Population Covered By The Guidance

This pathway provides guidance on the imaging of adult patients with unexplained painless visible haematuria.

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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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<th>SYMBOL</th>
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<th>EFFECTIVE DOSE RANGE</th>
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<td>&lt; 1 millisieverts</td>
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<tr>
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<td>Medium</td>
<td>&gt; 10 mSv</td>
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Pathway Diagram
**What do I need to know?**

1. Is this the first presentation of visible haematuria?
2. Is the patient at high risk or low risk?
3. Is there renal impairment?
4. Is the patient pregnant or do they have renal failure or a single kidney?

Any single episode of visible haematuria is considered significant and should be referred for urological assessment.

- Clinical examination including blood pressure
- Risk assessment
- Urea & electrolytes, eGFR, albumin : creatinine ratio
- Consider FBC, coagulation profile, PSA
- Urine dipstick, urine microscopy, urine culture and sensitivity

**Treat UTI if present and repeat urinary microscopy**

**Are the following present?**

- An increase in serum creatinine of ≥0.3 mg/dL (≥2.64 μmol/L), a percentage increase in serum creatinine of ≥50% (1.5-fold from baseline) or reduction in urine output (documented oliguria of less than 0.5 m/L per hour for more than six hours)
- eGFR <30 ml/min/1.73m² (Stage 4 or 5 chronic kidney disease)
- Significant proteinuria (ACR ≥30mg/mmol or PCR ≥50mg/mmol)
- Glomerular haematuria with macroalbuminuria
- Isolated haematuria with hypertension in those aged <30 years
- Visible haematuria coinciding with intercurrent (usually upper respiratory tract) infection

Note: ACR (albumin / creatinine ratio); PCR (protein / creatinine ratio)

**Yes**
- Nephrology referral

**No**
- Accompanying

**Low risk**
- Ultrasound urinary tract

**High risk**
- CT urography (CTU) or MR urography (MRU)

Flexible cystoscopy (under local anaesthesia) ↓
Rigid cystoscopy (under general or spinal anaesthesia) ↑
- Retrograde pyeloureterogram (RPUG)
- Urine cytology
  (in selected patients)

**Negative findings**
- CT Urography already performed?

**Yes**
- Appropriate management

**No**
- Consider CT Urography or MR Urography

**Positive findings**
- Appropriate management

Follow-up
Image Gallery

Note: These images open in a new page

1a

Transitional Cell Carcinoma (TCC)

Image 1a and 1b (Computed Tomography): Axial and coronal images of a large transitional cell carcinoma arising from the left lateral wall of the bladder and extending into the rectum and surrounding soft tissues. There is secondary hydronephrosis of the left kidney from ureteric obstruction.

1b

2

Transitional Cell Carcinoma (TCC)

Image 2: Cystoprostatectomy and bilateral nephroureterectomy showing severe bilateral hydroureter, hydronephrosis and renal cortical atrophy secondary to an extensive bladder transitional cell carcinoma causing ureteric obstruction.

3

Transitional Cell Carcinoma (TCC)

Image 3: Cystectomy showing a polypoid tumour arising from the mucosa of the bladder, confirmed to be a transitional cell carcinoma on histology.

Teaching Points

- Any single episode of visible haematuria (VH) is considered significant and should be referred for urological assessment. There is consensus that VH may be a sign of serious underlying disease, including malignancy, and warrants a thorough diagnostic evaluation, and this is usually done with a combination of
clinical examination, cystoscopy, and urinary tract imaging

- A cystoscopy should be performed on all patients who present with risk factors for urinary tract malignancies (e.g. irritative voiding symptoms, current or past tobacco use, chemical exposures) regardless of age
- Plain X-ray kidneys, ureters and urinary bladder (KUB) has no role in the detection of renal and urothelial carcinoma due to its limited sensitivity and should be avoided, especially in high-risk patients, as further imaging will almost always be required
- Ultrasound remains an important diagnostic tool for the evaluation of haematuria in radiation-sensitive populations, low-risk patients and for characterizing bladder abnormalities and cystic renal lesions
- MDCT urography (CTU) is the most sensitive and specific test for the diagnosis of urinary tract calculi and for detecting and characterizing renal masses. Split-bolus and low-dose imaging techniques are potentially effective methods of reducing radiation dose
- Magnetic Resonance Urography (MRU) is emerging as a potentially non-invasive comprehensive imaging test for evaluating the upper urinary tract without the use of ionizing radiation and thus is particularly useful in children and pregnant women. However, it is inferior to CTU in detection of urothelial lesions

