

CME Article

Renal tumours: a common incidental finding

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In the current era of increased frequency and sophistication of radiological imaging, the rate of incidental findings of renal cortical tumours has steadily increased. As a result, the apparent incidence of renal cell carcinoma (RCC) is increasing, as is the trend towards diagnosis at an earlier

stage. A simplified classification of space-occupying lesions in the kidney is shown in Table I.⁽¹⁾ An algorithm for investigation and management of a renal mass is suggested (Appendix 1), and some renal tumours are described below.

Table I. Pathological classification of renal masses.

	Benign	Malignant	Inflammatory
Common	Simple cyst Angiomyolipoma	Renal carcinoma Metastases	Abscess Pyelonephritis
Uncommon	Oncocytoma Pseudotumour Reninoma Pheochromocytoma Leiomyoma Haemangioma Cystic nephroma Fibroma Arteriovenous malformation Haemangiopericytoma Renal artery aneurysm	Lymphoma Leiomyosarcoma Haemangiopericytoma Liposarcoma Rhabdomyosarcoma Schwannoma Osteosarcoma Fibrous histiocytoma Neurofibrosarcoma Invasion by adjacent neoplasm Carcinoid Wilms' tumour Mesoblastic nephroma Leukaemia	Infected renal cyst Tuberculosis Xanthogranulomatous pyelonephritis Rheumatic granuloma

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BENIGN RENAL TUMOURS

Benign renal cysts

Simple cysts are the most common benign renal lesions, comprising more than 70% of all asymptomatic renal masses. Cysts may be unilateral or bilateral, and solitary or multiple. They are found in more than 50% of patients older than 50 years.⁽²⁾ Simple cysts are usually asymptomatic and of no clinical significance. They may, however, grow to a large size and become symptomatic. Diagnosis is achieved by ultrasonography (US), and further evaluation with computed tomography (CT) is only performed when suspect malignant features are seen (Appendix 1 and Fig. 1). Treatment options of symptomatic cysts comprise percutaneous drainage and multiple sclerosant instillations, or excision.

Cortical adenoma

Renal adenomas are benign lesions usually found incidentally, with an incidence of 7%–23% in autopsy series, although the radiological incidence is less than 1%, due to the small size of most lesions.^(3,4) The incidence is associated with increasing age, tobacco smoking, von Hippel-Lindau disease (VHL) and acquired renal cystic disease associated with end-stage renal failure.^(5,6) Most remain asymptomatic, although haematuria can occasionally occur. As small cortical adenomas are uncommon and are often difficult to distinguish from malignant lesions on CT, renal exploration and resection or other ablative therapies, are usually performed.⁽³⁾

Renal oncocytoma

Renal oncocytomas comprise 3%–7% of all solid renal masses and are essentially benign lesions.⁽⁷⁾ They are derived from the distal tubules. Grossly, these tumours are typically 4–6 cm in size, light brown or tan, homogeneous, well-circumscribed, and often have a central scar, but unlike renal cell carcinomas, lack prominent necrosis or hypervascularity. Microscopically, cytologically low grade, uniform round or polygonal eosinophilic cells are



Fig. 1 Axial CT images show (a) Bosniak category I bilateral small renal cysts (arrows); (b) Bosniak category II cyst with septations within the cysts (arrows); and (c) Bosniak category III cyst with non-enhancing solid component (arrows) and coarse calcifications (dashed arrows) within the cyst.

arranged in an organoid, tubulocystic, solid, or mixed growth pattern. Oncocytomas are usually unifocal but may be multicentric or bilateral (synchronous or asynchronous) in approximately 6% of cases. They are more common in males and their mean presentation age is similar to that of RCC.

Most oncocytomas are asymptomatic and discovered incidentally on imaging studies performed for other indications. Uncommonly, patients may present with gross or microscopic haematuria, abdominal pain or flank mass. A central scar, due to a central dense fibrous band with trabeculae extending in a stellate pattern, is often seen on imaging such as CT, magnetic resonance (MR) imaging and US, or a spoke-wheel pattern of feeding arteries observed on angiography, suggests diagnosis. However, these features are of poor predictive value and unreliable for diagnosis.^(8,9) Renal oncocytomas cannot be reliably differentiated from malignant RCC based on clinical or radiological means. Renal biopsy or aspiration is not recommended to differentiate oncocytoma from RCC, due to the difficulty in distinguishing it from the eosinophilic variant of chromophobe cell carcinoma or the granular type of conventional RCC.⁽¹⁰⁾ Renal oncocytomas are usually managed with open or laparoscopic, partial or radical nephrectomy.

