comparison of the Revised 2005 Bosniak Classification (Incorporating the 'IIF' Category) With the 2019 Update Proposed by Silverman et al

Class	Traditional Bosniak Classification	2019 Classification by Silverman	
	CT	CT	MRI
I	Benign simple cyst	Thin (≤2 mm) smooth walls; homogeneous simple fluid (−9 to +20 HU); no septa or calcifications	Thin (≤2 mm) smooth walls; homogeneous simple fluid (similar signal to CSF); no septa or calcifications
II	Two types:	Six subtypes, all well-defined with thin (≤2 mm) walls:	Three subtypes, all well-defined with thin (≤2 mm) smooth walls:
	1) Benign cyst with a few hairline septa, no measurable enhancement; can have thin or slightly thickened calcification	1) Cystic lesion with thin (≤2 mm) and few septa (n = 1-3); septa and wall may enhance; can have calcification	1) Cystic lesion with thin (≤2 mm) and few septa (n = 1-3); septa and wall may enhance; can have calcification
	2) Hyperdense cysts <3 cm	2) Homogeneous hyperdense mass on non-contrast CT (≥70 HU)	2) Homogeneous masses markedly hyperintense (similar to CSF) at T2w imaging
		3) Homogeneous non-enhancing mass >20 HU on Renal protocol CT	3) Homogeneous masses markedly hyperintense on non-contrast T1w imaging (>2.5× normal parenchymal signal intensity)
		4) Homogeneous mass -9 to +20 HU on non-contrast CT	
		5) Homogeneous mass 21 to 30 HU on portal venous CT	
		6) Homogeneous low attenuation masses that are too small to characterize	
IIF	Two types:	Cystic lesion with a smooth minimally thickened (3 mm) enhancing wall; or smooth minimally thickened septa (3 mm); or many (≥4) smooth thin septa (≤2 mm)	Two types:
	1) Multiple thin septa, or minimal smooth thickening of wall or septa; can contain thick/nodular calcification; no measurable enhancement		1) Cystic lesion with a smooth minimally thickened (3 mm) enhancing wall; or smooth minimally thickened septa (3 mm); or many (≥4) smooth thin septa (≤2 mm)
	2) Complete intra-renal hyperdense lesions >3 cm also in this category		2) Cystic lesion that is heterogeneously hyperintense on unenhanced fat-saturated T1w
III	Indeterminate cystic masses that have thickened irregular or smooth walls or septa with measurable enhancement	One or more enhancing thick (≥4 mm width) or enhancing irregular (≤3mm obtusely marginated convex protrusions) walls or septa	One or more enhancing thick (≥4 mm width) or enhancing irregular (≤3 mm obtusely marginated convex protrusions) walls or septa
IV	Clearly malignant lesions with similar characteristics to Bosniak III, but containing enhancing soft-tissue components	One or more enhancing nodules (≥4 mm convex protrusion with obtuse margins, or a convex protrusion of any size with acute margins)	One or more enhancing nodules (≥4 mm convex protrusion with obtuse margins, or a convex protrusion of any size with acute margins)

The key differences are inclusion of MRI imaging features; more precise definitions for thickness and number of septa; and homogeneous hyperdense cysts considered as category II, regardless of size (previously IIF if endophytic and >3 cm); calcification considered as category II, even if thick or nodular (previously IIF).

Adapted from: Israel and Bosniak[8] and Silverman et al.[10]

of malignancy for each category is known.[11] The use of Bosniak Class in imaging reports allows clear communication between radiologist and clinician, informs management plans and helps structure patient consultations.[15]

A Bosniak category I lesion corresponds to a simple cyst, containing no features of complexity; the likelihood of malignancy is reported as 3.2% (95% confidence intervals [CI] 0%-6.8%).

Bosniak II lesions are minimally complex, with a few thin septa and a low risk of malignancy (6.0%; 95% CI 2.7%-9.3%).

Bosniak IIF lesions are considered likely benign, but requiring a period of surveillance to be confidently classified as such. They include cysts with multiple thin septa, minimal non-enhancing thickening of the wall and septa, and thickened or nodular calcification (Figs. 1 and 2). The associated risk of malignancy is 6.7% (95% CI 5.0%-8.4%).

Bosniak III cysts are traditionally considered 'surgical lesions'. They have thickened or nodular septa or walls with measurable enhancement (Fig. 3). The chance of malignancy is 55.1% (95% CI 45.7%-64.5%).

Bosniak IV lesions are those with overtly malignant features and a very high likelihood of malignancy (91.0% 87.7%-94.2%; Fig. 4).

