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Incidentally detected small renal masses

Investigation and management

Background
With increasing use of imaging to diagnose other conditions, incidentally detected small renal masses and cysts are now a common clinical scenario for both the general practitioner and the urologist.

Objective
This article outlines a diagnostic and management approach to the incidental finding of a small renal mass or cyst.

Discussion
Renal cell carcinoma represent 2–3% of all cancers and more than 50% of these are detected incidentally. Small renal masses are defined as renal masses less than 4 cm in diameter. They comprise a heterogeneous group of lesions; 20% are benign and only 20–25% prove to be potentially aggressive kidney cancers at the time of diagnosis. Work-up involves a full history, looking for evidence of paraneoplastic syndromes and examination, which is usually normal. Recommended blood tests include basic biochemistry and haematology, and imaging. A four phase contrasted computerised tomography scan of the kidneys allows a detailed examination of each aspect of the functional anatomy of the kidney, which can help approximate risk of malignancy and direct management. Not all patients with small renal masses require a biopsy. However, biopsy is required in patients who opt for active surveillance or ablative therapy. Management options include surveillance, surgery and ablative techniques.

Keywords: kidney diseases; neoplasms; incidental findings

CPD

Case study

Joan, 64 years of age, has a past medical history of hypertension, rheumatic fever, appendicectomy and cholecystectomy. She presented to her general practitioner with difficulty in swallowing. Joan was otherwise well with no constitutional symptoms and no recent weight loss. She was suspected to have a foreign body lodged in her oesophagus.

Joan underwent an ultrasound which excluded a foreign body but detected an incidental finding of a right superior pole renal mass. A four phase computerised tomography scan was performed in order to further characterise the lesion. This showed a 25 mm enhancing lesion in the supero-posterior aspect of the right kidney (*Figure 1*). The contralateral kidney appeared normal. There was no renal vein tumour, thrombus or lymphadenopathy evident. Laboratory testing revealed renal impairment with a serum creatinine of 160 µmol/dL and an estimated glomerular filtration rate (eGFR) of 41.

With increasing use of imaging to diagnose other conditions, incidentally detected small renal masses (or 'incidentalomas') are now a common clinical scenario for both the general practitioner and the urologist. Latest database analysis shows that more than 50% of renal cell carcinomas (RCCs) are detected incidentally.[1–3] The classic textbook description of RCC presenting with a triad of flank pain, gross haematuria and abdominal mass is not commonly seen.

Small renal masses are classified as renal masses less than 4 cm in diameter and by definition these are primary tumour, nodes and distant metastases (TNM) stage T1a tumours.[4] They comprise a heterogeneous group of lesions. Around 20% of these lesions are benign and while the rest are by definition malignant, only about 20–25% of renal masses in this size are proven to be potentially aggressive kidney cancers at the time of diagnosis.[5–8]

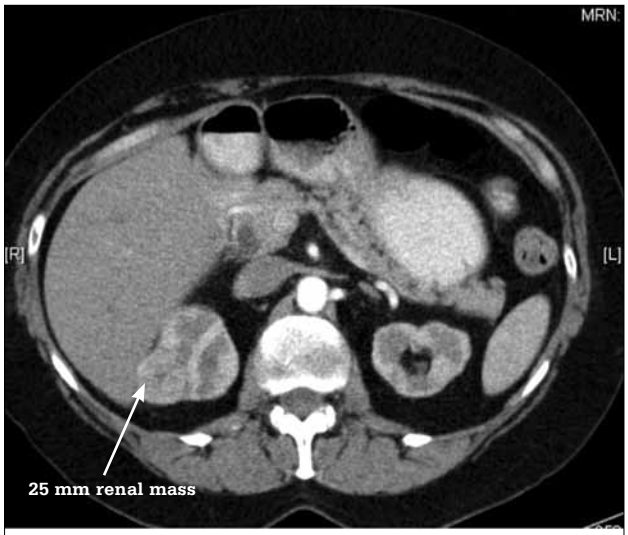

Figure 1. Joan's CT scan

Epidemiology

According to a European database, RCCs represents 2–3% of all cancers.[9] In Australia, there are just over 2000 new cases of primary kidney cancer diagnosed each year and Australians have a one in 74 risk of developing RCC during their lifetime. Kidney cancer caused 855 deaths in Australia in 2007 (539 men, 316 women), accounting for 0.6% of all deaths. There is a 1.5:1 predominance of men over women, with peak incidence occurring between 60–70 years of age.[10]

Aetiology

There are no defined risk factors for RCC, however an association between cigarette smoking and obesity has been shown in 22% (cigarette smoking) and 35% (obesity) of new cases.[11] Some studies also suggest that hypertension may be associated with the development of RCC.[11] Inherited forms of RCC comprise about 3% of new cases, making family history important in this subset of patients.[11]

Symptoms

Approximately 15–20% of patients with small renal masses will have evidence of paraneoplastic syndromes (*Table 1*).[12] It is prudent to take a full history, looking for evidence of these during the work-up of a small renal mass.