Haematuria (Painless Visible)

- The presence of haematuria, often intermittent but rarely factitious may be the sole symptom of an underlying disease, either benign or malignant. It is one of the most common presentations of patients with urinary tract diseases and of patients referred for urinary imaging. ‘Painless’ visible haematuria is the commonest presentation of bladder cancer
- The prevalence of carcinoma among patients with visible haematuria (VH) attending a haematuria clinic has been reported to be as high as 19% but more typically ranges between 3% and 6%. Other authors have reported that approximately 5% of patients with painless haematuria and up to 22% with VH will have bladder cancer, while the prevalence of all urologic malignancies among patients who presented with VH is between 22.0%-24.2%. Thus, there is consensus that VH may be a sign of serious underlying disease, including malignancy, and warrants a thorough diagnostic evaluation, and this is usually done with a combination of clinical examination, cystoscopic evaluation, and urinary tract imaging
- Urinary tract malignancy is four times more common in patients with VH than non-visible haematuria (NVH) with VH being the presenting symptom in 80% of bladder cancers and half of all renal cancers. The diagnosis is often delayed due to the similarity of these symptoms to benign disorders (e.g. urinary tract infection, interstitial cystitis, prostatitis, passage of renal calculi), and delays
can lead to a worsened prognosis due to more advanced stage at diagnosis 9

- Bladder tumours account for 90-95% of urothelial carcinomas (UCs) and are the most common urinary tract malignancy. The most common symptom of bladder cancer is haematuria, which usually occurs suddenly and is generally painless. 10 In 2011 alone, 2404 new cases of bladder cancer were diagnosed in Australia. It is significantly more common in men - the risk of bladder cancer by age 85 is 1 in 43 for men, compared to 1 in 166 for women. In 2012, there were 1038 deaths caused by bladder cancer in Australia. No screening test is routinely used for bladder cancer. Other less common symptoms include incomplete voiding, dysuria and frequency which again is seen with other benign conditions. The five year survival rate for Australians with invasive bladder cancer is 58% 11

**Treat Urinary Tract Infection (UTI): Exclude Transient Causes**

- Consensus from the British Association of Urological Surgeons (BAUS) 12, the Interregional Chiefs of Urology Service (IRCUS), Kaiser Permanente, America 13 and the American Urological Association 14 suggests that any single episode of visible haematuria (VH) is considered significant and should be referred to a urologist. Additionally, BAUS also recommends that patients with symptomatic non-visible haematuria (NVH) and those aged over 40 years with asymptomatic NVH, should be referred for urological assessment. Furthermore, the proposed evaluation should only be performed when the benefits outweigh the risks considering the evidence for the risk of cancer developing within two to five years in patients with haematuria is in the range of 0% to 3% 13

- In the interim, concurrent investigations should be carried out to determine transient, treatable causes and to arrange for primary imaging. UTI presenting with haematuria is not uncommon, though this is usually symptomatic, as opposed to “painless”. BAUS suggests that after one positive urinalysis, patients should be referred to a urologist for full evaluation of the upper and lower urinary tracts, principally to exclude life-threatening malignancy. 12 The presence of VH should also not be attributed to anti-coagulant or anti-platelet therapy and these patients should be evaluated regardless of these medications, 12 as reports of underlying malignancy was found in 24% and 7% of patients in two separate series. 8 This reinforces the need for thorough urological evaluation which should not be foregone in patients receiving anticoagulants

- Malignancy commonly coexists with or indeed can be the cause of UTI. UTI should be treated and there is a risk of uro-sepsis if cystoscopy is performed in the presence of active UTI

- Results from a study 15 reported that the current risk of urologic malignancy in patients with a positive mid-stream urine (MSU) specimen collected at the
one stop fast track haematuria clinic is as high as 20% and have concluded that the presence of UTI does not decrease the likelihood of having a urologic malignancy diagnosed. Therefore a patient with visible haematuria irrespective of urine culture status on a specimen collected at the haematuria clinic requires urgent investigation

- The differential diagnosis includes (though not limited to)
  - Urinary tract malignancy
  - Urinary calculi
  - Infections
  - Trauma
  - Benign prostatic hypertrophy
  - Haemorrhagic cystitis
  - Nephrological disease
  - Bleeding diathesis / anticoagulation therapy
  - Arteriovenous malformation / angiomyolipoma

