Population Covered By The Guidance

This pathway provides guidance on the further imaging investigation of adult patients with a renal mass that is clinically palpable or incidentally found on previous imaging.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points.
Clicking on the PINK text box will bring up the full text.
The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

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Pathway Diagram
Simple Renal Cyst

Image 1 (Ultrasound): Small simple benign cyst (arrow) in the upper pole of the right kidney with foci of calcification in or adjacent to the wall.

Renal Cell Carcinoma

Image 2 (Computed Tomography): Large right kidney mass with central necrosis consistent with renal cell carcinoma. There is tumour extension into the right renal vein (arrow).

Renal Cell Carcinoma

Go to Renal Cell Cancer (Staging) Pathway
Image 3a: Nephrectomy showing a circumscribed and encapsulated renal cell carcinoma arising from the lower pole of the kidney. The cut surface shows a heterogenous appearance typical of malignancy with patchy areas of necrosis (blue arrow) and haemorrhage (red arrow).

Image 3b (H&E, x10): Histological section of a conventional clear cell renal cell carcinoma showing sheets and nests of malignant cells with intervening thin-walled vessels. The cells demonstrate irregular and hyperchromatic nuclei surrounded by abundant clear cytoplasm (clear cells).

Teaching Points

- Is the mass a simple cyst? If not, further investigation is indicated
- If the mass is solid, urology review is indicated
- Solid masses or complex cysts (Bosniak IIF-IV) require active surveillance or intervention

Renal Mass

- An indeterminate renal mass is one that cannot be diagnosed confidently as either benign or malignant at the time of its discovery on imaging
- Renal cell carcinoma (RCC) represents 2% of cancers worldwide, with the highest incidence in Western countries
- There is a 1.5:1 male predominance, with peak incidence between 60 and 70 years. Aetiological factors include smoking, obesity and hypertension
- Due to increased detection of tumours by ultrasound (US) and computed tomography (CT), the number of incidentally diagnosed RCCs has increased. The majority of these tumours are smaller and of a lower stage
- The treatment paradigm for the past four decades is to remove solid renal masses on their detection, and thus the rate of surgery has paralleled the rise in incidence of renal cell carcinoma, most notably for tumours < 4cm
- However, data from a large cohort of 34,500 renal cancer patients demonstrates the increased detection and treatment of small renal cancers has not translated into improved mortality rates for renal cancer patients. This suggests a proportion of these smaller renal cell carcinomas may be an indolent form that does not warrant surgery

Clinically Suspected Mass

- More than 50% of RCCs are detected incidentally by non-invasive imaging used to investigate non-related abdominal diseases and symptoms
- The classic triad of flank pain, macroscopic haematuria and a palpable abdominal mass is rare (6-10%) and often correlated with advanced disease
- Physical examination has a limited role in the detection of RCC

Incidental Imaging Finding

- Most renal tumours are discovered incidentally by abdominal US or CT performed for other
indications

Ultrasound (US)

- US plays an important role in the detection and characterisation of renal masses. US is often sufficient as a standalone modality to characterize most cystic renal masses as benign, particularly those in Bosniak category I and II.
- The criteria for US diagnosis of renal cysts are well defined. To diagnose renal cysts via US, the mass must be sonolucent, demonstrate good through-transmission of the sound waves with posterior enhancement, and have a thin, well-defined wall.
- Complex masses not fulfilling the criteria of simple cysts are considered indeterminate and require further evaluation, usually by CT.
- There has been recent interest in the use of contrast enhanced US (CEUS) for the staging and characterisation of RCC.
- US contrast agents are composed of tiny bubbles of perfluorocarbon or sulfurhexafluoride gas, stabilised in a lipid or protein shell. These microbubbles avoid filtration in the lungs because of their comparable size to red blood cells. These bubbles are highly echogenic on US, and therefore provide what is essentially a real-time ultrasound angiogram.
- On CEUS, RCCs are typically heterogeneously hypervascular, with early washout in the delayed phase. CEUS can also help differentiate between benign and potentially neoplastic cysts by demonstrating contrast enhancement in septations and nodular protuberances.
- A study of 143 lesions demonstrating CEUS could predict malignancy with a sensitivity of 97% and specificity 45% and positive predictive value of 91%.