These reported malignancy rates are taken from a large 2017 meta-analysis.[16] The presence of selection and verification bias is acknowledged, in that only a relatively small number of Bosniak I, II and IIF cysts have been surgically resected, likely inflating the reported risk of malignancy in these categories. In reality, the likelihood of malignancy in Bosniak I and II cysts is thought to approach zero.[10]

The original Bosniak classification is based on triple-phase renal CT. Applying the classification directly onto US and MRI is not without problems, given the higher soft tissue contrast of these modalities. CEUS, for example, has been shown to up-classify cystic lesions compared to CT, as it depicts more numerous and thickened septa, and is more sensitive to subtle enhancement.[17] Another limitation of Bosniak classification is the reported inter-observer variability: while agreement is good for Bosniak I and IV lesions, inter-observer disagreement has been reported in up to 75% of Bosniak II, IIF and III cysts; this has high potential for impacting on management decisions.[18]

Proposed 2019 Update to the Bosniak Classification

Silverman et al proposed an update to the Bosniak classification in 2019, based on a multimodality approach including MRI[10] (Table). The aim was to overcome some of the key shortcomings of the previous classification, namely: high inter-observer variability; the exclusion of MRI imaging features; a high prevalence of benign lesions in the Bosniak III category (44.9% benign).[16]

To tackle inter-observer variability, further refinement and standardization of language are proposed, with regards to the following definitions:

- Enhancement: removal of the distinction between 'perceived' and 'measurable' enhancement. Enhancement is either present or not.
- Simple fluid: changed from 'homogeneous fluid ≤20 HU' to 'homogeneous fluid between −9 and +20 HU' or 'similar to signal intensity similar to CSF on T2w MRI'.
- Number of septa: previously vague description as 'few', 'more than a few' or 'many'. In the new proposal these

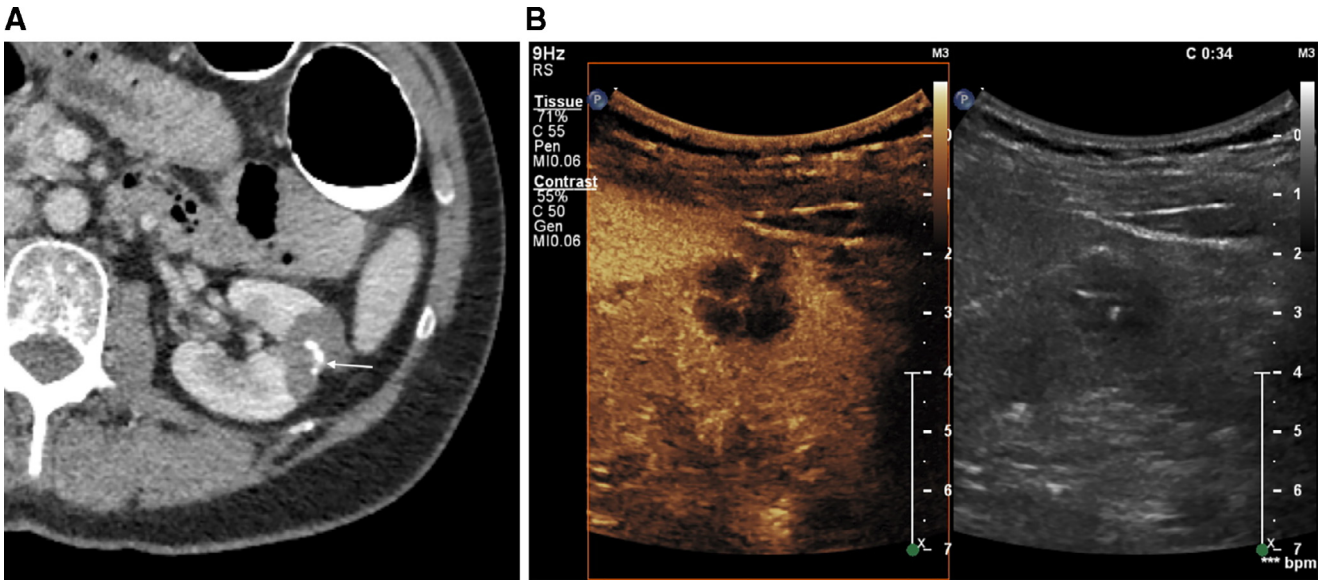

Figure 1 Incidental finding of a cystic lesion in a 56-year-old female. (a) Supine CT colonography performed in the portal venous phase demonstrates a complex cystic lesion in the interpolar region of the left kidney with clumped, nodular calcification. (b) On CEUS, this was shown to be a cluster of 1-1.5 cm cysts, separated by calcification. Using the original Bosniak Classification, this is IIF; based on the 2019 proposal this is II, as coarse calcification is now considered a benign finding.