Renal angiomyolipoma

Angiomyolipoma (AML) is a benign, perivascular epithelioid cell-derived tumour, composed of varying amounts of fat, smooth muscle and abnormal blood vessels. AMLs very rarely undergo malignant transformation. It occurs mainly in women, is rare before puberty, and is usually diagnosed between the third and fifth decades of life. AML may occur alone or in approximately 20% of cases with tuberous sclerosis syndrome (TS), an autosomal-dominant hereditary disorder characterised by mental retardation, epilepsy, adenoma sebaceum skin lesion, and multi-organ AMLs. Due to incomplete penetrance, approximately 50% of patients with TS develop AMLs. Among this group, mean age at presentation is 30 years, and renal AMLs tend to be larger, fast growing, symptomatic, multifocal and bilateral.

The majority of AMLs are asymptomatic and diagnosed incidentally on renal imaging. Fat within the mass suggests angiomyolipoma, as RCC usually does not contain fat. US show a well-circumscribed lesion, with a highly echogenic area within the mass, often associated with shadowing, suggesting the presence of fat. CT has been the most reliable modality for diagnosing AMLs, where the presence of even a small amount of fat within a renal mass (Hounsfield units ≤ 10) is considered diagnostic of AML (Fig. 2).⁽¹¹⁾ Larger AMLs can present with flank pain, haematuria, palpable mass, and potentially fatal massive retroperitoneal haemorrhage, causing sudden pain and

hypovolaemic shock (Wunderlich's syndrome) (Fig. 2).

AMLs > 4 cm are more likely to grow and become symptomatic.^(12,13) Currently, the recommendations for asymptomatic renal AML less than 4 cm in size, is conservative management, with repeat imaging 6–12 monthly. Symptomatic or large AML (> 4 cm) should be followed up more frequently, and partial nephrectomy or selective embolisation may be considered. In patients who present with haemorrhage from AML, selective embolisation should be considered as first-line therapy, and total nephrectomy reserved only for potentially life-threatening haemorrhage that is unsuitable for or had failed embolisation.

