PROVIDER LED ENTITY

Renal, Adrenal, & Urinary Tract AUC
2023 Update

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Appropriateness of advanced imaging procedures* in patients with the following renal, adrenal, and urinary tract clinical presentations or diagnoses:

*Including MRI, CT, renal scintigraphy, PET, and PET-CT

Abbreviation list:

AAFP	American Academy of Family Physicians
ACR	American College of Radiology
AI	Adrenal incidentaloma
AMH	Asymptomatic microhematuria
AUA	American Urological Association
AUC	Appropriate Use Criteria
CT	Computed tomography
CTU	Computed tomography urography
CUA	Canadian Urological Association
DTPA	Diethylene triamine pentaacetic acid
EAU	European Association of Urology
ENSAT	European Network for the Study of Adrenal Tumors
ESE	European Society of Endocrinology
HU	Hounsfield unit
IVU	Intravenous urogram
KUB	Kidneys, ureters, and bladder
MAG-3	Mercaptoacetyltriglycine
MDCT	Multidetector computed tomography
MET	Medical expulsive therapy
MH	Microscopic hematuria
MRI	Magnetic resonance imaging
MRU	Magnetic resonance urography
NCCT	Non contrast computed tomography
NICE	National Institute for Health and Care Excellence
PCN	Percutaneous nephrolithotomy
PET	Positron emission tomography
PLE	Provider Led Entity
RPG	Retrograde pyelogram
SWL	Shock wave lithotripsy
URS	Ureteroscopy
US	Ultrasound
UTI	Urinary tract infection

Appropriate Use Criteria: How to Use this Document

The CDI Quality Institute follows the recommendation framework defined by the Appraisal of Guidelines for Research & Evaluation (AGREE II), AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews) and a modified version of the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) to evaluate the strength of recommendations concerning advanced imaging. Considerations used to determine a recommendation are listed below.

Primary recommendation (green): A strong recommendation for initial imaging for this presentation; there is confidence that the desirable effects of imaging outweigh its undesirable effects.

Alternative recommendation (yellow): A conditional recommendation for imaging; the desirable effects of imaging likely outweigh its undesirable effects, although some uncertainty may exist. The individual patient's circumstances, preferences, and values should be considered on a case-by-case basis. This may include: contraindication to the primary recommendation, specific clinical circumstances that require use of the alternative recommendation, or the primary recommendation has results that are inconclusive or incongruent with the patient's clinical diagnosis. Case-by-case indications to consider have been noted in brackets when appropriate.

Recommendation against imaging (red): The undesirable effects of imaging outweigh any desirable effects. Additionally, the recommendation may be impractical or not feasible in the targeted population and/or practice setting(s).

Renal, Adrenal, & Urinary Tract AUC Summary:

- In most clinical scenarios, **CT** is the advanced imaging procedure of choice for renal/ureteral calculi and other disorders of the kidney and ureter:
  - A **non-contrast CT** is generally indicated for initial imaging of suspected or known renal/ureteral calculi.
  - CT urography is an imaging study that is tailored to improve visualization of both the upper and lower urinary tracts (Smith et al [ACR] 2022). **CT of the abdomen/pelvis without and with contrast** (with urography protocols preferred) is the primary imaging recommendation for hematuria not due to an identified benign cause.
  - CT can generally be helpful for preoperative planning, follow-up, infection that is unresponsive to therapy, or further evaluation of incidentally discovered renal or adrenal masses. In general, the addition of contrast can be used to assess abnormalities or indeterminate findings on non-contrast CT.
- **MRI** can be used in patients unable to receive CT contrast. It is helpful for evaluating hydronephrosis, however, can be limited in its detection of smaller stones. MRI can also be used as a first line imaging modality for indeterminate renal or adrenal masses. MR urography is tailored to improve imaging of the urinary system (Smith et al [ACR] 2022).
- **Renal scintigraphy** is limited to scenarios where further assessment of renal or urinary tract obstruction and/or loss of renal function is necessary.
- **PET or PET-CT** can further characterize indeterminate adrenal lesions seen on CT in those with history of PET-sensitive primary neoplasm.
- **Ultrasound** can be useful to identify stones, or for follow-up of patients being treated for renal or ureteral calculus. Ultrasound can also evaluate microhematuria, or hydronephrosis in patients with renal insufficiency or allergy to iodinated contrast. Ultrasound expertise may be limited and/or not available in some practice settings.

PICO 1: Hematuria:

Low-Risk Patient:

- **Yellow – Renal and bladder ultrasound**
- **Red – CT**
- **Red – MRI**
- **Red – Scintigraphy**
- **Red – PET or PET/CT**

Intermediate-Risk Patient:

- **Green – Renal and bladder ultrasound**
- **Green - CT abdomen/pelvis without and with IV contrast [urography protocols preferred]**
- **Yellow - MRI abdomen or abdomen/pelvis without and with IV contrast [urography protocols preferred]**
  [*patient unable to receive CT contrast*]
- **Yellow – MRI abdomen or abdomen/pelvis without IV contrast [urography protocols preferred]**
  [*patient unable to receive CT contrast and also unable to receive MRI contrast*]
- **Yellow – CT abdomen/pelvis without IV contrast***
  [*patient unable to receive CT contrast and also unable to undergo MRI*]
- **Red – CT with IV contrast**
- **Red – Scintigraphy**
- **Red – PET or PET/CT**

High-Risk Patient:

- **Green – CT abdomen/pelvis without and with IV contrast [urography protocols preferred]**
- **Yellow – MRI abdomen or abdomen/pelvis without and with IV contrast [urography protocols preferred]**
  [*patient unable to receive CT contrast*]
- **Yellow – MRI abdomen or abdomen/pelvis without IV contrast [urography protocols preferred]**
  [*patient unable to receive CT contrast and also unable to receive MRI contrast*]
- **Yellow – CT abdomen/pelvis without IV contrast***
  [*patient unable to receive CT contrast and also unable to undergo MRI*]
- **Yellow - Renal and bladder ultrasound**
- **Red – CT with IV contrast**
- **Red – Scintigraphy**
- **Red – PET or PET-CT**

* Consider urology consult for retrograde pyelogram

Level of Evidence: CT without and with contrast: moderate; MRI without and with contrast: low; CT without contrast: low; MRI without contrast: very low; CT with contrast: insufficient; scintigraphy and PET-CT: insufficient

Notes concerning applicability and/or patient preferences: none

Guideline and PLE expert panel consensus opinion summary:

Patients presenting with hematuria represent a heterogenous population with a broad spectrum of risk for underlying malignancy based on clinical and demographic features (Barocas et al [AUA/SUFU] 2020). The American Urological Association has proposed the following risk categories to better facilitate patient-center testing strategies (Barocas et al [AUA/SUFU] 2020):

Low risk: < 1% risk of urothelial carcinoma (patient meets all of the following):

- Women age < 50 years; men age < 40 years
- Never smoker or < 10 pack years
- 3-10 RBC/HPF on a single urinalysis
- No risk factors for urothelial cancer

In low-risk patients with microhematuria, clinicians should engage patients in shared decision-making to decide between repeating urinalysis within six months or proceeding with cystoscopy and renal ultrasound (Barocas et al [AUA/SUFU] 2020: moderate recommendation; grade C evidence level). Patients with microscopic hematuria, no risk factors, and a known benign cause such as vigorous exercise, infection, menstruation, trauma, or a recent urologic procedure are unlikely to gain benefit from a complete imaging workup (Wolfman et al [*ACR*] 2020; PLE expert panel consensus opinion).