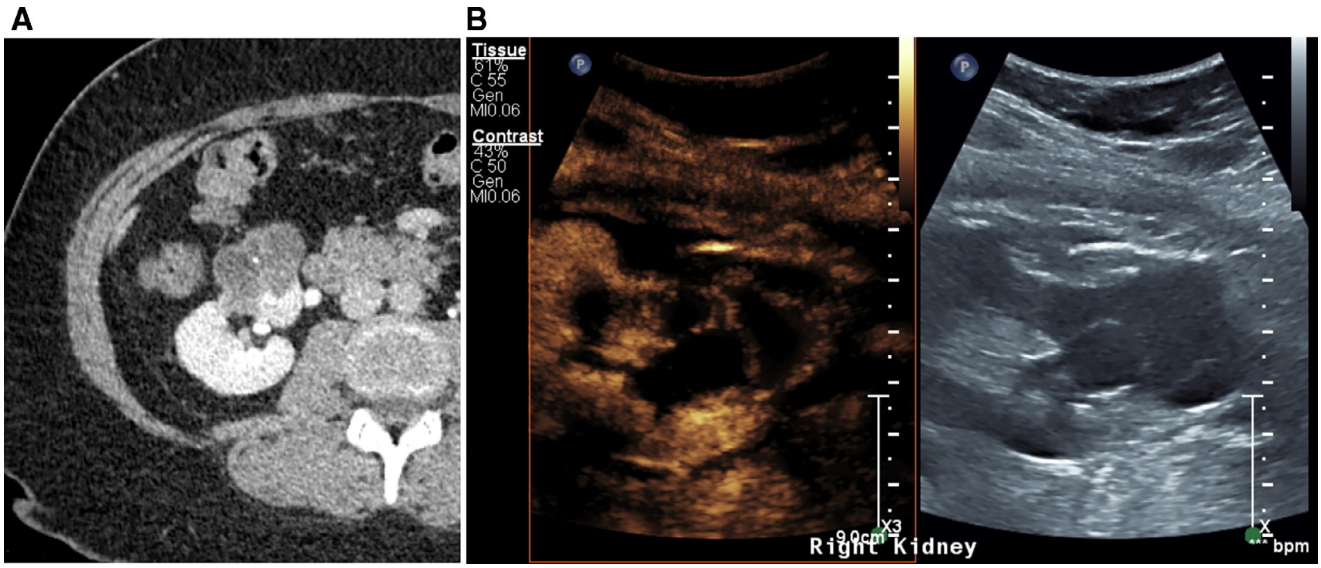

Figure 2 A 46-year-old female with a complex right-sided renal cyst. (a) Portal venous phase contrast-enhanced CT scan shows a 4.7 × 3.4 cm multi-loculated lesion. Some of the locules are of high attenuation, in keeping with haemorrhage. The septations are thin, with fine calcification. (b) CEUS reveals several (≥4) thin septa without nodularity. The lesion was categorized as IIF and has been stable on observation for the past 18 months.

are grouped specifically as 'one to three' and 'four or more'.

- Thickness of the cyst wall or septa: 'hairline' has been incorporated with 'thin' as ≤2 mm; 'minimally-thickened' corresponds to 3 mm; 'thick' is considered ≥4 mm.

Changes to the nomenclature applied to 'thickness' mean that only marked wall or septal thickening (≥4 mm and ≥3 mm, respectively) qualify for Bosniak category III. This is aimed to decrease the number of benign lesions that undergo resection. This can be done safely, as lesions that are down-classified will enter the IIF category, and will be followed up. It has been established there is only a small likelihood of metastatic disease developing in Bosniak III cysts under observation.[18]

As with the original Bosniak classification, the proposal by Silverman et al relies predominantly on anatomical information and does not take into account DWI. Lesion size is also not considered, even though smaller lesions have been shown to be more likely benign.[18] US features, aside from those of a simple cyst, are not included. Future prospective