- PSA is controversial in these patients but if performed (not unreasonable in men > 40) it should be done after UTI is excluded by MSU

**Nephrology Referral**

- Referral to nephrology if
  - An increase in serum creatinine of $>0.3$ mg/dl (>26.4 µmol/L), a percentage increase in serum creatinine of $>50\%$ (1.5-fold from baseline) or reduction in urine output (documented oliguria of less than 0.5ml/kg per hour for more than six hours
  - eGFR <30ml/min/1.73m² (stage 4 or 5 chronic kidney disease)
  - Significant proteinuria (ACR ?30mg/mmol or PCR ?50mg/mmol)
  - Glomerular haematuria with macroalbuminuria
  - Isolated haematuria (i.e. in the absence of significant proteinuria) with hypertension in those aged <40
  - Visible haematuria coinciding with intercurrent (usually upper respiratory tract) infection

- The presence of dysmorphic red blood cells, proteinuria, cellular casts, and/or renal insufficiency, or any other clinical indicator suspicious for renal parenchymal disease warrants concurrent nephrologic workup but does not preclude the need for urologic evaluation

**Urology Referral**

- Referral to urology if
  - Visible haematuria in all patient (regardless of age)
  - Patients with any symptomatic non-visible haematuria in the absence of UTI or other
transient causes (regardless of age)
- Male patients with asymptomatic non-visible
- All patients with asymptomatic non-visible and other risk factors
- Females with asymptomatic non-visible haematuria aged >40 years do not require urology referral

Risk Stratification

- Risk factors for the development of renal and urologic malignancies 14,16,17,18
  - Age >40 years
  - Men presenting with gross (visible / macroscopic) haematuria. Men have a 3x greater risk than women for urothelial tumour. Although the risk is still small in men <40 years of age, whether to place such patients in low or high risk categories is discretionary and should be based on clinical features and presence of other risk factors
  - Smoking
  - History of genito-urinary malignancy
  - Analgesic abuse (e.g. phenacetin)
  - Exposure to chemical carcinogens (e.g. aromatic amines)
  - Occupational carcinogens (e.g. metal workers, painters, rubber manufacture)
  - Chronic inflammation of urinary tract (e.g. calculi, diverticula, and infection)
  - Congenital anomalies (e.g. horseshoe kidney)
  - Pelvic irradiation

- Currently, there is insufficient data available to derive an evidence-based algorithm of the diagnostic pathway for haematuria. An algorithm based on the opinion and practice of clinical experts in the review team, other published algorithms and the results of economic modelling is currently being utilized as guidance 19
- Traditionally, first-line investigations often include conventional radiography, renal ultrasound, and/or intravenous pyelogram (IVP) in combination with cystoscopy. Second-line investigations include multi-detector computed tomography urogram (MDCTU) and magnetic resonance urography (MRU), often only carried out if the first-line tests reveal an abnormality. The imaging evaluation will almost always be accompanied by cystoscopy to evaluate the urinary bladder, since many bleeding urinary tract lesions arise in the urinary bladder and imaging procedures are not yet conclusively proven to be as sensitive as cystoscopy in diagnosing most of them 7
- IRCUS has recommended that a modified CTU or IVP with concurrent renal ultrasound be performed for patients with significant haematuria. As long as the renal ultrasound is done concurrently with IVP, there is no need for renal tomography. This approach will reduce the risk of ionizing radiation 13
- A method of triaging patients by incorporating the risk score has been proposed. Recommendations for patients with a risk score of 18
  - >3 should undergo CT urography
  - <3 undergo unenhanced CT of the kidney, ureters and bladder or ultrasonography

Risk factors and risk scores for UCC

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Score</th>
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<tr>
<td>Haematuria</td>
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Visible
Non-visible, persistent
Non-visible, unspecified

**Imaging findings**
- UUT-UCC
- Bladder cancer
- Renal mass
- Hydronephrosis, hydroureter
- Stone, large, for planning percutaneous nephrolithotomy

**Urine cytology**
- Normal, atypical probably benign, atypia of uncertain significance
- Atypia suspicious of malignancy and malignant
- Occupation al exposure to aromatic amines or benzenes, smoking, analgesic abuse, phenacetin
- Urethral stricture preventing cystoscopy

\(^a\) urothelial cell carcinoma
If ultrasonography or unenhanced CT reveal an increased risk for urothelial cell carcinoma (UCC) as defined by the risk score (≥3), then CTU becomes justified. The optimum diagnostic imaging strategy for patients at high risk for UCC consists of initial CT urography as a replacement for conventional upper tract imaging techniques and as a triage test for bladder assessment. For patients at low-risk of UCC, ultrasonography and unenhanced CT of the kidneys, ureters and bladder should be used instead. The European Society of Urogenital Radiology (ESUR) has suggested that the investigation of low-risk patients requires ultrasound and cystoscopy and high-risk patients require CTU and cystoscopy for thorough renal and urinary tract imaging.