Simple / Benign Cyst

- Simple cysts are diagnosed accurately by ultrasound.
- Characteristic findings of a simple cyst include:
  - Anechoic contents
  - Sharply defined far wall
  - Acoustic enhancement deep to lesion, and
  - Imperceptibly thin walls
- Cysts with thin septations or thin peripheral curvilinear calcifications still qualify as benign cysts.

Computed Tomography (CT)

- CT is the modality of choice for evaluating indeterminate renal lesions that are suspicious for malignancy.
- The sensitivity of CT in detecting small renal masses (< 3cm) is > 90%.
- This is similar to MRI, which demonstrates sensitivity of 95%.
- On unenhanced CT, homogenous lesions measuring < 20 HU or > 70 HU can be considered benign, whereas those 20-70 HU can be considered indeterminate and require further evaluation.
- For lesions of HU 20-70, enhancement after IV contrast determines whether a renal mass warrants treatment.
- Proper assessment of a renal mass requires at least 3 phases: non-contrast, corticomedullary and nephrogenic phases.
Non-contrast: important baseline for measurement of enhancement characteristics of the renal mass. Most RCCs are solid lesions with HU > 20 on NECT

Corticomedullary: 25-70 sec after contrast injection. Gives best delineation of arterial anatomy and tumour involvement, as well as hypervascular metastases

Nephrogenic: 80-180 sec post injection of contrast. Contrast filters through glomeruli into collecting tubules. Gives best opportunity for differentiation between normal medulla and masses

- The presence of enhancement is an important criterion for differentiating malignant from benign lesions, although this is not specific, such as in the case of minimal fat angiomyolipoma and oncocytoma
- In CT, evaluation of enhancement is performed by measuring HU both before and after the administration of contrast. Renal cell cancer enhancement is best identified in the nephrographic phase. Any enhancement that is identified must be unequivocal. Enhancement of the lesion may be assessed by comparing Hounsfield Unit (HU) increase from the non-contrast to the nephrographic phase. There is no universally agreed value suggesting malignancy. Anything over 20 HU increase should be regarded as likely malignant. Between 10-20 HU increase is indeterminate and requires further investigation

A fourth ‘excretory phase’ can be used for further evaluation of a centrally located mass within the collecting system. This phase starts at approximately 180 sec after injection of contrast. The comprehensive multiphase examination is known as CT Urography (CTU)

- CT urography has largely replaced intravenous urography for the evaluation of patients with haematuria. IV urography with nephrotomography has only 67% sensitivity in detecting renal masses < 3 cm in diameter
- CT urography provides a more comprehensive evaluation of the urinary tract, including detection of renal calculi and masses, as well as assessment of the urothelial tract

### Magnetic Resonance Imaging (MRI)

- MRI using IV gadolinium contrast agents provides sensitivity and specificity similar to that of CT in detecting contrast enhancement and identifying a mass requiring surgery
- Similar to CT, MRI allows accurate diagnosis of RCC, but cannot reliably distinguish oncocytoma and fat-free angiomyolipoma from malignant renal neoplasms
- There have been a number of recent systematic reviews and meta-analyses of diffusion weighted MRI for renal mass assessment. The meta-analysis by Lassel et al. suggests that evaluation of ADC values can help to determine between benign and malignant lesions, as well as differentiate oncocytomas from malignant tumours
- If the results of CT are indeterminate, MRI may provide additional information on enhancement of renal masses; local advanced malignancy; and venous involvement if the extent of IVC tumour thrombus is poorly defined on CT
- MRI is indicated in patients who are allergic to intravenous CT contrast medium
- Contrast enhanced MRI should not routinely be recommended to pregnant patients due to concerns regarding the safety of gadolinium-based contrast agents

### Angiomyolipoma (AML)

- AMLs are benign mesenchymal tumours that occur four times more commonly in women. 20% of AMLs are seen in the setting of tuberous sclerosis (TS)
- Diagnosis can be made by identifying adipose tissue within the lesion on imaging (CT or MRI)
The main complications of renal AML are bleeding into the retroperitoneum or collecting system, which can be life-threatening. The major risk factors for bleeding in AML are tumour size, grade of the angiogenic component, and the presence of TS (tuberous sclerosis). While active surveillance is the most appropriate option for most AMLs, typically, large AMLs are treated with surgery or selective arterial embolisation. Indications for intervention are pain, bleeding, or suspected malignancy. Recent European guidelines suggest that a recommended size threshold for prophylactic treatment does not exist (the formerly recommended size of > 4 cm can be disputed). The European Association of Urology Guidelines 2015 recommend that prophylactic intervention also may include women of childbearing age and patients with whom access to emergency care is limited.