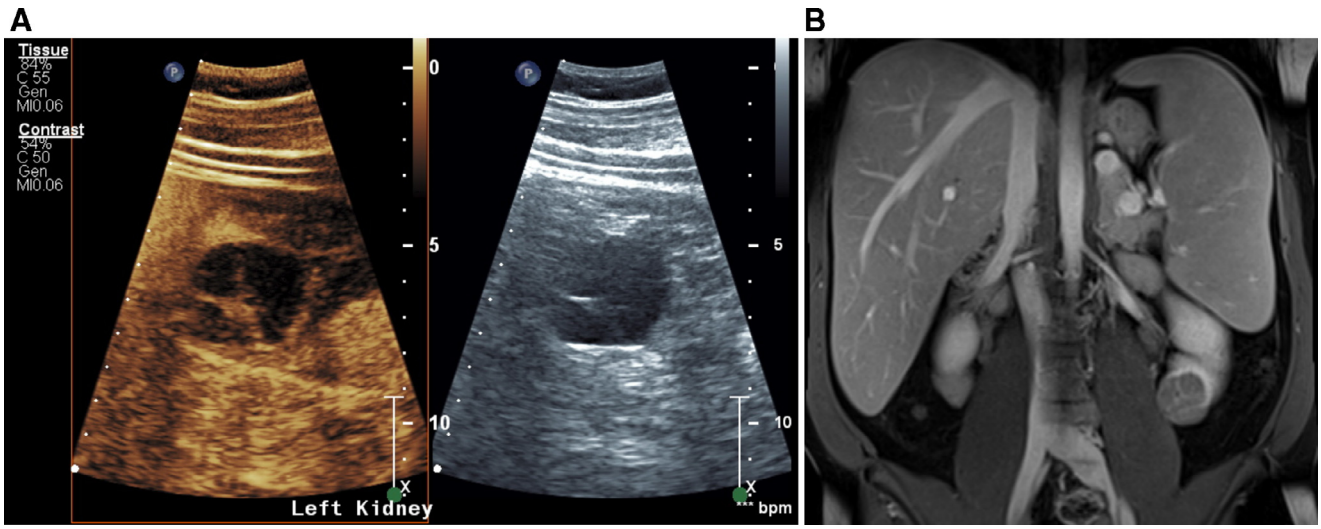

Figure 3 A 36-year-old female with a background of hereditary spherocytosis was found to have a Bosniak IIF cyst at the lower pole of the left kidney. During follow-up, the number and thickness of septations increased, re-classifying the lesion as Bosniak III. (a) CEUS showing florid septal enhancement with marked thickening on the 3.3 cm lesion. (b) Coronal post-contrast T1w fat-saturated MRI confirming the findings of a Bosniak III lower pole renal cyst. Incidental hepatosplenomegaly is due to hereditary spherocytosis. The lesion was resected by partial nephrectomy and was found to be a Fuhrman grade I clear cell RCC.