Physical examination

It is important to look for evidence of the paraneoplastic syndromes outlined in *Table 1* on physical examination. More commonly, nothing abnormal will be detected on physical examination of a patient with a small renal mass. This again underscores the point that many of these masses are detected incidentally.

Laboratory investigations

Table 2 lists the basic investigations that should be ordered. Some of these are aimed at identifying the paraneoplastic syndromes outlined in *Table 1*.

Table 1. Paraneoplastic syndromes that may be associated with RCC

Hypertension
Anaemia
Hypercalcaemia
Cachexia
Pyrexia
Weight loss
Polycythaemia
Raised erythrocyte sedimentation rate
Abnormal liver enzymes

Table 2. Recommended laboratory investigations in the patient with an incidentally detected small renal mass

Creatinine
Haemoglobin
Erythrocyte sedimentation rate
Alkaline phosphatase
Lactate dehydrogenase
Corrected serum calcium
Estimated glomerular filtration rate

Imaging

If a renal mass is detected on ultrasound, this should be followed by a four phase contrasted computerised tomography (CT) scan of the kidneys, provided renal function allows. These four phases include: arterial, corticomedullary, nephrographic and excretory phases and allow a detailed examination of each aspect of the functional anatomy of the kidney.

Some small renal masses are cystic in nature. The Bosniak classification is used to classify these lesions, approximate risk of malignancy and direct management.[13] *Table 3* lists the Bosniak classification and *Table 4* outlines the basic management and follow up plan for patients in each of the Bosniak classifications.

If the lesion is shown to be a renal mass on CT imaging, it is vital that the radiologist looks for enhancement by comparing the Hounsfield unit (HU) readings from before and after contrast administration. A Hounsfeld unit refers to the amount of information contained in each pixel of a CT image. An enhancement is present if a change in the HU is more than 20.[16] The lesion should be considered malignant until proven otherwise. *Table 5* outlines the possible underlying pathology of a small renal mass.

When a renal mass contains a fat component it can be safely diagnosed as an angiomyolipoma (AML), which is benign. However, if there is calcification in an AML, malignancy still needs to be suspected. Other than in the setting of an AML, none of the current imaging methods can safely distinguish between benign and malignant solid tumours of the kidney.[15]

Besides imaging for the primary tumour, contrasted CT images will also provide information on the status of the contralateral kidney, any

Table 3. Bosniak classification[13]

Bosniak	Description	Malignant %
I	A benign cyst with a hairline thin wall that does not contain septa, calcifications, or solid components. It measures as water density and does not enhance	±0%
II	A benign cyst that may contain a few hairline thin septa in which 'perceived' enhancement may be present. Fine calcification or short segment of slightly thickened calcification may be present in the wall or septa. Uniformly high attenuation lesions ≤3 cm that are well marginated and do not enhance are included in this group. Cysts in this category do not require further evaluation	±1%
IIF	Cysts that may contain multiple hairline thin septa or minimal smooth thickening of their wall or septa. Perceived enhancement of their septa or wall may be present. Their wall or septa may contain calcification that may be thick and nodular, but no measurable contrast enhancement is present. These lesions are generally well marginated. Totally intrarenal nonenhancing high attenuation renal lesions ≥3 cm are also included in this category. These lesions require follow up studies to prove them benign. 'F' in this classification stands for 'follow up'	5%
III	'Indeterminate' cystic masses that have thickened irregular or smooth walls or septa in which measurable enhancement is present. Surgery is recommended for these lesions; while some will prove to be benign (haemorrhagic cysts, chronic infected cysts and multiloculated cystic nephroma), some will be malignant (cystic RCC and multiloculated cystic RCC)	35%
IV	These are clearly malignant cystic masses that can have all the criteria of Category III, but also contain enhancing soft tissue components adjacent to, but independent of, the wall or septum. These lesions include cystic carcinomas and require surgical removal	90%

local metastasis and lymph nodes status. A chest X-ray is sufficient to look for lung metastases in small renal masses. Should the chest X-ray show any abnormality, a chest CT is mandatory. In a patient with raised corrected calcium levels or raised serum alkaline phosphatase levels, a bone scan is necessary to look for bony metastasis.

In some situations, such as locally advanced tumours, tumours with venous involvement, renal insufficiency and allergy to contrast, magnetic resonance imaging (MRI) with or without gadolinium may be ordered to provide additional information in order to characterise the lesion.