Solid Mass, Indeterminate

The differential diagnosis for solid renal masses includes RCC and benign lesions such as minimal fat angiomyolipomas (AMLs) and oncocytoma. CT allows accurate diagnosis of RCC, but cannot reliably distinguish oncocytoma and fat-free angiomyolipoma from malignant renal neoplasms. CT detection of small amounts of fat defines the benign AML. However there is a portion (5%) of AMLs containing minimal or no fat, making them indistinguishable from RCC. One study suggested oncocytomas could be reliably predicted based on arterial phase enhancement greater than 500% and washout values greater than 50%.

Solid Mass, Likely Malignant

There are three main RCC types: clear cell (ccRCC), papillary (pRCC - type I and II) and chromophobe (chRCC). Other renal tumours constitute the remaining 10-15% of renal cortical tumours. Oncocytomas are benign and make up 3-7% of all renal tumours. For a suspected malignant renal tumour, surgery is the mainstay of treatment. Biopsy may be considered for confirmation of RCC if

- Surgical risk is high
- Disease is locally advanced or metastatic
- Prior to ablative therapies
- Mass is present in a single or transplant kidney
- Or when alternative diagnoses such as lymphoma, metastasis or infection are considered

Cystic Mass

The Bosniak system classifies renal cysts into five categories, based on CT imaging appearance, to predict malignancy risk.

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<tr>
<th>Bosniak Category</th>
<th>Features</th>
<th>Work-up</th>
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<tr>
<td>Bosniak Category</td>
<td>A summary of the Bosniak classification of renal cysts is below.</td>
<td>29</td>
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<table>
<thead>
<tr>
<th>I</th>
<th>A simple benign cyst with a hairline thin wall that does not contain septa, calcification or solid components. It measures as water density and does not enhance with contrast material</th>
<th>Benign</th>
</tr>
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<tbody>
<tr>
<td>II</td>
<td>A benign cyst that might contain a few hairline thin septa. Fine calcification might be present in the wall or septa. Uniformly high-attenuation lesions of &lt; 3 cm that are sharply marginated and do not enhance</td>
<td>Benign</td>
</tr>
<tr>
<td>IIIF</td>
<td>These cysts might contain more hairline thin septa. Minimal enhancement of a hairline thin septum or wall can be seen and there might be minimal thickening of the septa or wall. The cyst might contain calcification that might be nodular and thick but there is no contrast enhancement. There are no enhancing soft-tissue elements. Totally intrarenal non-enhancing high-attenuation renal lesions of ≥ 3 cm are also included in this category. These lesions are generally well marginated</td>
<td>Follow-up. Some are malignant</td>
</tr>
<tr>
<td>III</td>
<td>These lesions are indeterminate cystic masses that have thickened irregular walls or septa in which enhancement can be seen</td>
<td>Surgery or active surveillance. Over 50% are malignant</td>
</tr>
<tr>
<td>IV</td>
<td>These lesions are clearly malignant cystic lesions that contain enhancing soft-tissue components</td>
<td>Surgery. Most are malignant</td>
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**Urology Review Options**

- A systematic review of studies that reported surveillance of localised renal masses concluded that active surveillance for localized solid renal masses should only be considered as an alternative to definitive therapy in select patients with limited life expectancy, competing health risks precluding surgery, or significant potential for requiring renal replacement therapy. 44
- Analysis of a large renal cancer database has found that nephrectomy appears to have an overall cancer-specific survival over non-surgical management by as much as 9.4% at 5 years, age-adjusted. 45
- However, analysis of the same SEER database demonstrated no improvement in mortality rates from all causes despite increased surgery of smaller renal cancers. 8
- Active surveillance as a diagnostic strategy for the small indeterminate renal mass is concluded as being appropriate in more current epidemiologic series. 8,46
- In a meta-analysis by Kunkle et al, no statistical differences were detected in the incidence of metastatic progression of small renal masses regardless of whether lesions were excised, ablated or observed. 46
There is no optimal diagnostic and management pathway when it comes to small renal masses in the elderly