Ultrasound Urinary Tract

Ultrasound is still vital in the initial assessment of haematuria. Apart from being readily available at point-of-care, it involves no exposure to radiation and is an inexpensive imaging technique. US allows unlimited scan planes thus permitting good visualisation of the kidneys and urinary bladder. Additionally, Doppler studies can provide further information regarding vascularity. It is especially useful in radiation-sensitive populations, such as children and pregnant or child-bearing age women. Ultrasound is effective in the detection of upper urinary tract tumours, though more sensitive for renal cell carcinoma than for upper tract transitional cell carcinoma. Compared to the use of US and IVP, US alone provided a sensitivity of 94.5% for the detection of all upper tract malignancies. This is supported by more recent studies that show US being more sensitive than IVU in diagnosing urological malignancy including the detection of renal and bladder tumours. The sensitivity of ultrasonography is, however, not sufficient to obviate the need for cystoscopy because of its lack of sensitivity in detecting small tumours <0.5 cm in diameter. In a prospective study of 141 patients, US showed a higher sensitivity (96% versus 25%) and negative predictive value (98% versus 91%) than IVP in detecting abnormalities of the upper urinary tract in patients present with haematuria. However, in comparison to cross-sectional imaging modalities such as MDCTU or MRU, US has a lower sensitivity in detecting urinary tract abnormalities. The authors therefore concluded that, US should replace IVU for first-line screening of the upper tracts in radiation-sensitive populations and patients with glomerular disease as the cause of haematuria.

Ultrasound is useful in detecting obstructive uropathy, such as hydronephrosis and hydroura, secondary signs of bladder tumours obstructing the vesicoureteric junction. Synchronously, it allows for interventional procedures such as renal biopsy in the same setting if indicated. Ultrasound allows for lesion characterization as it can accurately distinguish cystic from solid masses. It is excellent for defining the internal architecture of a renal mass and determining the Bosniak grade, which guides management and prognosis. Ultrasound has also been reported to be the most cost effective method for the assessment of renal masses detected at IVU as over 80% of these masses are found to be simple cysts. Apart from operator and patient’s body habitus dependency, the low spatial and contrast resolution compared to other modalities, another inherent disadvantage which limits the
acceptance of US as a comprehensive single-step screening test in case of haematuria is its variable sensitivity in detection of urothelial carcinomas, \(8, 20\) with moderate (82%) sensitivity for renal pelvis carcinoma detection and sensitivities as low as 12% for the detection of urothelial carcinoma of the ureter. \(8\) The sensitivity of ultrasound for the detection of bladder TCC however has been reported as being as high as 95% \(16\).

- Therefore utilizing US as a first line imaging modality in the assessment of haematuria seems justifiable. \(20\) Ultrasound remains an important diagnostic tool for the evaluation of haematuria in children and in low-risk patients and for characterizing bladder abnormalities and cystic renal lesions \(16\).
- Other protocols have used a combination of ultrasound and IVU with success for a comprehensive assessment of the upper urinary tract in the evaluation of haematuria \(1\).
- More recently, the European Society of Urogenital Radiology (ESUR) had suggested that the investigation of low-risk patients requires ultrasound and cystoscopy and high-risk patients require CT urography and cystoscopy for thorough renal and urinary tract imaging \(17\).
- In efforts to define which patients require a CT urography (CTU) for further evaluation of haematuria, a large prospective study of 841 patients, revealed that for patients who present with NVH, ultrasonography is sufficient to exclude significant UUT disease while for patients with VH, in-view the likelihood of finding UUT disease is higher, CTU as a first-line test seems valid \(24\).