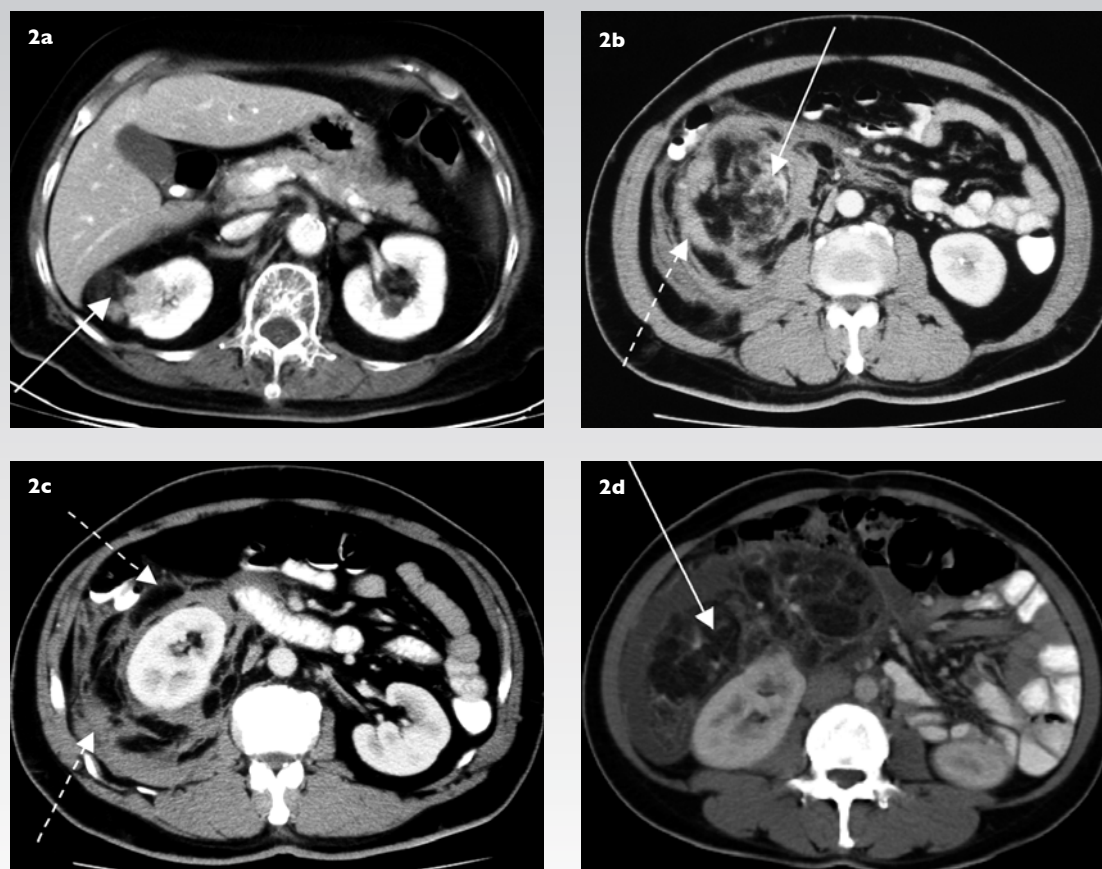


Fig. 2 Axial CT images show (a) non-complicated renal angiomyolipoma (arrow); (b & c) renal angiomyolipoma (arrow) in the lower pole of the right kidney, complicated by perinephric haemorrhage (dashed arrows); and (d) large renal angiomyolipoma with adipose tissue component (arrow).

MALIGNANT RENAL TUMOURS

Renal cell carcinoma

RCC accounts for approximately 3% of all adult malignancies, with a male: female ratio of 2:1. The incidence of RCC has been increasing, almost doubling in the last 35 years, with age-standardised rates of 5.4 and 2.9 per 100,000 population per year, for Singaporean males and females, respectively.⁽¹⁴⁾ Typical presentation of RCC is in the fifth to seventh decades of life, and is more common in Chinese compared to Indians and Malays.⁽¹⁴⁾

RCCs arise primarily from the proximal renal convoluted tubules, but some histological subtypes of RCC are derived from the distal convoluted tubules or



Fig. 3 Axial CT image shows right RCC (arrow) in a patient with multicystic kidney disease secondary to prolonged haemodialysis for end-stage renal failure.

Table II. Pathological types of renal cell carcinomas.

Renal tumour type	% incidence	Prognostic significance
Clear cell (conventional)	70%–80%	–
Papillary	10%–15%	Tendency to be of low stage & grade
Chromophobe	4%–5%	Better prognosis than conventional RCC
Collecting duct	< 1%	Poor prognosis
Medullary cell	< 1%	Poor prognosis
Oncocytoma	2%–5%	Benign

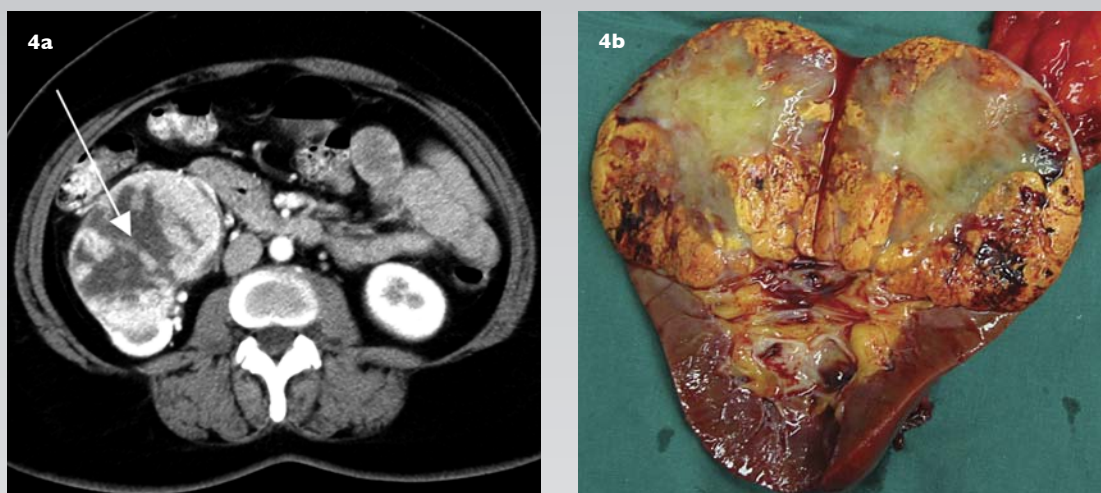


Fig. 4 (a) Axial CT image shows RCC in the upper pole of the right kidney, with areas of central necrosis (arrow). (b) Bivalved gross nephrectomy specimen of the same tumour shows corresponding central necrosis and areas of haemorrhage with the RCC.

collecting ducts. The risk factors for RCC are tobacco smoking, patients with tuberous sclerosis, and end-stage renal failure patients on dialysis, who develop acquired renal cystic disease (Fig. 3). Familial forms of RCC have also been identified. The clear cell variant of RCC develops in about 50% of patients with VHL, where they present early in the third, fourth, or fifth decades of life, and are often bilateral and multifocal. VHL is an autosomal-dominant disorder of chromosome 3p, with a worldwide incidence of one in 36,000 live births, and has major manifestations including pheochromocytoma, retinal angiomas, haemangioblastomas of the brain stem, cerebellum or spinal cord, renal and pancreatic cysts, pancreatic tumours, inner ear tumours, and papillary cystadenomas of the epididymis.⁽¹⁵⁾ Hereditary papillary RCC is another uncommon autosomal-dominant disorder, arising from mutations of the MET proto-oncogene at 7q31. Patients tend to present with multifocal and bilateral papillary variant of RCC.