For patients with a prior negative hematuria evaluation and subsequent negative urinalysis, clinicians may discontinue further evaluation for microhematuria (Barocas et al [AUA/SUFU] 2020: conditional recommendation; grade C evidence level). For patients with a prior negative hematuria evaluation who have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision-making regarding need for additional evaluation (Barocas et al [AUA/SUFU] 2020: expert opinion). Low-risk patients who initially elected not to undergo imaging and who are found to have microhematuria on repeat urine testing should be reclassified as intermediate- or high-risk. In such patients, clinicians should perform cystoscopy and upper tract imaging in accordance with recommendations for these risk strata (Barocas et al [AUA/SUFU] 2020: strong recommendation; grade C evidence level).

Intermediate risk: 1-2% risk of urothelial carcinoma (patient meets any one of these criteria):

- Women age 50-59 years; men age 40-59 years
- 10-30 pack years
- 11-25 RBC/HPF on a single urinalysis
- Previously low-risk patient with no prior evaluation and 3-10 RBC/HPF on repeat urinalysis
- Additional risk factors (irritative lower urinary tract symptoms, prior pelvic radiation therapy, family history of urothelial cancer, occupational exposures, etc)

Clinicians can perform cystoscopy and renal ultrasound in patients with microhematuria categorized as intermediate risk for malignancy (Barocas et al [AUA/SUFU] 2020: strong recommendation; grade C evidence level). In patients with persistent or recurrent microhematuria previously evaluated with renal ultrasound, clinicians may perform additional imaging of the urinary tract (Barocas et al [AUA/SUFU] 2020: conditional recommendation; grade C evidence level). The ACR notes that CTU without and with IV contrast is usually appropriate for the initial imaging of microhematuria in patients with risk factors, without any of the following: history of recent vigorous exercise, presence of infection or viral illness, present or recent menstruation, or renal parenchymal disease (Wolfman et al [ACR] 2020).

High risk: ≥ 10% risk of urothelial carcinoma (patients meets any one of these criteria):

- Women or men age ≥ 60 years
- > 30 pack years
- > 25 RBC/HPF on a single urinalysis
- History of gross hematuria

Clinicians should perform cystoscopy and axial upper tract imaging in patients with microhematuria categorized as high-risk for malignancy (Barocas et al [AUA/SUFU] 2020: strong recommendation; grade C evidence level).

CT

If there are no contraindications to its use, clinicians should perform multiphasic CT urography (including imaging of the urothelium) (Barocas et al [AUA/SUFU] 2020: moderate recommendation; grade C evidence level). Multiphasic CT urography without and with intravenous contrast is the imaging procedure of choice for hematuria as its use is tailored to improve visualization of both the upper and lower urinary tracts, and it has the highest sensitivity (91-100%) and specificity (94-97%) for imaging the upper tracts (Wolfman et al [*ACR*] 2020). Typically, CT urography consists of unenhanced images followed by IV contrast-enhanced images, including nephrographic and excretory phases, and providing excellent diagnostic information in a single imaging session (Wolfman et al [ACR] 2020; Sharp et al [*AAFP*] 2013). If there are contraindications to multiphasic CT urography and MR urography, clinicians may utilize retrograde pyelography in conjunction with non-contrast CT or renal ultrasound (Barocas et al [AUA/SUFU] 2020: expert opinion; PLE expert panel consensus opinion). Although invasive, retrograde pyelography combined with renal ultrasonography has a sensitivity and specificity of 97% and 93%, respectively, for detecting urothelial filling defects (Sharp et al [*AAFP*] 2013).

MRI

If there are contraindications to multiphasic CT urography (e.g., chronic kidney disease or allergy to iodine-based contrast), clinicians may utilize MR urography (Barocas et al [AUA/SUFU] 2020: moderate recommendation; grade C evidence level). MR urography is also tailored to improve imaging of the urinary system: unenhanced MRU relies upon heavily T2-weighted imaging of the intrinsic high signal intensity from urine for evaluation of the urinary tract, and IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, and focal lesions (Wolfman et al [ACR] 2020). Patients undergoing MR urography should have a low likelihood for renal calculus, as it is poor at detecting stone disease, which is a common etiology of microscopic hematuria (Sharp et al [*AAFP*] 2013; PLE expert panel consensus opinion). When collecting system detail is important, but the patient has contraindications to both CT and MRI contrast, MR urography without IV contrast, or combining non-contrast MRI with retrograde pyelogram provides an alternative evaluation of the entire upper tract (PLE expert panel consensus opinion).

Follow-up evaluation:

For patients with a prior negative hematuria evaluation who have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision-making regarding need for additional evaluation (Barocas et al [AHA/SUFU] 2020: expert opinion). For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of microhematuria, or new urologic symptoms, clinicians should initiate further evaluation (Barocas et al [AUA/SUFU] 2020: moderate recommendation; grade C evidence level; Wolfman et al [ACR] 2020; PLE expert panel consensus opinion).

Clinical notes:

- Microhematuria is defined as > 3 red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen (Barocas et al [AUA/SUFU] 2020).
- In patients with microhematuria, a history and physical examination should be performed to assess risk factors for genitourinary malignancy, medical renal disease, gynecologic, and non-malignant genitourinary causes (Barocas et al [AUA/SUFU] 2020; Wolfman et al [ACR] 2020).
- In patients with microhematuria who have a family history of renal cell carcinoma (RCC) or a known genetic renal syndrome, clinicians should perform upper tract imaging regardless of risk category (Barocas et al [AUA/SUFU] 2020: expert opinion). Patients with suspected benign prostatic hyperplasia or interstitial cystitis should undergo an appropriate clinical work-up prior to advanced urologic imaging (Wolfman et al [*ACR*] 2020).

Technical notes:

- Sagittal and coronal reconstructions should be utilized to increase the sensitivity and specificity of CT for ureteral calculi (PLE expert panel consensus opinion).
- A contrast-enhanced T1-weighted MR urography series should include corticomedullary, nephrographic, and excretory phase. Thin-slice acquisition and multiplanar imaging should be obtained (Wolfman et al [*ACR*] 2020).