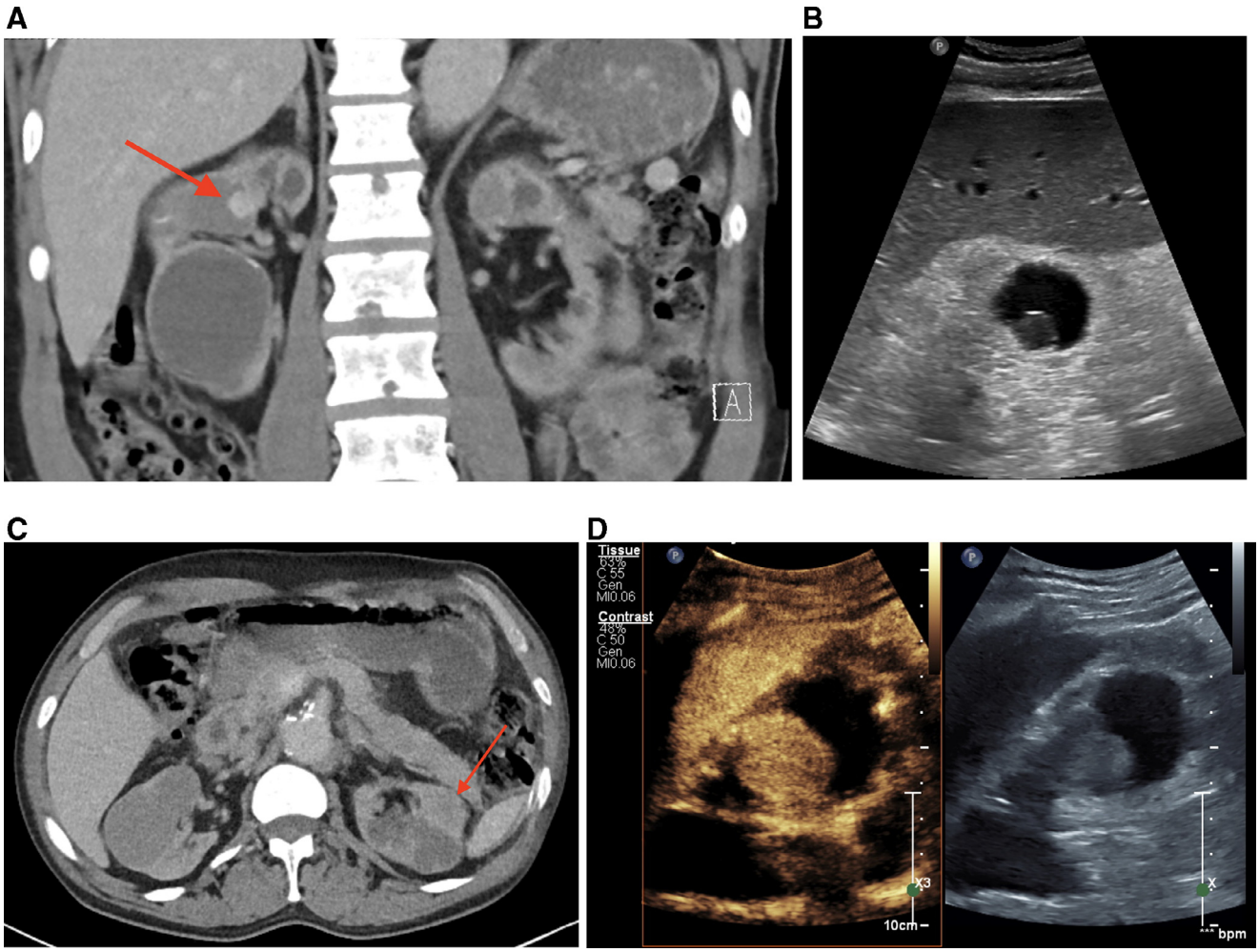

Figure 4 A 57-year-old male on long-term peritoneal dialysis. Both kidneys were atrophic and contained bilateral cysts in keeping with acquired cystic kidney disease. (a) Coronal portal venous phase CT scan shows an enhancing 1.2 cm mural nodule in a right upper pole cyst. (b) The nodule within the cyst is clearly demonstrated on US and has acute margins with the cyst wall in keeping with a Bosniak IV lesion. (c,d) CT and CEUS showed a 2.0 cm avidly enhancing nodule within a left interpolar region cyst, which washed-out after 20 seconds. Following nephrectomy, this was confirmed to be a Type 1 papillary RCC. The right-sided lesion is awaiting surgical management.

studies will be needed to validate this revised classification system.

As to the length of follow-up for IIF lesions, between 1 and 4 years has been previously suggested, depending on the complexity of the lesion.[19] Silverman et al advise imaging at 6 months, 12 months, then annually for a total of 5 years.[10] It appears realistic to expect the rates of malignancy or progression within the IIF category to be low, so that less frequent imaging follow-up could be recommended in the future, particularly for smaller lesions.[20]

A Role for CEUS?

Robbin et al[21] first proposed an adapted Bosniak classification for CEUS in 2003. CEUS is very sensitive to enhancement, and will often demonstrate occasional microbubbles flowing within 'hairline' septa; in the absence of constant flow of bubbles, septal thickening or septal nodularity, this can be considered a benign finding.[22]

A possible revised classification for CEUS is the following[23]:

- Bosniak I: no enhancement.
- Bosniak II: minimal enhancement within hairline septa.
- Bosniak IIF: constant flow of microbubbles within linear minimally-thickened septa.
- Bosniak III: thick or irregular enhancing walls or septa. No solid enhancing nodules.
- Bosniak IV: Enhancing nodules arising from walls or septa.

A large retrospective study investigating the diagnostic performance of CEUS in 1018 indeterminate renal masses, predominantly Bosniak II-III cysts, showed a sensitivity for malignancy of 100% (95% CI 97.1%-100%), specificity of 95% (95% CI 89.9%-98%), positive predictive value of 94.7% and negative predictive value of 100%.[22]

Pathology of Renal Cysts

The aim of this section is to provide the reader with a concise summary of the more common pathologic entities accounting for cystic renal masses.

Simple Renal Cyst

Simple cysts are common and their incidence increases with age, such that approximately 50% of patients aged 50 will have one or more.[1] Simple cysts are lined with simple epithelium and contain serous fluid. They are separate from the collecting system. The vast majority of simple cysts are asymptomatic; rarely, haemorrhage, infection, rupture and hydronephrosis secondary to mass effect can occur.

Pelvicalyceal Diverticulum

Pelvicalyceal diverticula are rare, seen historically on <0.5% of intravenous urograms.[24] They are cavities lined with transitional epithelium, which communicate with the collecting system. They frequently have similar appearances to simple cysts on US, CT and MRI, but will normally fill with contrast on urographic phase imaging. The most common complication is stone or milk of calcium formation, seen in approximately 50%.[3] Other complications include haemorrhage, infection and rupture, usually presenting with pain. A theoretical risk of malignancy due to urinary stasis has not been proven in practice.[25]

Infective Cysts

Hydatid Disease

Hydatid disease is a parasitic infection, caused by tapeworms of the Echinococcus type. Renal involvement is rare, with the liver (>75% of cases) and lung most frequently involved.[26] It is endemic in large parts of the world, and often presents many years after being acquired. Renal hydatid is generally asymptomatic but can present with flank pain and haematuria.

Hydatid cysts are usually solitary and unilateral. They most commonly occur in the renal cortex and can be uniocular or multilocular. They are often greater than 10 cm at the time of presentation.[27] Brood capsules arise from the internal layer of the cyst wall, and once they detach can enlarge and move freely within the dominant cyst.[28]

Typical sonographic findings are those of a septated cyst containing daughter cysts, which lie dependently.[28] Parasitic hooklets can cause internal echoes within the hydatid fluid. On CT, cyst walls are usually thickened. The daughter cysts are often of lower attenuation than the parent cyst, causing a 'Rosette' appearance. Many patients will have coexistent hepatic involvement.[26] Removal of the cysts carries a risk of rupture, which can precipitate a serious immune response leading to anaphylaxis.