Sporadic RCCs tend to be unilateral and unifocal. However, synchronous or asynchronous bilateral tumours are found in 2%–4% of sporadic RCCs. RCCs are typically round to ovoid, yellow or brown tumours interspersed with areas of fibrosis, necrosis, or haemorrhage, and circumscribed by a pseudocapsule of compressed parenchyma and fibrous tissue rather than a true histologic capsule (Fig. 4). Cystic degeneration and stippled or plaque-like calcification can also be found within the tumour. RCCs commonly displace the collecting system rather than invade it, and may sometimes invade beyond Gerota's fascia, which usually forms its natural barrier. A unique feature of RCC is its predilection for involvement of the venous system (10%), forming a tumour thrombus that can extend into the inferior vena cava (IVC), up to as high a level as the right atrium. The histological classification of RCCs and their prognostic significance are shown in Table II. Common sites of metastases are the lung, liver, subcutaneous tissue and central nervous system.

RCCs are now increasingly found as incidental asymptomatic renal masses on imaging studies obtained for other purposes. The classic triad of flank pain, gross haematuria and palpable/ballotable abdominal mass, is now rarely found, and generally indicates advanced disease. Gross or microscopic haematuria occurs in 40%–60%, flank pain in about 40%–50%, and flank mass in about 20%–30% of RCCs. Other general manifestations include weight loss, fever or night sweats, a non-reducing varicocele (due to a blocked testicular vein) or bilateral lower extremity

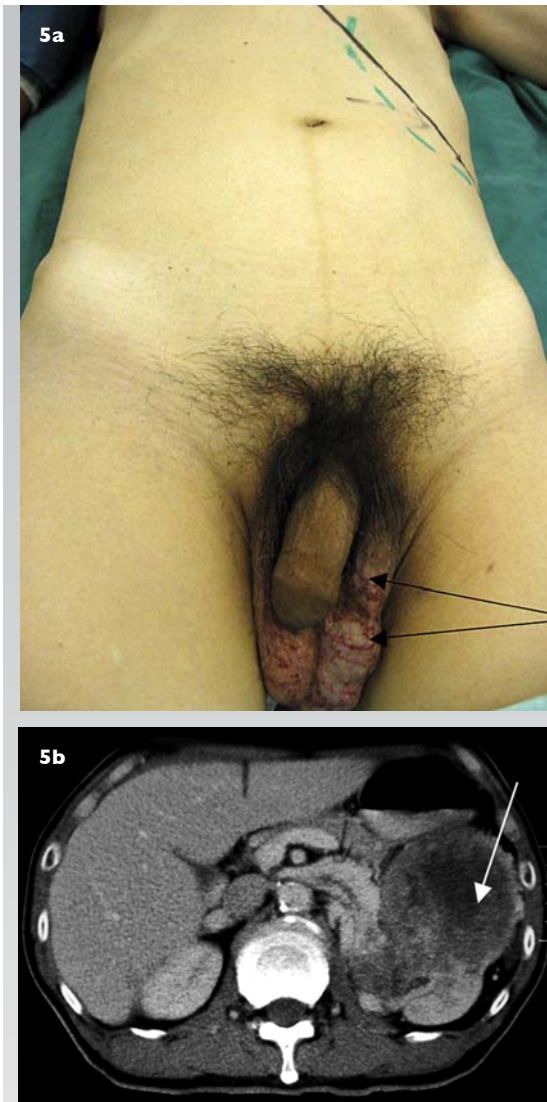


Fig. 5 (a) Clinical photograph of a middle-age man presenting with a non-reducing left varicocele (arrows) and a ballotable left renal mass. (b) Axial CT image shows a large left RCC (arrow).

oedema, which suggests venous involvement (Fig. 5). The sudden development of a varicocele in a man over 40 years of age warrants renal imaging.