### Computed Tomography Urography (CTU)

- With the advent of multi-detector row CT, it is possible to perform a comprehensive evaluation of haematuria with a single investigation. There is evidence to suggest that multi-detector CTU (MDCTU) should be employed in the evaluation of patients, when other diagnostic tests fail to elucidate a cause of painless VH. The scan protocol should include; non-contrast scan, nephrographic and excretory phase \(25, 26, 27, 28\).
  - The non-contrast images are used to detect renal calculi
  - The nephrographic phase (acquired 90-100 seconds after administration of a non-ionic contrast) has the highest sensitivity in the detection of renal masses, and correlation with unenhanced images is required to show unequivocal enhancement
  - The pyelographic phase / excretory phase (acquired 5-15 minutes after contrast administration) is used to assess the collecting system, ureters and bladder
- Compression, an IV saline bolus, and diuretics have been used to optimize ureteric distention with variable results
- Computed tomography has been shown to be superior to trans-abdominal ultrasound in the detection and characterisation of <3 cm renal masses \(29\).
- Small retrospective studies have reported promising results. Sensitivities of 57-89% have been reported on a ‘per lesion’ identification of urothelial tumours when compared to surgery, other invasive procedures or follow-up \(30\).
- Excretory phase CT urography was comparable with IVU for evaluation of the urinary tract in patients with painless haematuria. \(31\) Furthermore, sensitivity of MDCTU is superior to IVU in the detection of upper urinary tract-urothelial cell carcinoma. \(22, 32\) Other authors report sensitivity and specificity for upper urothelial urinary cancer detection with CTU between 67-100% and 93-99% respectively. \(10\) However cystoscopy remains the gold standard in the detection of lower urinary tract (bladder) urothelial tumours, \(19\) as neither IVU nor MDCTU have significant sensitivity to exclude an abnormality of the bladder mucosa \(26, 32\).
- Whether CTU should replace excretory urography (IVU) in the evaluation of haematuria remains controversial. Definitive resolution of this question is limited by a lack of randomized studies. \(27, 28\)
- The radiation exposure is much higher in MDCTU when compared to IVU and is highly dependent on the exact CT protocol / technique used \(33\).
Currently, there have been differing views on haematuria guidelines on how to specifically utilize CTU.

When applied to selected high-risk groups of VH, transitional cell carcinoma (TCC) tumour prevalence may increase to 25-30% and it has been shown that CTU of the UT is equivalent to retrograde pyelogram (RP). CT may still have problems of correctly staging advanced tumours.

CTU can also be powerful in the diagnosis of bladder tumours, but results differ depending on the specific population studied where in the high risk group with macroscopic haematuria, unequivocal CTU results were 93% sensitive and 99% specific for detection of bladder cancer with an overall negative predictive value (NPV) for CT urography (95%, 649 of 681) as high as cystoscopy (99%, 634 of 641). The high negative predictive value (NPV) of CT urography in patients with haematuria may obviate cystoscopy in selected patients.

A large cohort study consisting of 747 consecutive high-risk patients reported that the optimum diagnostic strategy for investigating patients with visible haematuria aged >40 years with infection excluded is a combined strategy using CT urography and flexible cystoscopy. Patients’ positive for bladder cancer on CTU should be referred directly for rigid cystoscopy and so avoid flexible cystoscopy with an advantage of a 17% reduction in the number of flexible cystoscopies performed.

A systematic review and meta-analysis reported that CTU proved to be a very sensitive and specific method for the detection of urothelial malignancy, with sensitivity ranging between 88% and 100%, and specificity between 93% and 100%. Pooled sensitivity was 96% (95% CI: 88–100%) and pooled specificity was 99% (95% CI: 98–100%). Direct comparison of the method with intravenous urography (IVU), confirmed the superiority of CTU over IVU in terms of sensitivity and specificity. Again, it was concluded that CTU is the method of choice for the detection of pathology in “high risk” haematuria patients, i.e. patients older than 40 years of age presenting with gross haematuria. The combination of CTU with conventional cystoscopy should be considered as a complete imaging investigational algorithm in this patient category.

Other advantages:
- CT outperforms ultrasound, excretory urography, and radiography in the evaluation of renal parenchymal masses and urinary tract calculi.
- CTU is reliable in demonstrating signs of obstruction, including hydronephrosis, hydroureter, ipsilateral renal enlargement, perinephric and periureteric fat stranding, perinephric fluid, and uretero-vesical oedema.
- CT urography can also be used to depict structures outside the urinary tract and thus is useful in detecting unsuspected extra-urinary disease.
- CTU is more sensitive and specific modality than excretory urography (IVP) and have a greater diagnostic accuracy than retrograde pyelography in the detection of urothelial tumors and can reliably detect bladder tumours.