Renal Abscess

Renal abscess most commonly occurs as a complication of acute pyelonephritis, but can also be due to haematogenous spread in a bacteraemic patient. Immunocompromised, diabetic and pregnant patients are at increased risk.[3] On US, a complex cyst with internal echoes, septations and loculations is normally seen. On CT, abscess will usually present as a thick-walled, hypoattenuating round mass. MRI will usually demonstrate central high T2w signal, a low T2w wall and central restricted diffusion.[3]

Cystic Nephroma

Cystic nephroma is an uncommon benign cystic neoplasm of the kidney. Cysts are lined with simple columnar or cuboidal epithelium.[29] It has a strong female predominance (80%),[29] and a peak age at presentation of 55 years.[30] Lower renal poles are more commonly affected. The average size at presentation has been reported to be 7.3 cm.[29]

Typical US appearances are those of a unilateral cyst with many irregular septa of varying thickness[29] (Fig. 5). On CT, the mass is usually well circumscribed. Cyst contents have densities equal to, or slightly higher than water. The multiseptated cyst is separated from the adjacent renal parenchyma by a thick fibrous capsule. This capsule is well demonstrated on MRI and is T1w and T2w hypointense.[3,29] Cystic nephroma often corresponds to a Bosniak III cyst, implying crossover with the imaging characteristics of cystic renal cell carcinoma (RCC).

Mixed Epithelial and Stromal Tumour

Mixed epithelial and stromal tumour (MEST) is a rare, mixed solid and cystic renal tumour with stromal and epithelial elements. In almost all reported cases, MEST has been benign.[30] Radiologically, MEST will combine cystic and solid components.[31] It cannot be distinguished from cystic RCC on imaging, and is likely to be classified as Bosniak III or IV due to thickened septations, enhancing nodules and curvilinear calcification.[31,32]

Cystic RCC

Cystic clear cell RCC accounts for 4%-15% of all RCC.[33] Pathologically, it represents either a primary cystic tumour, or a secondary tumour developing within a pre-existing cyst. It is a subtype of clear cell RCC defined by clear or eosinophilic cytoplasm, characteristic vasculature and common molecular signatures.[34] Cystic RCCs have been shown to have better prognosis compared to solid lesions of the same size.[35] On imaging, cystic RCC will have the appearances of a Bosniak III or IV cyst.[7,10] Progression of a Bosniak IIF cyst to a III or IV on follow-up imaging is strongly predictive of malignancy (~85%).[18] The presence of marginal or septal foci of restricted diffusion can be useful in differentiating benign complex cysts from cystic RCC.[36]

Polycystic Kidney Disease

Autosomal Dominant Polycystic Kidney Disease

Autosomal dominant polycystic kidney disease (AD-PCKD) affects approximately 3-4 people per 10,000.[37] It has 100%