Evidence update (2016-present):

Moderate Level of Evidence

Taylor et al (2023), in a systematic review and meta-analysis, summarized diagnostic test characteristics of CT urography, renal ultrasound, and MR urography in comparison with surgical pathology for the diagnosis of upper urinary tract cancer in microhematuria and gross hematuria patients. A search identified 20 studies, or which six were included in the quantitative analysis. For the detection of renal cell carcinoma and upper urinary tract carcinoma in patients with microhematuria and gross hematuria, CT urography had a sensitivity of 94% (95% CI, 84%-98%) and a specificity of 99% (95%CI, 97%-100%) when 4 studies were pooled. In comparison, ultrasound demonstrated a sensitivity ranging from 14%-96% (low certainty of evidence) and a specificity of 99%-100% in 2 studies (moderate certainty of evidence), while MR urography demonstrated a sensitivity of 83% and specificity of 86% in 1 study with a low certainty of evidence. The authors conclude that, in a limited data set, CT urography appears the most sensitive imaging modality for the diagnostic evaluation of hematuria.

Tan et al (2018), in a prospective, multicenter, observational study, reported incidence of upper tract disease and bladder cancer in patients with hematuria. The authors also sought to determine whether CT urography (CTU) can be safely replaced by renal and bladder ultrasound (RBUS) in patients presenting with microscopic hematuria. A total of 3,556 patients (median age 68) were recruited from 40 hospitals; 2,166 underwent RBUS and 1,692 underwent CTU; all patients also underwent cystoscopy. The incidence of bladder, renal, and upper tract urothelial cancer was 11.0%, 1.4% and 0.8%, respectively, in macroscopic hematuria cases. Patients with microscopic hematuria had a 2.7%, 0.4% and 0% incidence of bladder, renal, and upper tract urothelial cancer, respectively. The sensitivity and negative predictive value of RBUS to detect renal cancer were 85.7% and 99.9%; but were 14.3% and 99.7%, respectively, for detection of upper tract urothelial cancer. RBUS was poor at identifying renal calculi and had lower sensitivity than CTU to detect bladder cancer. Cystoscopy had 98.3% specificity and 83.9% positive predictive value. The authors suggest that CTU can safely be replaced by RBUS to image the upper tracts in conjunction with cystoscopy following a presentation of microscopic hematuria. They note the risk of upper tract urothelial cancer in patients with microscopic hematuria is extremely low and RBUS can identify renal parenchymal cancer with high sensitivity. Imaging for patients with suspected renal calculi should include non-contrast renal tract CT. Imaging cannot replace cystoscopy to diagnose bladder cancer.

Pandharipande et al (2016), in a prospective multicenter observational study, identified outpatients referred by primary care providers for CT evaluation of abdominal pain, hematuria, or weight loss. In these three groups, leading diagnoses changed after CT in 53% (131 of 246), 49% (36 of 73), and 57% (27 of 47) of patients, respectively. Changes in provider's leading diagnoses and management after CT were common, and diagnostic confidence increased substantially.

Low Level of Evidence

Kravchick et al (2019), in a retrospective study, assessed the role of CT urography (CTU) in 140 patients ≥ 50 years old (mean age 70) presenting with differing types of hematuria. To estimate accuracy of CTU in detection of upper urinary tract urothelial carcinoma (UTUC), findings were compared to ureteroscopy results. Factors predicting ureteroscopic confirmation of CTU-based diagnoses were also evaluated. CTU suspected urothelial carcinoma in 24 (17%) of patients (UTUC in eight and bladder urothelial carcinoma in 16). CTU had a sensitivity of 66.7%, specificity of 98.5%, positive predictive value of 75% and negative predictive value of 97.7%. Logistic regression revealed five strong predictors for UTUC: positive/atypical cytology, recurrent hematuria, CTU signs, age, and Warfarin treatment. The authors conclude that CTU should be primarily performed in patients > 55 years, with recurrent microscopic or a single episode of gross hematuria, especially in patients who take Warfarin. CTU results may be used to exclude patients who do not need further ureteroscopy.

PICO 2: Suspected renal or ureteral calculus:

- Green – **CT KUB without IV contrast**
- Yellow **– Renal and bladder ultrasound**
- Yellow – **CT abdomen/pelvis with IV contrast** or **CT abdomen/pelvis without and with IV contrast**
  [*further evaluate abnormalities, obstruction, or indeterminate findings on recent ultrasound or non-contrast imaging*]
- Yellow - **MRI abdomen** or **abdomen/pelvis (urography protocols preferred)**
  [*further evaluate abnormalities, obstruction, or indeterminate findings on recent ultrasound or non-contrast imaging*]
- Yellow – **Renal scintigraphy**
  [*further evaluate obstruction on recent ultrasound or non-contrast imaging*]
- Red – **PET** or **PET-CT**

Level of Evidence: CT without contrast: high; CT with contrast: insufficient; CT without and with contrast: insufficient; MRI: very low; renal scintigraphy: low; PET-CT: insufficient

Notes concerning applicability and/or patient preference: none

Notes concerning use of contrast:
CT contrast can be used when unexplained pain, uncertainty, or abnormality is revealed on previous ultrasound or non-contrast CT. If the patient has had a previous non-contrast CT and cannot receive CT contrast, MRI [urography] without and with IV contrast can be used to further assess unexplained pain or indeterminate findings, or can be used to assess for obstruction of the collecting system.

Guideline and PLE expert panel consensus opinion summary:
Diagnostic imaging is recommended in patients with acute flank pain and a suspicion for a renal or ureteral stone. Given the often nonspecific presentation of acute onset flank pain, imaging allows for the diagnosis of stones and assessment of alternative diagnoses, complications, and appropriateness of potential therapies (Gupta et al [ACR] 2023).

CT KUB without IV contrast:
Non-contrast CT has become the standard for diagnosing acute flank pain, and in evaluating patients with suspected acute urolithiasis; with a median sensitivity and specification of 98% and 97% for detecting ureteral calculi, it is significantly more accurate than ultrasound and intravenous urography (IVU) (Skolarikos et al [EAU] 2023: level 1a evidence; Fulgham et ak [AUA] 2013: level A evidence; NICE 2019). Virtually all renal calculi are radiopaque on CT, allowing for accurate detection of even small stones at CT without the use of IV contrast (Gupta et al [ACR] 2023). Secondary signs of urolithiasis and complications such as periureteral and perinephric inflammation and ureteral dilatation can also be visualized with noncontrast CT (Gupta et al [ACR] 2023). CT allows for rapid acquisition with high spatial resolution and ability for multiplanar reformations (Gupta et al [ACR] 2023).

The radiation dose of noncontrast CT can be reduced with low-dose CT. Reduced-dose NCCT scans have been shown to maintain sensitivities and specificities from 90–97%, while preserving enough detail to identify alternate diagnoses (Lee et al [CUA] 2021). Low dose CT has been shown to have a sensitivity of 86% for detecting ureteral stones > 3mm and 100% for calculi > 3mm (Skolarikos et al [EAU] 2023).

A noncontract CT may be inconclusive for stones when it is unclear whether an identified calcification is located within the ureter or an adjacent structure, with common mimics of ureteral stones including phleboliths or arterial calcifications (Gupta et al [ACR] 2023). Contrast enhanced CT can be helpful in these cases (Gupta et al [ACR] 2023).