Disadvantages:
- Increased radiation risk
- Associated side effects and increased costs with intravenous iodinated contrast media injection

In cases of diagnostic dilemma where the need for further characterizing of filling defects detected on other modalities, a non-diagnostic CTU, or in patients with renal failure or cases of contrast medium allergy, retrograde pyelography (RP) may have a role. However, RP shows only the ureteric lumen and cannot directly depict extrinsic abnormalities which is why it is not routinely used.

While things are rather quite clear with “high-risk” patients, for all other patient categories including younger patients and patients with more benign indications and lower pre-test cancer probabilities, CTU examination technique modifications to reduce radiation exposure (see below), consisting of
limited protocols and scan phase combinations, could be utilized alternatively or complementary to the other imaging tests. \textsuperscript{17,36}

- Radiation doses in CT urography can be reduced by limiting the number of imaging phases through the use of dual-energy CT (DECT) or split-bolus technique. \textsuperscript{17} Omission of the non-enhanced acquisition can reduce radiation exposure by almost 50\% \textsuperscript{38} with low dose protocols yield total patient dose as low as IVU. \textsuperscript{20} Dual-energy CT provides information about how substances behave at different energies, the ability to generate virtual unenhanced datasets, and improved detection of iodine-containing substances on low-energy images. \textsuperscript{39,40,41} Other advantages of DECT include good temporal and spatial registration and good spectral separation between high- and low-energy scans easy to equalize dose and noise. \textsuperscript{42}

- A prospective study demonstrated that the single-phase DECT urography with synchronous nephrographic-excretory phase enhancement represents an accurate “all-in-one” approach with a radiation dose saving up to 45\% compared with a standard dual-phase protocol and good opacification in 86.9\% of cases and excellent or good virtual unenhanced (VUE) images in 83.3\% of cases. \textsuperscript{43}

- Other authors concluded that split-bolus MDCT urography provided at least 50\% opacification of the majority of upper urinary tract segments and had high sensitivity (88.9-100\%), specificity (99-99.5\%), and accuracy (98.5-99.5\%) for the detection of upper urinary tract tumours. \textsuperscript{44}

- In patients who have contraindications to CTU, are sensitive to radiation, or who have a very low-risk of having a malignant cause of haematuria, US is the first-line imaging modality. \textsuperscript{20,24,36}

### Magnetic Resonance Urography (MRU)

- An MRI examination of the urinary collecting system is performed by two main methods: static-fluid urography with ultrafast T2-weighted sequences, as used for MRCP, and excretory urography with T1-weighted sequences after IV contrast (gadolinium-based) administration. \textsuperscript{28,45,46} Although T2-weighted sequences do not require IV contrast enhancement, imaging modifications often are necessary to optimize ureteral imaging. A complete MRU protocol can be used for imaging all components of the kidneys and the urinary collecting system in a single imaging session. At excretory MRU, IV administration of saline solution and a diuretic in addition to IV contrast material improves contrast distribution so that it is closer to uniform. \textsuperscript{45,46} To avoid the risk of nephrogenic systemic fibrosis, static-fluid MRU is preferable to excretory MRU in the imaging of patients with impaired renal function, pregnant patients, and patients with ureteral obstruction. \textsuperscript{46}

- **Advantages** \textsuperscript{46}
  - Better contrast resolution than CT urography without exposure to ionizing radiation and does not require IV contrast administration (static-fluid MRU), making it more suitable for examination of pediatric and pregnant patients and patients with renal impairment. \textsuperscript{7,10,14,28,46}
  - MRI may have a role in screening patients with inherited conditions affecting the kidneys, such as Von Hippel Lindau disease, which is characterized by hemangioblastomas of the CNS with a high prevalence of renal cysts, angiomas, and renal cell carcinoma.
  - As effective as excretory urography, ultrasound, and nuclear medicine techniques for the investigation of most pediatric uropathologic conditions. \textsuperscript{19,28} MRU is better than IV urography for depiction of renal scarring in patients with spinal dysraphism.
  - The combination of static-fluid and excretory MRU can be useful in the evaluation of obstructive uropathy because T2-weighted images can show the extent of dilatation of the obstructed system and excretory MRU can provide information on the functional effects on excretion.
  - Use of MRI facilitates simultaneous evaluation of the kidneys, ureters, renal arteries, renal
veins, and inferior vena cava, which is useful for assessing renal parenchymal, perinephric, and periureteral tumor extension