The role of renal mass biopsy

The role of renal biopsy is controversial in the setting of a small renal mass. In particular there is disagreement as to whether it is necessary to biopsy these lesions before planning management and in what settings. Importantly, postsurgical histopathological review shows that about 20% of lesions that were highly suspicious of RCC on imaging were proven to be benign lesions after surgery.[16,17] It is also more likely to find benign lesions when the tumour is less than 3 cm in diameter and if found in younger women.[16] In practice, renal tumour biopsies are increasingly being used in diagnosis, follow up surveillance and in ablative therapies.[18,19]

The safety of CT guided biopsies of renal masses is well accepted. The risk of bleeding is minimal, and more importantly, the risk of needle tract seeding of tumour cells is extremely rare.[20] The sensitivity of a CT guided biopsy of a renal mass is in the range of 85–92%, with a specificity of 85–100%.[21–23] It is important to note that renal masses less than 3 cm in diameter have higher false negative rates on biopsy with a negative predictive value of about 60%.[21] Also, biopsy is generally avoided in cystic lesions.

Certainly, not all patients with small renal masses should be subjected to biopsy. Common indications include patients who opted for either active surveillance or ablative therapy (see below).[22] The decision about whether or not to biopsy a small renal mass will generally be made in the specialist setting by a urologist.

Management options

Management options for patients with a small renal mass include surveillance, surgery and ablative techniques. Current available data suggests that all three options are valid with similar short term and intermediate term oncologic outcomes.[24–26] Careful selection of patients by a urologist will largely determine the choice of management option.

Surveillance

Even if a small renal mass has imaging characteristics highly suspicious for RCC, active surveillance may be appropriate, particularly in patients with medical comorbidities that will increase the risk of active intervention such as surgery, in elderly patients and those with decreased life expectancy.[27,28] Renal impairment may also be an indication for active surveillance in some patients. Active surveillance means that the patient will either have delayed treatment or no treatment at all.

In some patients considered fit for surgery, active surveillance may be offered as a delayed intervention strategy as there is no correlation between local tumour progression and an increased risk of metastatic disease in patients with T1a lesions undergoing active surveillance.[29] Therefore, active surveillance is an appropriate strategy to initially monitor small renal masses followed by treatment for progression if required, as

Table 4. Basic management plan for patients in each of the Bosniak classification groupings[14]

Classification	General population	Comorbidities or limited life expectancy
I	No follow up	No follow up
II	No follow up	No follow up
IIF	Follow up*	Follow up or no follow up
III	Surgery	Surgery or follow up
IV	Surgery	Surgery or follow up

* CT or MRI at 6 and 12 months, then yearly for 5 years; interval and duration of observation may be varied (eg. longer intervals may be chosen if the mass is unchanged; longer duration of follow up may be chosen for greater assurance)

Table 5. Possible underlying pathology of a small renal mass

Benign	Malignant
Angiomyolipoma	Renal cell carcinoma, includes all subtypes
Renal adenoma	Urothelial cell carcinoma
Abscess	Metastatic lesion
Oncocytoma	Carcinoma of the collecting ducts of Bellini
Vascular malformation	Renal medullary carcinoma
Infarction	Renal epithelial and stromal tumours (REST)
Pseudotumour	

the short and intermediate oncological outcomes are no different from immediate surgery.[30–32]

Importantly, it must be emphasised that active surveillance is not generally recommended for young, healthy patients because, while there is some evidence it may be an option if the lesion is less than 1 cm; more data is needed before adopting this as standard protocol in this group of patients.[29] Another issue of concern when considering active surveillance in young patients is the number of scans they will require over a lifetime, which is associated with a not inconsiderable amount of radiation.

Serial CT or MRI is the preferred monitoring method for T1a lesions undergoing active surveillance. They are better than ultrasound due to better reproducibility and better resolution. Surveillance involves measurements including tumour size and growth. The recommended interval for repeat imaging is every 6–12 months.

Surgery

Surgical resection of localised RCC is the active treatment of choice for this condition as disease specific survival benefits from this treatment have been clearly shown.[33] Furthermore, patients with metastatic RCC have dismal survival rates, as most salvage systemic therapies have poor outcomes.[34] The cancer specific survival rates of patients undergoing radical or partial nephrectomy for pathological classification T1a (<4 cm) tumours are around 95% at 5 years.[33] Similar results have also been shown for laparoscopic partial nephrectomy.[35]

Traditionally, radical nephrectomy was the standard surgery offered for all kidney tumours, including T1a lesions. With this approach, cancer specific survival rates are extremely high.[36] However, current literature suggests radical nephrectomy may not be the best approach for the management of clinical stage T1 renal masses, particularly stage T1a lesions.[37] Data from multiple studies has shown an increased risk of chronic kidney disease related to radical nephrectomy and compelling correlation between chronic kidney disease and morbid cardiovascular events and mortality on a longitudinal basis.[38–41] Therefore, preservation of as many nephrons as possible is an important aspect in the decision making as this results in preservation of renal function. Based on this evidence, nephron sparing approaches should be considered the preferred approach for surgery in all patients with a clinical T1 renal mass, provided the procedure can be completed safely with good oncologic control.