CT abdomen/pelvis with IV contrast

The presence of enhancing renal parenchyma during the nephrogenic phase may obscure stones within the renal collecting system, and therefore CT abdomen and pelvis with IV contrast is usually not appropriate as a first-line test in the evaluation of the patient with acute onset flank pain and suspicion of stone disease (Gupta et al [ACR] 2023). However, its use may help differentiate a ureteral stone from a phlebolith, enhance detection of urinary obstruction, or allow for the evaluation of other etiologies of flank pain (Gupta et al [ACR] 2023; PLE expert panel consensus opinion). In studies evaluating the use of CT abdomen and pelvis with IV contrast following a noncontrast CT, contrast-enhanced CT provided additional information or revealed a new diagnosis in 5% to 18% of cases (Gupta et al [ACR] 2023).

There is no relevant literature documenting the additional benefit of nonexcretory phase contrast CT in addition to noncontrast CT in the initial evaluation of urolithiasis (Gupta et al [ACR] 2023). However, CT (CTU) with a delayed excretory phase can better confirm the degree of obstruction caused by a ureteral stone and can potentially also aid in the diagnosis of a radiolucent stone, albeit a rare entity (Gupta et al [ACR] 2023).

MRI abdomen or abdomen/pelvis:

There is limited literature on the use of MRI for the initial evaluation of patients with suspected urolithiasis, and MRI can also be limited in its ability to detect smaller stones (Gupta et al [ACR] 2023; Skolarikos et al [EAU] 2023; Assimos et al [AUA] 2016). However, MR urography can be an excellent tool for the evaluation of secondary signs of obstruction in the presence of urolithiasis, detailed anatomical information about the urinary collecting system, and renal parenchymal morphology (Gupta et al [ACR} 2023; Skolarikos et al [EAU] 2023).

Renal scintigraphy:

General indications for renal scintigraphy include detection and evaluation of renal perfusion and function, and distinction between obstructive and nonobstructive hydronephrosis (Bartel et al [ACR-ACNM-SPR] 2022; PLE expert panel consensus opinion).

Ultrasound:

Ultrasound can also be used as the primary diagnostic imaging tool for stones when expertise is available, although limited evidence has shown that it is not as sensitive for renal and ureteral calculi as non-contrast CT (Skolarikos et al [EAU] 2023; *NICE* 2019). Compared with noncontrast CT, ultrasound demonstrates an overall sensitivity of 24% to 57% for renal stone detection with decreased sensitivity for smaller stones, (Gupta et al [ACR] 2023). Detection of ureteral calculi is also reduced compared with CT, demonstrating sensitivity up to 61% with a specificity of 100%, although sensitivity is improved (up to 100%) if there are associated signs of obstruction, such as hydronephrosis or ureterectasis (Gupta et al [ACR] 2023). However, within the first 2 hours of presentation, these findings are less sensitive because secondary signs of obstruction may not have had time to develop (Gupta et al [ACR] 2023).

Ultrasound can be combined with radiography to improve stone detection and has been pursued as an alternative to CT, particularly for the detection of clinically significant stones or among known stone formers who have previously had radiopaque stones (Gupta et al [ACR] 2023; Fulgham et al [AUA] 2013). This modality can enhance the sensitivity of detecting a ureteral stone, with studies demonstrating that the combination results in sensitivity ranging from 79-100% and specificity up to 100% (Lee et al [CUA] 2021).

Ultrasound expertise may be limited and there is known to be widespread variation in the quality of ultrasound (Lee et al [CUA] 2021; *NICE* 2019; PLE expert panel consensus opinion).

Clinical notes:

- KUB radiography should not be performed if NCCT is being considered but can be helpful in differentiating between radiolucent and radiopaque stones (Skolarikos et al [EAU] 2023. However, not all stones are visible at radiography, with KUB detecting only 8% of stones ≤ 5 mm, and 78% overall for stones >5 mm (Gupta et al [ACR] 2023).
- Unenhanced MR urography (MRU) relies upon heavily T2-weighted imaging of the intrinsic high signal intensity from urine for evaluation of the urinary tract and IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones (Wolfman et al [*ACR*] 2020).
- Dual-energy CT allows for the characterization of stone composition (able to differentiate uric acid containing stone from calcium-containing stones) and the generation of virtual unenhanced images simulating noncontrast CT images (Gupta et al [ACR] 2023; Skolarikos et al [EAU] 2023).

Technical notes:

- Optimization of CT includes limited scanning protocols confined to an anatomical region of interest, adjustments of CT parameters for tissue thickness and body habitus, and limitation of phases (e.g., non-contrast only or combined injection and delayed phases) to reduce total radiation exposure (Fulgham et al [*AUA*] 2013).
- In patients with a BMI > 30, ultrasound may be less effective at identifying renal and ureteral calculi, and CT may therefore be more efficacious (PLE expert panel consensus opinion).
- Sagittal and coronal reconstructions should be utilized to increase the sensitivity and specificity of CT for ureteral calculi (PLE expert panel consensus opinion).
- A contrast-enhanced T1-weighted MR urography series should include corticomedullary, nephrographic, and excretory phase. Thin-slice acquisition and multiplanar imaging should be obtained (Wolfman et al [*ACR*] 2020).

Evidence update (2014-present):

High Level of Evidence

Moore et al (2015), in a prospective, blinded observational study of 201 patients, examined the sensitivity and specificity of a reduced-dose CT protocol for symptomatic ureteral stones, particularly those large enough to require intervention, using a protocol stratified by patient size. CT scans with both regular and reduced doses were conducted, with 63% of patients receiving the high BMI reduced-dose protocol. Ureteral stone was identified in 102 patients (50.7%) receiving regular-dose CT, with a ureteral stone > 5 mm identified in 26 (12.9%). CT with substantial dose reduction was 90.2% sensitive and 98.9% specific for ureteral stones in ED patients with a wide range of BMIs. Reduced-dose CT was 96.0% sensitive for ureteral stones requiring intervention within 90 days.

Smith-Bindman et al (2014), in a multicenter comparative effectiveness RCT, randomly assigned 2,759 patients (age 18 -76 years) presenting to the emergency department (ED) with suspected nephrolithiasis to point-of-care ultrasonography (US) (n = 908), radiology US (n = 893), or CT (n = 958). Diagnostic accuracy for nephrolithiasis showed that US had lower sensitivity and higher specificity than CT. The sensitivity was 54% for US, 57% for radiology US, and 88% for CT ($P < 0.001$), and specificity was 71%, 73%, and 58%, respectively ($P < 0.001$). Patients in US groups were less likely to undergo additional diagnostic testing with CT when they reported history of nephrolithiasis. Mean 6-month cumulative radiation exposure was significantly lower in US groups than CT group ($P < 0.001$). Serious adverse events occurred in 12.4% of patients assigned to point-of-care US, 10.8% to radiology US, and 11.2% to CT ($P = 0.50$). Related adverse events were infrequent (0.4%) and similar across groups. Return ED visits and hospitalizations did not differ significantly among groups. The authors concluded that although US was less sensitive than CT for diagnosis of nephrolithiasis, using US as initial test in patients with suspected nephrolithiasis (and using other imaging as needed) resulted in no need for CT in most patients, lower cumulative radiation exposure, and no significant differences in risk of subsequent serious adverse events, pain scores, return ED visits, or hospitalizations.