- Sequential imaging
  - of the ureters with MRU can be used to overcome problems with intermittent lack of ureteral distention due to peristalsis, which can lead to misdiagnosis of stricture and obstruction at CT urography
  - can be used to map the pattern of renal and lesional enhancement after contrast administration, which can be useful for characterizing lesions and quantifying renal function

- Disadvantages
  - Lower spatial resolution compared with CT and conventional radiography
  - Limited availability
  - Long imaging time
  - Increased cost
  - Risk of nephrogenic systemic fibrosis
  - Sensitivity to motion and susceptibility to artifacts
  - The timing of imaging in relation to contrast administration needs to be carefully considered for excretory MRU, to avoid misinterpretation of bladder lesions

- Due to its poorer diagnostic confidence (ROC area 0.994 vs. 0.938) in detecting urothelial malignancy when compared to CTU, MRU with static-fluid technique may be reserved for the evaluation of obstructed patients with impaired excretory function and who is at low risk for malignancy.

- Moreover, MRU surveillance for urothelial carcinoma should be performed for both upper and lower tract when CTU is contraindicated due to its moderate accuracy in detecting bladder carcinoma.

- The additional use of DWI to T1- and T2-weighted imaging increases the sensitivity of MRI in identifying upper urinary tract cancer with excellent interobserver agreement.

- Although there is a potential role for static-fluid MRU (sensitivity 75%) and combining DWI with MRI (sensitivity 84%) in urinary tract imaging, CTU (sensitivity 94% and accuracy 91%) is still the better choice for the diagnosis of upper urinary tract cancer. Combining DWI with CTU can help improve confidence in upper urinary tract cancer diagnoses.

- Future directions for MRU are the development of faster sequences and optimization of 3-T MRI protocols, which should help improve spatial resolution and reduce acquisition time and motion artefact.

Cystoscopy

- Cystoscopy is still the method of choice for the evaluation of the urinary bladder and should by no means be replaced by any excretory imaging technique. The recent EAU guidelines also recommends that cystoscopy should be performed to rule out concomitant bladder tumour.

- Visible haematuria should be assessed with cystoscopy within two weeks of initial presentation with up to 5% survival advantage over delayed referral as a large number (55%) of diagnosed bladder cancers are usually invasive disease.

- This is supported by a prospective study of 150 patients who underwent CTU, MRU and flexible cystoscopy where the sensitivity and specificity for detection of tumours by CTU and MRU were 61.5% and 94.9%, and 79.9% and 93.4%, respectively. When using histopathology as a reference standard, the false-positive and false-negative results for the detection of bladder tumours of both imaging modalities cannot be ignored and therefore, split-bolus CTU or MRU cannot replace cystoscopy in cases of visible haematuria.

- Additionally, in a study where MDCTU detected 32 of 50 (17 of which were <1cm) neoplasms for a sensitivity of 64%, specificity of 98%, positive predictive value of 76% and negative predictive value...
of 96%, there were 10 false-positive and 18 false-negative results (16 of which were from the bladder, including flat TCC in 14 cases and carcinoma in-situ in two, 12 of which were less than 1 cm). The authors concluded that despite MDCTU being relatively sensitive and highly specific for detecting urinary neoplasms, it does not eliminate the role of cystoscopy in the evaluation of haematuria in high risk patients 3

- A cystoscopy should be performed on all patients who present with risk factors for urinary tract malignancies (e.g. irritative voiding symptoms, current or past tobacco use, chemical exposures) regardless of age 14
- Flexible cystoscopy is simple, quick and safe procedure performed under local anaesthesia as a day case. The ‘one stop’ clinic service enables reduction in hospital presentation with reliable reassurance and allowing operative patients to be diagnosed and prepared for their surgery in the same visit 2
- Rigid cystoscopy is performed under general or spinal anaesthesia. It is performed if more complex additional procedures are anticipated
- Retrograde pyelo-ureterogram (RPUG) to image the upper tracts can be performed at the time of rigid cystoscopy if CTU has not been performed (i.e. renal impairment) 23

**Urine Cytology**

- Urinary cytology, although controversial, often constitutes part of the initial work up for haematuria. It has a sensitivity of 25%, specificity of 91%, high positive predictive value but low negative predictive value.