Paraneoplastic syndromes are associated in about 20% of patients with RCC, due to various substances produced by RCC in pathological amounts. These include hypercalcaemia (about 10%, due to parathyroid hormone-like peptide production or osteolytic metastatic involvement of the bone), hypertension (due to increased renin production, compression of the renal artery or its branches, causing renal artery stenosis; or arteriovenous fistula within the tumour), polycythaemia (due to tumour production of erythropoietin), pyrexia of unknown origin (may be related to tumour production of necrosis factors) and Stauffer's syndrome (3%–20%, non-metastatic hepatic dysfunction characterised by abnormal liver function tests, neutropenia, thrombocytopenia, fever, areas of hepatic necrosis). Other less common RCC-associated paraneoplastic syndromes include Cushing's syndrome, hyperglycaemia, erythrocytosis, protein-wasting enteropathy, galactorrhoea, neuro-myopathy, clotting disorders and amyloidosis. Nephrectomy usually normalises most abnormalities of paraneoplastic syndromes.

Diagnosis of RCCs usually begins with imaging such as an intravenous urogram or US detecting a renal mass (Figs. 6 & 7). This is best further evaluated using CT, which is the method of choice in diagnosing and staging RCCs. MR imaging is the preferred study for the evaluation of IVC tumour thrombus, compared to venography (Fig. 8).⁽¹⁶⁾ Percutaneous renal biopsy or aspiration of renal masses are now uncommonly performed due to the high diagnostic accuracy of CT or MR imaging, and the known problems of sampling error

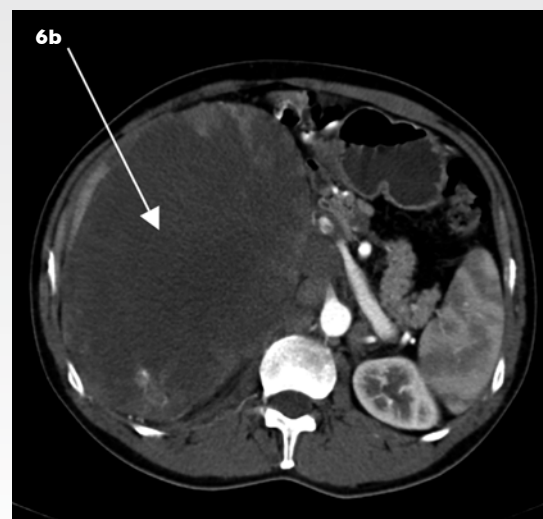
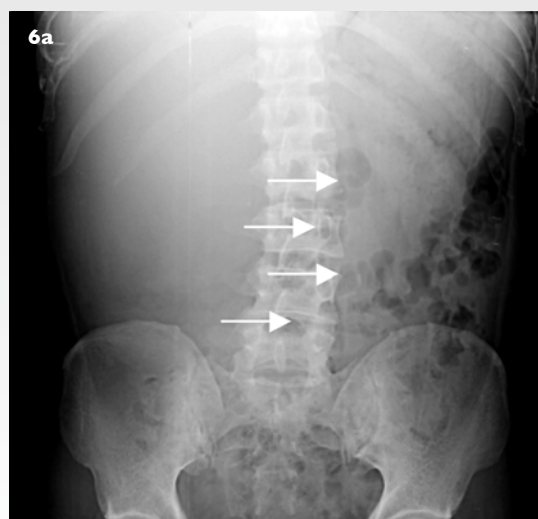


Fig. 6 (a) Frontal abdominal radiograph shows a large right-sided RCC displacing bowel, as seen by the displacement of bowel shadows (arrows). (b) Corresponding axial CT image shows a very large right-sided RCC (arrow).

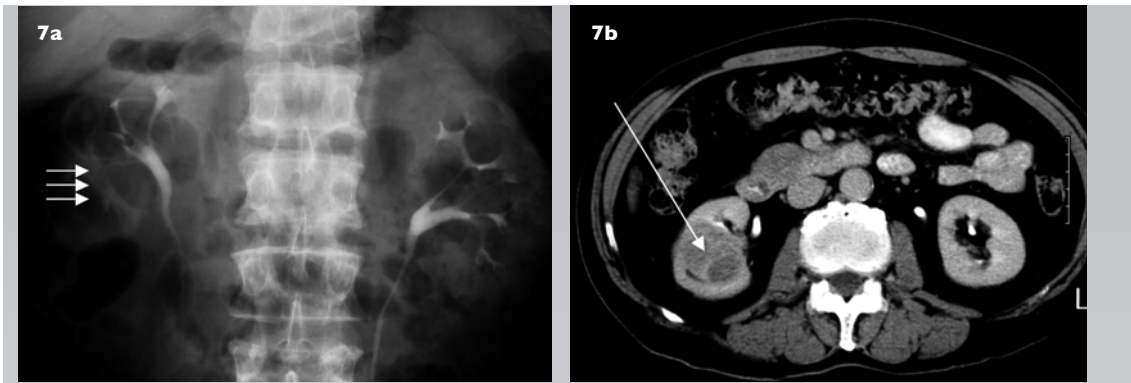


Fig. 7 (a) Intravenous urogram coned image shows absence of the lower pole calyces due to a space-occupying lesion (arrows), compared to the opposite side. (b) Corresponding axial CT image shows RCC in the lower aspect of the right kidney (arrow).