Moderate Level of Evidence

Rob et al (2017), in a systematic review, investigated whether reducing radiation dose of CT KUB impacts specificity, sensitivity, and detection of urolithiasis. Literature was reviewed for adult patients undergoing a CT scan of the kidneys, ureters, and bladder (CT KUB) or non-contrast CT for renal colic or urolithiasis. 417 articles were identified, and after screening, seven articles (n = 1,104 patients) were included. Ultra-low dose CT and low-dose CT were found to be effective techniques, yielding high sensitivity and specificity. Although they yield comparable results against standard-dose CT KUB in detecting alternative diagnoses, they may not be as effective in detecting stones < 3 mm in size or in patients with body mass index of > 30. However, this should be first-line investigation for majority of renal colic patients.

Rapp et al (2016), in a retrospective cohort study, aimed to evaluate incidence of ureteral calculi on non-contrast CT in patients with flank pain (FP) and determine if clinical variables are associated with higher detection rates. 613 patients underwent non-contrast CT; no stone disease was identified in 175 patients (28.5%). Analysis demonstrated a statistically significantly increased relative risk of stone formation given four clinical variables (hematuria, nausea/vomiting, and prior stone history) when compared with FP alone. Whereas isolated FP is associated with a lower rate of ureteral calculus detection, a significant increased relative risk of ureteral calculus is seen in patients with additional clinical variables associated with stone disease.

Dym et al (2014), in a cohort of 97 cases of non-contrast and contrast-enhanced CTs, demonstrated that the detection of nephrolithiasis of ≥ 3mm is unhindered on routine portal-venous phase images, and that single-phase contrast-enhanced imaging may be utilized in evaluation of patients with suspected abdominal or flank pain secondary to renal stones without a decrement in the ability to detect such stones versus a non-contrast study. This reduces radiation dose and increases the sensitivity for the detection of non-stone-related causes for the patient's presenting symptoms.

Low Level of Evidence

Moore et al (2019), in a systematic review, sought evidence-based multispecialty consensus on optimal imaging for patients with suspected renal colic in the acute setting. A nine-member panel consisting of physician representatives from the ACEP, the ACR, and the AUA was formed, and a literature review was used as the basis for a modified Delphi process to seek consensus in 29 specific clinical scenarios. A total of 232 relevant articles were selected to guide the literature summary. Key recommendations were: 1) for suspected uncomplicated kidney stones and adequate pain relief, even without prior history of kidney stones, CT can be avoided in younger patients with typical presentation; 2) in middle-aged patients (~ 55 years), CT may be avoided if there is a prior history of kidney stones; 3) in older patients (~ 75 years), CT should generally be obtained; and 4) point-of-care ultrasound (POCUS) may help guide clinical suspicion and need for further imaging in patients with less typical signs and symptoms.

Odenrick et al (2019) retrospectively investigated detectability of renal stones in corticomedullary (CMP) and nephrographic (NGP) phases on contrast-enhanced CT in fifty patients (n = 136 renal stones – ureteral stones were excluded). Two radiologists evaluated the NGP from each exam; three abdominal radiologists blinded to the findings of the NGP reviewed independently the CMP and NGP on two different occasions. For inter-observer agreement, intra-class correlation coefficient was 0.86. There was no statistically significant difference between CMP and NGP phases (p = 0.94). The detection rate for renal stones measuring 3–5 mm was 82–88%, and 98% for stones ≥ 6 mm. The authors conclude that these findings show that renal stones with a higher risk of not passing spontaneously can be safely diagnosed. This could imply benefit to doing an examination with IV contrast from the beginning in cases where the patient's diagnosis is uncertain and renal stones is only one out of many differential diagnoses.

Rodger et al (2018), in a systematic review, investigated the diagnostic accuracy of low dose (LD) and ultra-low dose (ULD) CT of the urinary tract for detection of urinary tract stones in patients with renal colic. A total of 12 studies were included, with a total of 1,529 patients (475 in LD group and 1,054 in ULD group). Specificity/sensitivity values were calculated for LD (< 3.5 mean radiation dose [mSv]) and ULD (< 1.9 mSv) CT separately, with standard dose CT serving as the reference standard. Results found the sensitivity of LD CT ranged from 90-98% and specificity from 88-100%. The sensitivity of ULD CT ranged from 72-99% and specificity from 86-100%. The diagnostic accuracy for LD CT was 94.3% and for ULD CT was 95.5%. The authors conclude that LD and ULD CT provide effective methods of identifying urinary tract stones, and that high diagnostic accuracy, sensitivity, and specificity are maintained despite significant radiation dose reduction.

Weinrich et al (2018), in a retrospective study, assessed the diagnostic yield of low-dose (LD) CT for alternative diagnoses in 776 patients with suspected urolithiasis. The leading LD CT diagnosis was recorded for each patient and compared with final clinical diagnosis, which served as the reference standard. The mean (± SD) effective dose of CT was 1.9 ± 0.6 mSv. The frequency of urolithiasis was 82.5% (640/776). LD CT reached a sensitivity of 94.1% (602/640), a specificity of 100.0% (136/136), and an accuracy of 95.1% (738/776) for the detection of urolithiasis. The most common clinical alternative diagnoses were urinary tract infections (n = 22). For 43 of 776 patients (5.5%), neither LD CT nor clinical workup could establish a final diagnosis. The sensitivity, specificity, and accuracy of LD CT for the detection of alternative diagnoses were 91.9% (57/62), 95.6% (43/45), and 93.5% (100/107), respectively. The authors conclude that LD CT enables the diagnosis of most alternative diagnoses in the setting of suspected urolithiasis.

PICO 3: Preoperative planning for known renal or ureteral calculus:

- Green – **CT KUB without IV contrast**
- Green – **CT abdomen/pelvis without and with IV contrast (urography protocols preferred)**
- Yellow – **CT abdomen/pelvis with IV contrast (urography protocols preferred)**
  [*further evaluate abnormalities, obstruction, or indeterminate findings on recent non-contrast imaging*]
- Yellow – **MRI abdomen** or **abdomen/pelvis (urography protocols preferred)**
  [*further evaluate abnormalities, obstruction, or indeterminate findings on recent non-contrast imaging*]
- Yellow – **Renal scintigraphy**
  [*evaluate suspected loss of renal function*]
- Red – **Renal and bladder ultrasound**
- Red – **PET or PET-CT**

Level of Evidence: CT without contrast: low; CT with contrast: low; CT without and with contrast: very low; MRI with contrast: insufficient; MRI without contrast: insufficient; MRI without and with contrast: insufficient; renal scintigraphy: low; PET-CT: insufficient

Notes concerning applicability and/or patient preferences: none

Notes concerning use of contrast: In patients with complex stones or anatomy, clinicians may obtain additional contrast imaging if further definition of the collecting system and the ureteral anatomy is needed (Assimos et al [*AUA*] 2016: conditional recommendation; evidence level grade C), but it is not required in all cases (PLE expert panel consensus opinion).