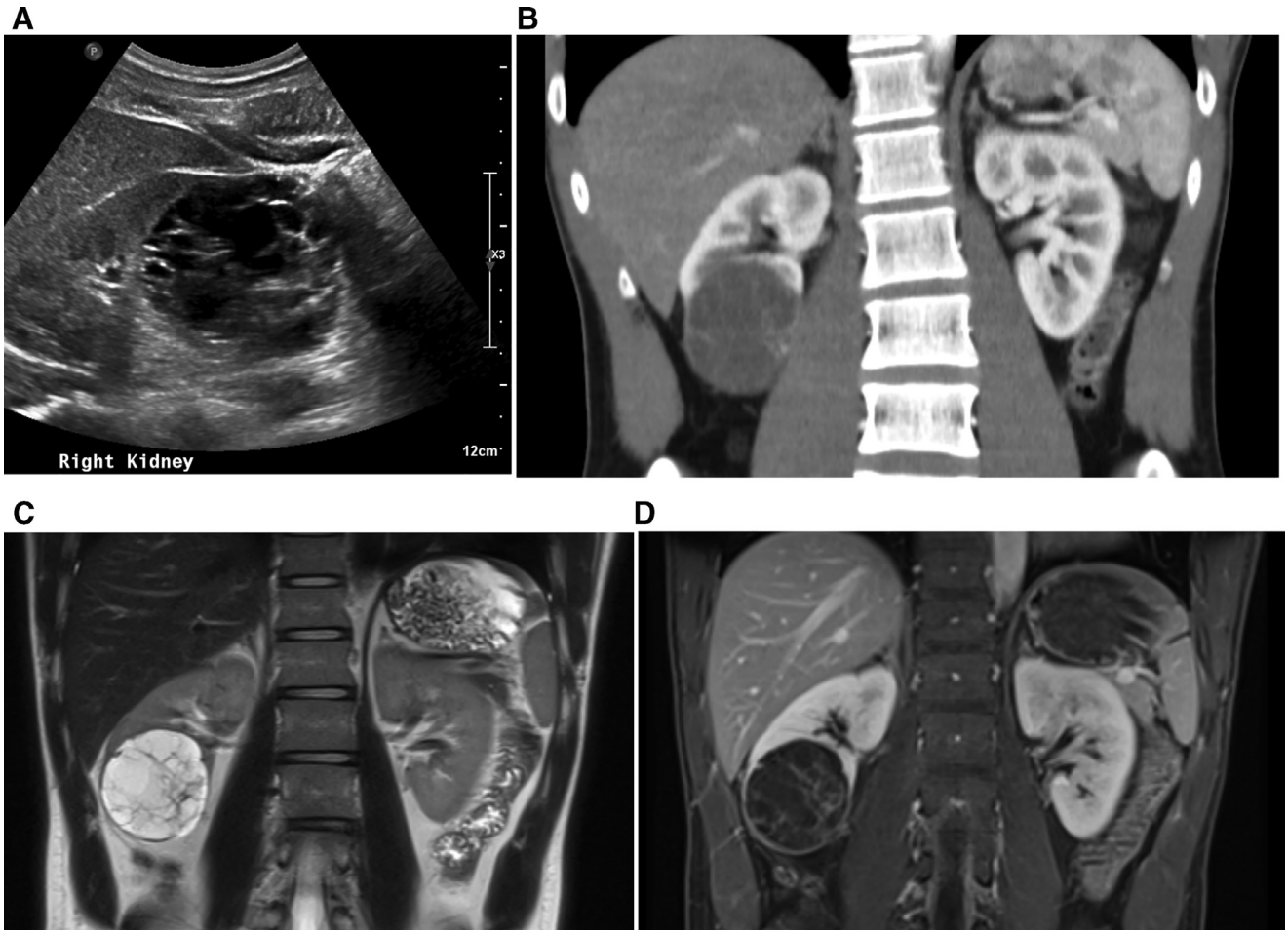

Figure 5 A 45-year-old female with an incidental right lower pole renal lesion. (a) US shows a multi-loculated cyst with many septations and some internal debris. (b) Similar findings are shown on coronal CT. (c) Coronal T2w and (d) Coronal post-contrast T1w fat-saturated MRI confirm a multiloculated cystic lesion. There is a low signal capsule around the lesion, suggestive of cystic nephroma. The patient opted for conservative management and the lesion has been stable on follow-up imaging.

penetrance but variable expression, such that many patients may not have a family history of renal disease. It is responsible for 7%-15% of patients on dialysis.[38]

Renal cysts frequently calcify. Due to the large number of cysts, these may not be completely round and can form irregular or bizarre shapes. Both kidneys are affected, but involvement can be asymmetrical. Cysts are often seen in other organs, most commonly the liver.

Even in the absence of end-stage renal disease, AD-PCKD carries an increased risk of RCC.[39] It can be an arduous task, particularly on US, to look for traits of cyst complexity due to the number of cysts. In many patients, iodinated contrast is contraindicated; unenhanced CT will demonstrate calcification but will not provide full cyst characterization. Unenhanced MRI with DWI is often the investigation of choice.[36]

Localized Cystic Disease

Localized cystic disease is a rare sporadic benign condition. It is characterized by replacement of one portion of parenchyma with multiple simple cysts. Unlike cystic nephroma, the cluster of cysts is not encapsulated. Microscopic evaluation reveals dilated ducts and tubules measuring from millimetres to several centimetres.[40]

Cysts Associated With Phakomatoses

Phakomatoses are a group of neurocutaneous disorders, 2 of which are associated with renal cysts.

Tuberous Sclerosis

Tuberous sclerosis (TS) is a multisystem disorder characterised by hamartoma formation in ectodermal (ie, skin and brain) and mesodermal (ie, kidney, heart, lung and bone) elements. Inheritance is autosomal dominant with incomplete penetrance, but many cases arise sporadically.[41] It classically presents with a triad of typical skin lesions, seizures and mental retardation.

At least 50% of patients have renal involvement,[31] most commonly in the form of angiomyelolipoma, commonly multifocal and bilateral, but also renal cysts. Many patients will have a few cysts, and these are usually simple and smaller than 3 cm. Patients can develop diffuse cystic change, similar to

that in AD-PCKD, due to the contiguous location of TSC2 and PKD1 genes on chromosome 16.[41] In cases where cyst formation predominates, patients can develop renal failure, which is the second most common cause of death after CNS involvement. RCCs occur in 2%-4% of patients, which is a similar rate to the general population, although these occur at a younger age.[42] Current recommendations are for brain and abdominal imaging every 3 years after diagnosis.[43]

Von Hippel-Lindau

Von-Hippel Lindau syndrome (VHL) is an autosomal dominant condition predisposing patients to cerebellar, retinal and spinal haemangioblastomas, pheochromocytomas, RCCs, pancreatic tumours and cysts involving the abdominal organs including the kidneys.

Renal cysts can become visible in late childhood, but increase in number and size thereafter. The cysts are usually multiple and bilateral, and progress along a continuum from apparently simple cysts to cystic RCCs (Fig. 6). The cysts are lined exclusively by clear cells,[31] and even those with simple appearances are thought to be pre-malignant.[44] In VHL, RCCs rarely develop before the age of 20 (the mean age of onset is 44), and 69% of patients reaching 60 will have had RCC.[45,46] Tumours are typically low grade, either Fuhrman 1 or 2.[31] Management involves a delicate balance between excising tumours before they metastasize and preserving renal function. Patients typically undergo yearly imaging and nephron-sparing surgery or ablation for lesions measuring 3-4 cm. The Bosniak classification is not reliable in these patients.