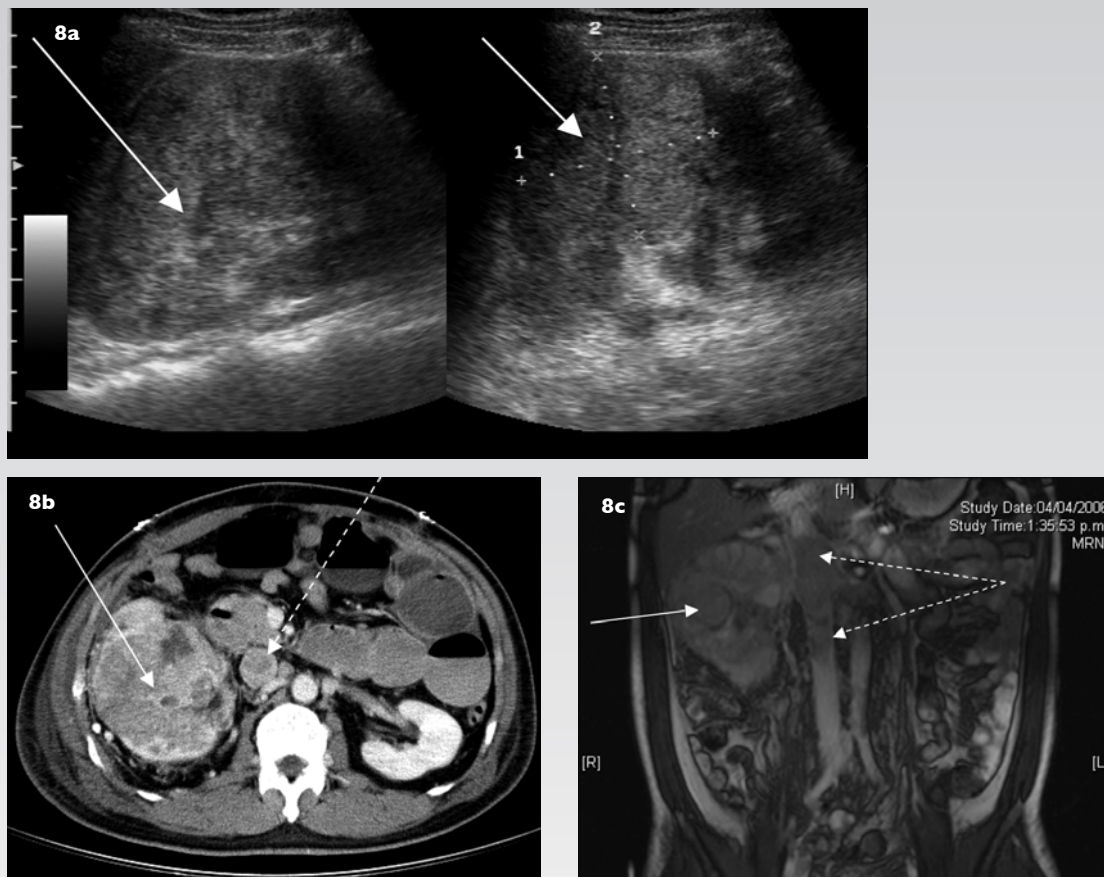


Fig. 8 (a) US images show a large renal mass (arrows) in the right kidney in a man who presented with gross haematuria. (b) Corresponding axial CT image shows the large RCC (arrow) with tumour thrombus (dashed arrow) causing a filling defect in the IVC. (c) Coronal MR image shows the RCC (arrow) as well as extensive tumour thrombus (dashed arrow) in the IVC.

or difficulty in interpretation of biopsy specimens, in addition to complications of biopsies. Staging investigations include chest radiographs or CT, CT of the abdomen and pelvis, liver function tests, and bone scan (in patients with bone pain or elevated alkaline phosphatase).