Guideline and PLE expert panel consensus opinion summary:
Pre-procedural imaging should be performed to assess stone comprehensiveness and anatomy of the collecting system to ensure safe access to the renal stone (Skolarikos et al [EAU] 2023: strong recommendation). Additionally, imaging should be offered if passage of stones is suspected or if stone movement will change management; this imaging should be focused on the region of interest and should limit radiation exposure to uninvolved regions (Assimos et al [*AUA*] 2016, clinical principle). Use of CT for preoperative assessment in nephrolithiasis has gained widespread acceptance, as it defines stone burden and distribution, and provides information regarding collecting system anatomy, position or peri-renal structures, and relevant anatomic variants (Assimos et al [AUA] 2016). It may also be used to predict operative outcomes and, in some instances, stone composition (Assimos et al [*AUA*] 2016).

CT KUB without IV contrast:
Non-contrast CT imaging is the most sensitive and specific imaging investigation in the diagnosis of upper urinary tract stone disease (Assimos et al [*AUA*] 2016). Stone location and size can be accurately depicted on noncontrast CT, which is important in planning urologic management (Gupta et al [ACR] 2023). Clinicians may obtain a non-contrast CT scan to help select the best candidate for shock-wave lithotripsy (SWL) vs. ureteroscopy (URS) (Assimos et al [*AUA*] 2016, Conditional Recommendation; Evidence Level Grade C). Clinicians may also obtain a non-contrast CT scan on patients prior to performing percutaneous nephrolithotomy (PCNL) (Assimos et al [*AUA*] 2016, Strong Recommendation; Evidence Level Grade C).

CT abdomen/pelvis:
CT with IV contrast can be useful if stone removal is planned and the anatomy of the renal collecting

system needs to be assessed (Skolarikos et al [EAU] 2023: strong recommendation). When treating a complex stone burden or patient with complex anatomy, a clinician may obtain additional contrast-enhanced imaging with urographic phases to help determine the best treatment approach (Assimos et al [*AUA*] 2016; PLE expert panel consensus opinion)*.* CT urography with IV contrast can be useful for patients who have had a non-contrast CT performed within the past 6 months (PLE expert panel consensus opinion).

MRI abdomen or abdomen/pelvis:
MR urography can be useful in defining renal collecting system anatomy in patients with CT contrast allergy, although stones are typically not well visualized directly with MR imaging (Assimos et al [*AUA*] 2016; PLE expert panel consensus opinion). In the case of staghorn/complex stones, renal function may be compromised and must be adequately assessed a contrast-enhanced imaging study, such as MR urography (Assimos et al [*AUA*] 2016). MRI without contrast can be useful for further evaluation of complex stone or to assess renal collecting system anatomy in patients who are unable to receive both CT contrast and MRI contrast (PLE expert panel consensus opinion).

Renal scintigraphy:
In general, indications for renal scintigraphy include detection and evaluation of renal perfusion and function, and distinction between obstructive and nonobstructive hydronephrosis (Bartel et al [ACR-ACNM-SPR] 2022). Clinicians may obtain a functional imaging study if clinically significant loss of renal function in the involved kidney is suspected (Assimos et al [*AUA*] 2016, conditional recommendation; evidence level grade C). In the case of staghorn/complex stones, renal function may be compromised and must be adequately assessed with nuclear renal scan or another contrast-enhanced imaging study (Assimos et al [*AUA*] 2016).

Ultrasound
The use of ultrasonography alone to direct SWL or URS treatment planning should be discouraged as US is inherently inaccurate in determination of stone size and provides no information on stone density (Assimos et al [*AUA*] 2016).

<u>Clinical notes:</u>

- CT urography (CTU) is tailored to improved visualization of both the upper and lower urinary tracts; it usually involves unenhanced images followed by IV contrast-enhanced images, including nephrographic and excretory phases, acquired at least 5 minutes after contrast injection (Wolfman et al [*ACR*] 2020).
- MR urography (MRU) is also tailored to improve imaging of the urinary system. IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones (Wolfman et al [*ACR*] 2020).
- Pyelography (either antegrade or retrograde) is routinely performed at the time of PCNL and yields superior anatomical detail for the purposes of surgical decision-making (PLE expert panel consensus opinion).

<u>Technical notes:</u>

- 3D reconstructive techniques are advocated by some for their perceived utility in improving preoperative PCNL planning (Assimos et al [*AUA*] 2016).
- Optimization of CT includes limiting scan protocols to an anatomical region of interest for evaluation of the distal ureter, adjusting CT parameters for tissue thickness and body habitus,

and limiting contrast phases (e.g., non-contrast only or combined injection and delayed phases) to reduce total radiation exposure (Fulgham et al [*AUA*] 2013; Assimos et al [*AUA*] 2016).

- Sagittal and coronal reconstructions should be utilized to increase the sensitivity and specificity of CT for ureteral calculi (PLE expert panel consensus opinion).
- A contrast-enhanced T1-weighted MR urography series should include corticomedullary, nephrographic, and excretory phase. Thin-slice acquisition and multiplanar imaging should be obtained (Wolfman et al [*ACR*] 2019).

Evidence update (2015-present):

Low Level of Evidence

Bayrak et al (2016) conducted a retrospective cohort study of 736 patients with ureteral stones undergoing pre-operative imaging before ureteroscopy for stone removal. Patients were placed into 4 groups— (1) reference standard contrasted imaging study (IVU), (2) non-contrast CT, (3) both, and (4) neither (ultrasound + abdominal radiographs). The stone-free rate after primary ureteroscopy was 87.1% in group 1, 88.2% in group 2, 96.7% in group 3, and 89.9% in group 4 (P=0.093). No significant differences were seen among the groups for complication rates. The authors conclude that ureteroscopic treatment of ureteral stones can be safely and effectively performed without the use of contrast study imaging, except in doubtful cases of anatomical abnormalities.

PICO 4: Follow-up imaging during or after treatment of renal or ureteral calculus:

- Green – **Renal and bladder ultrasound** (with or without **KUB radiography**)
- Yellow – **CT KUB without IV contrast**
- Yellow – **CT abdomen/pelvis with IV contrast** or **CT abdomen/pelvis without and with IV contrast**
  [*further evaluate abnormalities, obstruction, or indeterminate findings on recent ultrasound or non-contrast imaging*]
- Red – **MRI**
- Red – **PET or PET-CT**
- Red – **Scintigraphy**

Level of Evidence: CT without contrast: high; CT with contrast: insufficient; CT without and with contrast: insufficient; MRI with contrast: insufficient; MRI without contrast: very low; MRI without and with contrast: insufficient; renal scintigraphy: insufficient; PET-CT: insufficient

Notes concerning applicability and/or patient preferences: none

Guideline and PLE expert panel consensus opinion summary:

Overview:

The need for an imaging study to confirm stone/fragment clearance, to monitor for the resolution of hydronephrosis, or to evaluate for the development of hydronephrosis after shock wave lithotripsy (SWL) or ureteroscopy is widely accepted (Fulgham et al [*AUA*] 2013). Neither resolution of symptoms nor patient reports of successful passage of obstructing ureteral stones is always confirmatory, and follow-up imaging to ensure passage of an obstructing ureteral stone is suggested (Lee et al [CUA] 2021: level 3; strong recommendation; Fulgham et al [AUA] 2013). The goal of postoperative imaging is to assess for residual stone burden and screen for ongoing obstruction, as residual stone fragments may lead to additional stone-related episodes and surgical intervention (Lee et al [CUA] 2021; Fulgham et al [AUA] 2013).