Acquired Renal Cystic Disease

Renal Failure

The most common cause of acquired renal cystic disease is chronic kidney disease, particularly in patients on long-term dialysis, with 44% affected after 3 years, and 90% after

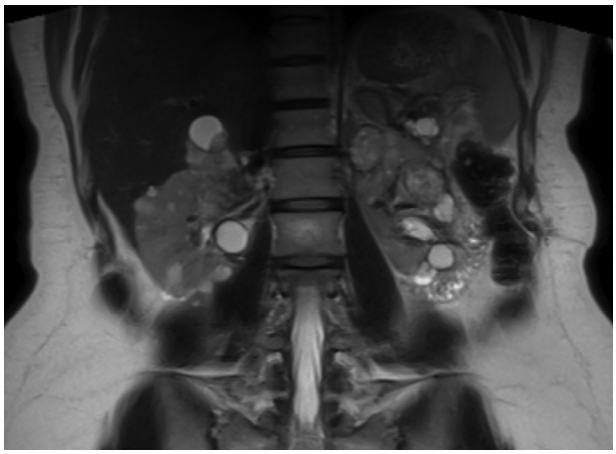

Figure 6 A 35-year-old female patient with Von Hippel-Lindau syndrome. Coronal T2w MRI imaging performed as part of screening demonstrates multiple bilateral renal cysts of varying complexity. Several solid renal lesions are shown bilaterally which have gradually developed from cysts whilst under observation. The patient has had multiple resections of Fuhrman grades I and II clear cell RCCs.

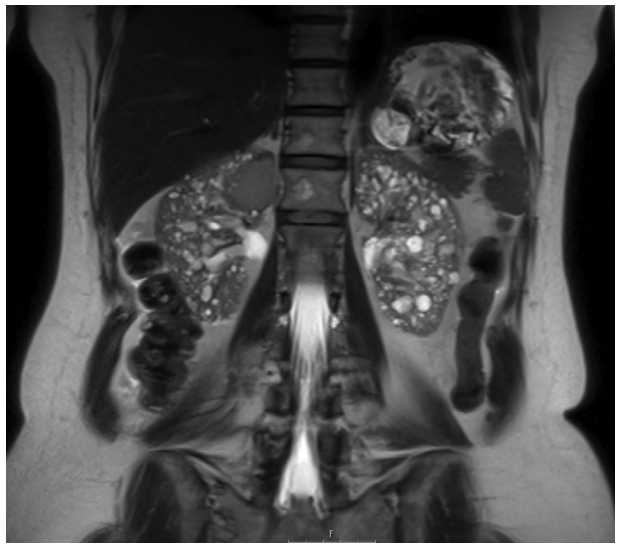

Figure 7 A 54-year-old female with a long history of lithium use for schizoaffective disorder. The kidneys contain innumerable small simple cysts within the cortex and medulla, with classic appearances of lithium nephropathy.

10 years.[47] Multiple cysts of varying complexity develop in the cortex and medulla of the atrophic kidneys. Patients are at increased risk of developing tumours, with an incidence of 3%-7% per year (approximately 100× greater than the general population).[31] They develop RCCs, oncocytomas and adenomas. RCCs vary in appearance, many arising within cyst walls or septa. US imaging of these patients is challenging due to renal atrophy and frequent calcification in cyst walls.[31]

Lithium

Nephrotoxicity due to long-term use of the mood stabiliser lithium is well described[3] (Fig. 7). Renal biopsy shows tubular atrophy, glomerulosclerosis, interstitial fibrosis and distal tubular atrophy.[48] Macroscopically, normal-sized kidneys contain uniformly distributed cysts in the cortex and medulla, most of which range from a few millimetres to a centimetre but are quite uniform in size.[49] Cysts are absent in the liver and other abdominal organs.

Conclusion

Imaging characterization of renal cysts relies on a multimodality approach in modern radiological practice, and is pivotal in estimating the associated likelihood of malignancy and in guiding management. The Bosniak classification is based on contrast CT and remains widely accepted as a reliable and practical system for risk estimation. Ultrasound and MRI are increasingly used for renal cyst characterization; they benefit from excellent soft tissue contrast, even in the absence of intravenous contrast, and are radiation free. An update to the Bosniak classification has been recently proposed, incorporating MRI imaging features and refining category definitions; it aims to improve inter-observer agreement and to reduce the number of benign lesions currently

classified as Bosniak III, but requires validation in future studies. Contrast-enhanced ultrasound is gaining ground as an alternative to cross-sectional imaging to characterize complex renal cysts; unlike contrast CT and MRI, it can be safely used in patients with chronic kidney disease.

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