Other Imaging

- Nuclear medicine: FDG PET may prove useful in detecting renal tumours and characterising indeterminate renal cysts, however low sensitivity and diagnostic accuracy of FDG-PET for RCC detection has limited its use for this purpose. There may be a role of PET for detection of distant metastases in RCC 55,56
- Intravenous urography: IV urography with nephrotomography has only 67% sensitivity in detecting small renal masses (< 3cm diameter). 1 It is now seldom used in the investigation of the indeterminate renal mass and has largely been replaced by CT urography for evaluation of patients with haematuria 2
- For central renal masses abutting or invading the collecting system, urine cytology and possibly endoscopic assessment should be considered in order to rule out urothelial cancer 9

Biopsy, Surgery, Tumour Ablation

- Surgical excision of renal cancer is considered to be the standard of care in most patients
- However, ablative therapy is highly advantageous in selected patients. Active surveillance may be appropriate in others, particularly the elderly and those with co-morbidities with small tumours
- The use of percutaneous sampling of renal tumours has previously been limited due to concerns about diagnostic yield, safety and lack of impact on clinical management 47
- However, modern biopsy techniques and improved expertise and understanding of the clinical indications of biopsies have resulted in a recent increase in the number of renal biopsies performed 48
- Core biopsy is preferred over fine needle aspiration (FNA) due to better diagnostic accuracy for malignancy 48
- A meta-analysis and systematic review of the literature has shown that renal tumour core biopsy has sensitivity and specificity of 99.1% and 99.7% respectively for the diagnosis of malignancy, as well as good accuracy for histological sub-type, and fair accuracy for predicting tumour grade 48
- While FNA has a lower sensitivity and specificity (93.2% and 89.8%), there may be a potential advantage to FNA in that intraprocedural assessment of the cytological specimen can be performed 48
- Complications from renal biopsy include: lumbar pain, haematuria, perirenal haematoma, pseudoaneurysm and pneumothorax. Both core biopsy and FNA have low reported complication rates, with the median complication rate of about 8%. However most complications were mild and self-limiting 48

Indications, contraindications and potential complications of percutaneous renal tumour biopsies [reproduced from Volpe, 2012 49]

Indications

- Small renal masses that are indeterminate on
abdominal imaging (including selected indeterminate cystic lesions)
- Renal masses that are suspicious for metastatic disease in the presence of a known extrarenal malignancy
- Incidentally diagnosed small renal masses in patients who are potentially candidates for active surveillance or minimally invasive ablative therapy to support treatment decisions
- Renal tumours during follow-up of thermal ablation to confirm histologic success and monitor for recurrence
- Primary renal tumours in the setting of metastatic disease to select the optimal biologic systemic therapy, particularly when a cytoreductive nephrectomy is not indicated or neoadjuvant systemic therapy is planned
- Unresectable retroperitoneal renal tumours involving the kidney

**Contraindications**

**Complications**

**Nephron-sparing surgery**

- Most RCCs are diagnosed at a localised stage (T1-2N0M0 or stage I-II)
- Until recently, open radical nephrectomy has been the mainstay of curative treatment of RCC
- Nephron sparing surgery (NSS; partial nephrectomy) is now accepted treatment, particularly in T1 (< 7cm) lesions, when a nephrectomy would render the patient anephric or at high risk of requiring dialysis
- One meta-analysis demonstrated partial nephrectomy results in significantly better preservation of renal function when compared to radical nephrectomy
- Based on current available oncological and quality of life outcomes, localised renal cancers
are better managed by nephron sparing surgery rather than radical nephrectomy, irrespective of the surgical approach 50,51
- Partial nephrectomy may not be appropriate due to unfavourable tumour location, locally advanced tumour growth or significant deterioration in patient health

Tumour ablation

- The treatment strategy for small renal masses is currently evolving
- About 25% of renal masses measuring 3 cm or smaller will be benign, and of those that are malignant, most will be of low grade 52
- Tumour ablation is a form of nephron sparing surgery, which includes radiofrequency ablation (RFA) and cryoablation, and can be performed both intra-operatively and percutaneously under imaging guidance
- Tumour ablation is considered a less-invasive treatment option for small renal cell carcinoma, which may be advantageous in the high surgical risk patient, acknowledging the increased risk of local tumour recurrence compared to surgical excision 53
- Disadvantages of percutaneous tumour ablation include lack of long-term data, inadequacy for treating large or central tumours and the likelihood of making any future extirpative surgery more difficult 54
- The available evidence around minimally invasive ablative techniques is weak and there is no definite evidence of superior perioperative or quality of life outcomes compared to nephrectomy 50

References

Date of literature search: December 2015

The search methodology is available on request. Email

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

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