For patients undergoing medical expulsive therapy (MET) for a ureteral calculus and who have ongoing symptoms, imaging can assess stone progression as well as ongoing hydronephrosis (Fulgham et al [*AUA*] 2013). In these MET patients in whom there is documented stone passage and resolution of symptoms, no further imaging is necessary (Fulgham et al [*AUA*] 2013). When stones are not treated, follow-up can be periodic (e.g., initially at six months and then yearly if the patient is stable) and can be tailored based on stone activity or clinical signs (Skolarikos et al [EAU] 2023: strong recommendation; Pearle et al [AUA] 2014).

Ultrasonography/KUB radiography:

An ultrasound with or without KUB radiography is recommended following ureteroscopy for ureteral stones (Skorlarikos et al [EAU] 2023; Lee et al [CUA] 2021: level 4; strong recommendation; Pearle et al [AUA] 2014). Although not considered to be an advanced imaging modality, ultrasound is often used for initial follow-up of patients treated for renal or ureteral calculus (Fulgham et al [*AUA*] 2013; PLE expert panel consensus opinion). For patients undergoing medical expulsive therapy (MET) in whom there is documented stone passage and persistent symptoms, ultrasound is used to demonstrate whether there is persistent obstruction (Fulgham et al [*AUA*] 2013). After a period of MET in patients with a known radiopaque ureteral calculus < 10 mm in diameter with minimal to moderate associated hydronephrosis and no evidence of renal damage, ultrasound offers the best combination of sensitivity/specificity with minimal radiation exposure (Fulgham et al [*AUA*] 2013). For patients undergoing shock wave lithotripsy (SWL), follow-up renal sonogram with KUB (for radiopaque stones) or without KUB (for radiolucent stones) can document stone clearance and demonstrate presence or absence of hydronephrosis (Fulgham et al [AUA] 2013). If the patient is asymptomatic and ultrasound/KUB shows no stones or hydronephrosis, no further imaging is required. If follow-up ultrasound/KUB demonstrates hydronephrosis and/or residual fragments, further observation with repeat imaging may be indicated (Fulgham et al [*AUA*] 2013). For patients who undergo intact stone removal and whose symptoms have resolved, a renal ultrasound is sufficient to document resolution of hydronephrosis (Fulgham et al [*AUA*] 2013).

CT:
While noncontrast CT is the best modality for identifying residual fragments and postoperative obstruction, the effective dosage of radiation has prevented its routine use in this population (Lee et al [CUA] 2021). In complicated cases or when further intervention is required, NCCT can be performed (Skolarikos et al [EAU] 2023: strong recommendation; Lee et al [CUA] 2021: level 4; strong recommendation). Non-contrast CT has emerged as the most sensitive and specific modality for detecting ureteral calculi and is used to a lesser extent in the follow-up of known ureteral calculi after treatment (Fulgham et al [*AUA*] 2013). CT of the abdomen and pelvis without and with IV contrast may be indicated in patients with hydronephrosis on follow-up ultrasound to identify additional stones, residual edema, or obstruction (Fulgham et al [*AUA*] 2013). For patients undergoing treatment for radiolucent stones, low dose non-contrast CT can assess stone progression and degree of hydronephrosis (Fulgham et al [*AUA*] 2013). Patients with radiolucent stones and no hydronephrosis who remain symptomatic and/or have not passed fragments should be further observed with repeat imaging (low dose non-contrast CT) or intervention as indicated (Fulgham et al [*AUA*] 2013). CT of the abdomen and pelvis without and with IV contrast may also be indicated in patients with persistent symptoms and no hydronephrosis on ultrasound to evaluate for retained calculi (Fulgham et al [*AUA*] 2013).

<u>Clinical notes:</u>

- Silent obstruction, described as asymptomatic, persistent, postoperative obstructive hydronephrosis, has been shown to occur at a rate of 2–10% following ureteroscopy, highlighting the importance of routine postoperative imaging (Lee et al [CUA] 2021).
- Obstruction with or without associated symptoms after ureteroscopy is generally due to obstructing stone fragments or ureteral stricture. With the low incidence of stricture (< 1% in most series), obstructing fragments is the most common etiology (Fulgham et al [*AUA*] 2013).

<u>Technical notes:</u>

- Optimization of CT includes limited scanning protocols confined to an anatomical region of interest for evaluation of the distal ureter, adjustments of CT parameters for tissue thickness and body habitus, and limitation of phases (e.g., non-contrast only or combined injection and delayed phases) to reduce total radiation exposure (Fulgham et al [*AUA*] 2013).
- Sagittal and coronal reconstructions should be utilized to increase the sensitivity and specificity of CT for ureteral calculi (PLE expert panel consensus opinion).

<u>Evidence update (2015-present)</u>:

Low Level of Evidence

Meltzer et al (2020), in a secondary analysis of a multicenter prospective trial, examined if patient-reported stone passage (capture or visualization) could detect stone expulsion as accurately as follow-up CT scan. A total of 237 patients with symptomatic ureteral stone < 9 mm (mean = 3.8 mm) in diameter underwent a follow-up CT scan after initial presentation (range: 29-36 days). In those reporting stone passage, 94% demonstrated passage on follow-up CT. Of patients who did not report stone passage, 72% demonstrated passage of stone on follow-up CT. The authors conclude that patient-reported stone passage was strongly associated with stone passage on follow-up CT scan. Routine follow-up CT imaging of patients with ureteral stones who have visualized or captured their stone thus may not be necessary.

PICO 5: Suspected infection in any of the following:

- **Immunocompromised patients,**
- **Patients with ≥ 72 hours of unsuccessful therapy, and/or**
- **Patients with progressive, recurrent, or atypical symptoms:**

  - Green – **CT abdomen/pelvis without and/or with IV contrast**
  - Yellow **– Renal and bladder ultrasound** or **abdominal ultrasound**
  - Yellow – **MRI abdomen** or **abdomen/pelvis without and with IV contrast (urography protocols preferred)**
    [*patient unable to receive CT contrast*]
  - Yellow – **MRI abdomen or abdomen/pelvis without IV contrast (urography protocols preferred)**
    [*patient unable to receive CT contrast and also unable to receive MRI contrast*]
  - Red – **PET** or **PET-CT**
  - Red – **Renal scintigraphy**

Level of Evidence: CT without contrast: insufficient; CT with contrast: low; CT without and with contrast: very low; MRI: insufficient; renal scintigraphy: low

Notes concerning applicability and/or patient preferences: none

Guideline and PLE expert panel consensus opinion summary:
Overview:
Cystoscopy and/or imaging of the upper urinary tract is not mandatory for asymptomatic bacteriuria if the medical history is otherwise unremarkable (Bonkat et al [EAU] 2023), and a diagnosis of uncomplicated cystitis can be made with a high probability from a focused history of lower urinary tract symptoms (dysuria, frequency, and urgency) and the absence of vaginal discharge (Bonkat et al [EAU] 2023). Similarly, recurrent UTIs are common, and an extensive routine workup including cystoscopy and imaging is not routinely recommended as the diagnostic yield is low (Bonkat et al [EAU] 2023).