Partial nephrectomy consists of planned and selective excision of the tumour with an acceptable margin of normal renal tissue, allowing for preservation of the rest of the kidney which is normal. It is worth mentioning that the complication rates for partial nephrectomy compared to radical nephrectomy is slightly higher, namely significant bleeding (3.1% vs. 1.2%), urinary leak (4.4% vs. 0%), and re-operation (4.4% vs. 2.4%).[42] The 5 and 10 year cancer specific mortality rates after open partial nephrectomy are 2.4% and 5.5% respectively, similar to rates seen after radical nephrectomy.[42] A 10 year observational study has shown that the risk of renal insufficiency (12% vs. 22%) and proteinuria (35% vs. 55%) is significantly lower in partial nephrectomy compared to radical nephrectomy.[43]

Laparoscopic partial nephrectomy is becoming widely accepted and being performed as the standard approach for T1a renal lesions. Although oncological outcome is comparable to open partial nephrectomy, many series conclude that laparoscopic partial nephrectomy is associated with greater warm ischaemia time (30 minutes vs. 20 minutes) and an increased risk of postoperative haemorrhage (4.2% vs. 2%) when compared to open partial nephrectomy.[44] Furthermore, laparoscopic partial nephrectomy involves advanced laparoscopic techniques, such as suturing, and the treatment has been largely confined to centres of surgical excellence where there is a high volume of cases. The main advantage of laparoscopic partial nephrectomy is lesser postoperative pain and earlier recovery than open partial nephrectomy.[44] Some centres are able to offer robotic assisted laparoscopic partial nephrectomy. There is no adequate data at the moment to prove the superiority or otherwise

of this approach. As expected, a recent study concluded that the use of the robot to be significantly more costly than laparoscopic and open partial nephrectomy.[45]

Ablative techniques

Since the late 1990s, ablative techniques have been employed to manage small renal masses, especially in patients with advanced age and comorbidities. The main limiting factor for ablative techniques is location; if the tumour is too close to important structures, these may be injured.

Thermal ablative energy is delivered into the renal mass via needle applicators and this generates either high or low temperatures that are lethal to the cells in the lesion. Various energy generators, ablation probes and energy delivery systems are available. The most commonly used thermal energy therapies are radiofrequency ablation (RFA) and cryoablation. Before an ablative approach, a pretreatment biopsy to clarify the histology of the renal mass should be carried out. In some centres, this is done at the time of the treatment via the same needle tract used to deliver the energy.

In RFA, radiofrequency waves cause ionic agitation which results in the generation of temperatures ranging from 50–100°C, and this causes tissue damage and coagulative necrosis.[46] Cryotherapy causes tissue destruction using repeated freeze/thaw cycles. Ice crystals are formed during the freeze cycle and this causes weakening of the cell membrane and protein denaturation. The cell then undergoes thawing, which allows water movement into the cell via oncotic pressure and lyses the cell.

Both RFA and cryoablation of small renal mass can be done via open, laparoscopic, or percutaneous image guided techniques. Percutaneous image guided ablative techniques are becoming the standard of care for treatment of small renal masses. Short term data shows tumour control was achieved in 90% of the patients undergoing RFA for small renal masses.[47–49] In patients who had cryoablation, 73% of these masses were not detectable on MRI at 5 years.[50] However, long term data is lacking for both these techniques.

Complications of thermal ablations are bleeding, hematomas, visceral injury, damage to collecting system and hematuria. Major complications following RFA and cryoablation were 2.2% and 1.4% respectively, while minor complications were 6% and 12.2%.[51]

Case follow up

Joan underwent a successful laparoscopic partial nephrectomy. She was discharged home on day three of surgery and had minimal pain. Her histopathology confirmed an RCC with Fuhrman (the RCC histopathological grading system) 'Grade 2' and clear surgical margins. Her follow up renal function was similar to her pre-operative parameters.

Summary of important points

- Renal cell carcinoma represents 2–3% of all cancers and more than 50% of these are detected incidentally.
- Small renal masses are defined as renal masses less than 4 cm in diameter. Some are cystic in nature.
- 20% of small renal masses are benign, and 20–25% prove to be potentially aggressive kidney cancers at the time of diagnosis.
- Work-up involves a full history, looking for evidence of paraneoplastic syndromes, and examination, which is usually normal. Recommended blood tests include basic biochemistry and haematology, and imaging.
- A four phase contrasted CT scan of the kidneys allows a detailed examination of each aspect of the functional anatomy of the kidney, which can help approximate risk of malignancy and direct management.
- Management options include active surveillance, surgery and ablative techniques.
- Not all patients with small renal masses require a biopsy. However, biopsy is required in patients who opt for active surveillance or ablative therapy.

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