Radical nephrectomy is the gold standard curative treatment for localised RCC. A variety of approaches are available, including open (using abdominal, loin, or thoraco-abdominal incisions) and laparoscopic (transperitoneal and retroperitoneal) techniques. More recently, nephron-sparing surgeries (NSS) have been performed for indications such as small peripheral tumours, patients with poorly-functioning contralateral kidney or solitary kidney, and bilateral/multiple RCCs. NSS techniques include open or laparoscopic partial nephrectomy and a variety of

minimally-invasive energy-based ablation techniques, such as renal cryotherapy, radiofrequency ablation, high intensity focused ultrasound, microwave thermotherapy, laser interstitial thermal therapy and interstitial photon radiation ablation. While open partial nephrectomy is a more established procedure, the other minimally-invasive NSS techniques still require validation with long-term studies. IVC tumour thrombectomy can be performed together with nephrectomy, and the operative approach is determined by the level of vena caval involvement, which may or may not involve adjunctive cardiopulmonary bypass with hypothermic circulatory arrest for thrombus extending to the right atrium.^(17,18)

In patients with advanced RCC, palliative nephrectomy or renal angioinfarction may be performed to control symptoms. Nephrectomy and surgical resection of a solitary metastasis, either in the lung, adrenal gland, or brain, may confer an improved prognosis. RCCs tend to be chemotherapy-resistant, and immunotherapy with agents such as Interleukin-2 and interferon alpha, conferring modest effect. For patients with a good performance status [WHO status 0 (fully active) or status 1 (restricted in physically strenuous activity but able to do light or sedentary work)], the combination of nephrectomy and immunotherapy has shown some survival benefits.^(19,20) Newer agents targeting angiogenic factors, such as small molecule inhibitors of kinases and monoclonal antibodies, are being investigated, and show considerable promise in the management of advanced RCCs.

SUMMARY

With the increase in utilisation of abdominal imaging, more incidental benign and malignant renal tumours are being detected. Initial imaging study showing indeterminate solid lesions or cystic lesions with suspicious features, warrant either further evaluation or periodic monitoring. The risk factors and possible features of RCC are summarised:

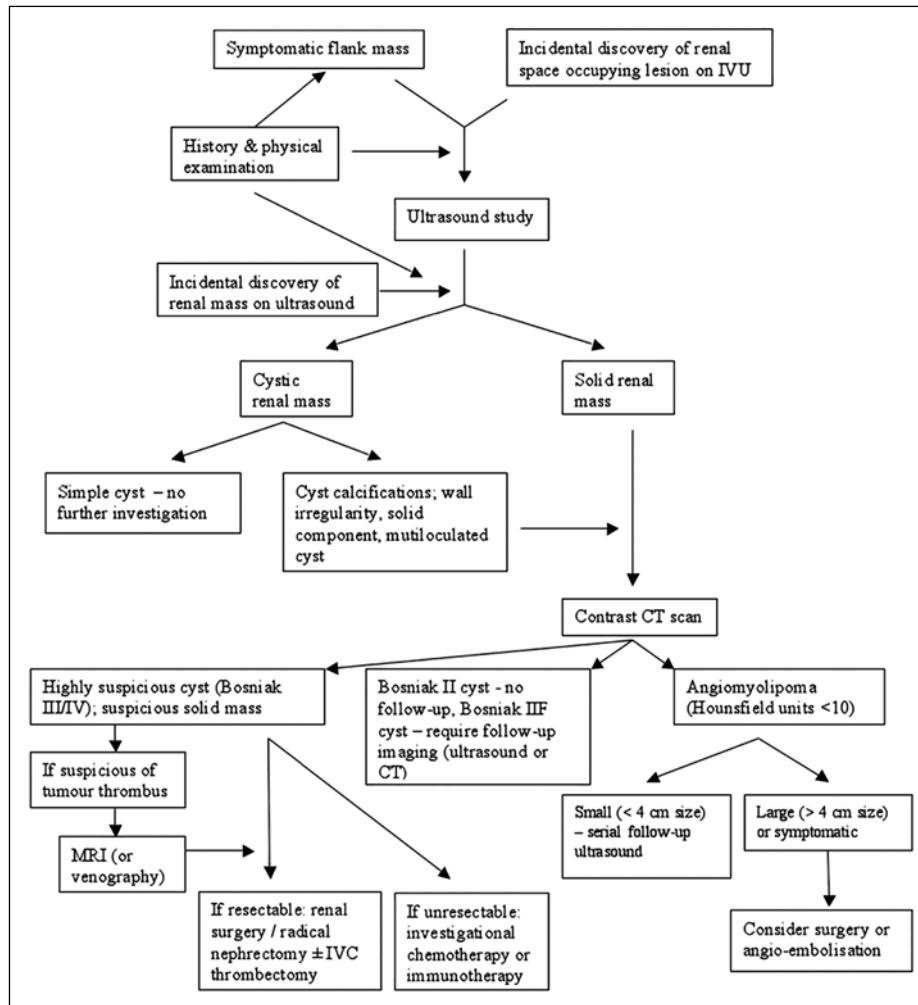
Features of RCC	Risk factors of RCC
Common/Important <ul style="list-style-type: none"> • Incidental • Haematuria (gross or microscopic, without dysuria) • Flank pain • Loin mass Non-specific <ul style="list-style-type: none"> • Weight loss • Fever • Night sweats • Anaemia Less common <ul style="list-style-type: none"> • Non-reducing varicocele • Paraneoplastic syndromes 	<ul style="list-style-type: none"> • Age 40 years or more • Tobacco smoking • End-stage renal failure on dialysis with acquired renal cystic disease • Von Hippel-Lindau disease • Family history of RCC • Tuberous sclerosis

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Appendix I. Algorithm for investigation and management of a renal mass.



Key: Bosniak CT scan classification of cysts:⁽²¹⁻²³⁾ Category I (benign) – simple cysts; Category II (minimally complicated, benign) – septated or minimally-calcified cyst, or infected cyst; Category IIF (minimally-complicated cysts that require follow-up) – most likely benign but have worrisome features, that require follow-up imaging to prove that the lesion is benign, such as some hyperdense cysts and cysts with more calcium in the wall; Category III (moderately complicated, suspicious for malignancy) – multiloculated haemorrhagic, coarse or pleomorphic calcifications, or non-enhancing solid component; Category IV (probably malignant) – wall irregularity and enhancing solid component.

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
Multiple Choice Questions (Code SMJ 200706A)

	True	False
Question 1. Regarding benign renal tumours:		
(a) Renal cysts are the most common incidentally-discovered renal masses.	<input type="checkbox"/>	<input type="checkbox"/>
(b) All renal cysts found on US should be further evaluated by CT.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Renal cysts are only treated when they are symptomatic or are suspected to be malignant in nature.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Renal cortical adenomas are commonly diagnosed, as they are clinically and radiologically distinct from renal cell carcinoma.	<input type="checkbox"/>	<input type="checkbox"/>
Question 2. Regarding benign renal tumours:		
(a) Clinically and radiologically, renal oncocytomas are commonly mistaken for renal cell carcinomas.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Patients with tuberous sclerosis syndrome tend to have symptomatic, large, bilateral and multiple renal angiomyolipomas.	<input type="checkbox"/>	<input type="checkbox"/>
(c) It is difficult for radiological imaging to distinguish between renal angiomyolipomas and renal cell carcinomas.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Large renal angiomyolipomas can cause potentially fatal haemorrhage.	<input type="checkbox"/>	<input type="checkbox"/>
Question 3. Regarding renal cell carcinoma:		
(a) It presents typically in the third and fourth decades of life.	<input type="checkbox"/>	<input type="checkbox"/>
(b) It has many known chemical aetiological factors.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Tobacco smoking is not a risk factor.	<input type="checkbox"/>	<input type="checkbox"/>
(d) It has been associated with acquired renal cystic kidneys in renal failure patients and Von Hippel-Lindau disease.	<input type="checkbox"/>	<input type="checkbox"/>
Question 4. Regarding renal cell carcinoma:		
(a) It commonly presents with a classic triad of gross haematuria, flank pain and a ballotable mass in at least 50% of patients.	<input type="checkbox"/>	<input type="checkbox"/>
(b) It is rarely found as an incidental renal mass on imaging for other purposes.	<input type="checkbox"/>	<input type="checkbox"/>
(c) It is important to obtain renal imaging in a 50-year-old man who presents with a non-reducing varicocele.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Hypercalcaemia, polycythaemia, poorly-controlled hypertension, liver dysfunction or pyrexia of unknown origin may be paraneoplastic manifestations of renal cell carcinoma.	<input type="checkbox"/>	<input type="checkbox"/>
Question 5. Regarding renal cell carcinoma:		
(a) Spread occurs into the renal vein and inferior vena cava, resulting in lower limb oedema in 30% of patients.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Preoperative diagnosis is usually achieved by CT, rather than performing renal biopsies.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Surgery (radical nephrectomy) is the method of choice in treating localised renal cell carcinomas.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Nephrectomy has a role in relieving symptoms and improving survival in patients with metastatic disease.	<input type="checkbox"/>	<input type="checkbox"/>

Doctor's particulars:

Name in full: _____
MCR number: _____ Specialty: _____
Email address: _____

SUBMISSION INSTRUCTIONS:

(1) Log on at the SMJ website: www.sma.org.sg/cme/smj and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

RESULTS:

(1) Answers will be published in the SMJ August 2007 issue. (2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 15 August 2007. (3) All online submissions will receive an automatic email acknowledgment. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

Deadline for submission: (June 2007 SMJ 3B CME programme): 12 noon, 25 July 2007