Imaging is not typically beneficial in the initial evaluation for the first-time presentation of suspected acute pyelonephritis in an uncomplicated patient (Smith et al [ACR] 2022; Bonkat et al 2023). In most patients, uncomplicated pyelonephritis is diagnosed clinically and is responsive to treatment with appropriate antibiotics (Smith et al [ACR] 2022).

Some patients, however, are at high risk for developing complications from acute pyelonephritis. In these instances, imaging studies are often used to aid with the diagnosis, identify precipitating factors, and differentiate lower UTI from renal parenchymal involvement (Smith et al [ACR] 2022). Imaging should also be performed without delay in atypical cases of infection, including whenever renal calculi, outflow obstruction, interstitial cystitis, or urothelial cancer is suspected (Bonkat et al [EAU] 2023). Therefore, additional investigations for pyelonephritis, such as a contrast enhanced CT scan, or excretory urography should be considered if the patient remains febrile after 72 hours of treatment, or immediately if there is deterioration in clinical status (Bonkat et al [EAU] 2023).

CT abdomen/pelvis:
There is widespread agreement that CT of the abdomen and pelvis with IV contrast is a useful study to diagnose acute pyelonephritis in a complicated patient, including those with diabetes or who are immunocompromised (Smith et al [ACR] 2022; PLE expert panel consensus opinion). CT imaging may be useful if symptoms persist for 72 hours, as studies have demonstrated nearly 95% of patients with uncomplicated pyelonephritis become afebrile within 48 hours after appropriate antibiotic therapy, and nearly 100% within 72 hours (Smith et al [ACR] 2022). In the absence of a history of renal stones, the benefit of performing unenhanced CT in combination with contrast-enhanced CT is negligible in a complicated patient with suspected acute pyelonephritis (Smith et al [ACR] 2022). However, unenhanced CT has higher sensitivity than contrast-enhanced CT for detection of small renal calculi, and therefore may be useful for initial imaging in those with history of stones or renal obstruction (Smith et al [ACR] 2022; PLE expert panel consensus opinion).

MRI abdomen or abdomen/pelvis:
Similar to CT, MRI does not provide benefit early in uncomplicated cases of acute pyelonephritis (Smith et al [ACR] 2022). When indicated, MRI of the abdomen without or with IV contrast may be useful to detect and characterize congenital anomalies of the kidneys, and imaging of the pelvis can improve detection of congenital abnormalities of the distal ureters and abnormalities of the urinary bladder (Smith et al [ACR] 2022). MRI may be particularly useful for patients in whom the use of iodinated contrast material must be avoided (particularly those with contrast sensitivity) (PLE expert panel consensus opinion). Disadvantages of MRI include relatively poor accuracy for detecting urolithiasis and reduced ability to detect gas in emphysematous pyelonephritis (Smith et al [ACR] 2022).

Ultrasound:
In patients with pyelonephritis, evaluation of the upper urinary tract with ultrasound can be performed to rule out urinary tract obstruction or renal stone disease in patients with a history of urolithiasis, renal function disturbances, or a high urine pH (Bonkat et al [EAU] 2023). Although ultrasound has similar accuracy to CT for detecting urolithiasis and hydronephrosis, it has a lower rate of detection of acute pyelonephritis and renal abscess; however, it can be performed portably and without IV contrast (Smith et al [ACR] 2022). Therefore, when appropriate expertise is available, evaluation of the upper urinary tract with ultrasound may be performed in patients with acute uncomplicated pyelonephritis to rule out urinary obstruction or renal stone disease (Bankot et al [*EAU*] 2019, Level 4/Grade C Evidence; PLE expert panel consensus opinion).

Clinical notes:

- Acute pyelonephritis often presents with signs and symptoms of both systemic inflammation (e.g., fever, chills, fatigue) and bladder inflammation (e.g., urgency, dysuria, urinary frequency (Smith et al [ACR] 2022; Bonkat et al [EAU] 2023).
- Patients at greater risk for developing complications from acute pyelonephritis include those with a prior history of pyelonephritis, a lack of response to therapy for urological infection, diabetes, anatomic or congenital abnormalities of the urinary system, infections by treatment-resistant organisms, nosocomial infection, urolithiasis, renal obstruction, prior renal surgery, advanced age, and immunosuppressed or immunocompromised patients (Smith et al [ACR] 2022).

Evidence update (2014-present):
There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

PICO 6: Evaluation of incidental/indeterminate renal mass or complex cyst:

- Green – **CT abdomen without and with IV contrast**
- Green – **MRI abdomen without and with IV contrast**
- Yellow **– Renal ultrasound**
- Yellow – **MRI abdomen without IV contrast**
  [*patient unable to receive CT contrast and also unable to receive MRI contrast*]
- Yellow – **CT abdomen without IV contrast**
  [*patient unable to receive CT contrast and also unable to undergo MRI*]
- Yellow – **CT abdomen with IV contrast**
  [*further evaluate findings on recent ultrasound or non-contrast imaging*]
- Red – **Scintigraphy**
- Red – **PET** or **PET-CT**

Level of Evidence: CT without contrast: very low; CT with contrast: very low; CT without and with contrast: low; MRI with contrast: low; MRI without contrast: insufficient; MRI without and with contrast: low; renal scintigraphy: insufficient; PET-CT: insufficient

Notes concerning applicability and/or patient preferences: none

Guideline and PLE expert panel consensus opinion summary:
Overview:
Most renal masses are incidentally discovered on routine imaging, with up to 30% of identified as benign, and the majority of malignant lesions having low metastatic potential (Richard et al [CUA] 2022). However, cystic renal lesions cannot be diagnosed confidently as benign or malignant at the time of discovery (Wang et al [ACR] 2020). Therefore an abdominal, multiphasic, contrast-enhanced CT or MRI is mandatory to characterize the mass or cyst, as enhancement is the most important criterion to confirm its solid nature (Richard et al [CUA] 2022; Richard et al [CUA] 2023: strong recommendation, moderate certainty in evidence of effects).

The Bosniak renal cyst classification was originally described using CT imaging but other modalities, such as MRI, ultrasound, or contrast-enhanced ultrasound, are now being used to help better delineate these lesions (Richard et al [CUA] 2022).

Patients identified with a renal cyst should be classified according to the v2019 Bosniak classification, with suggested terms and phrases to use when reporting cystic renal masses as follows (Silverman et al 2019):

- Bosniak I: "Benign simple renal cyst requiring no follow-up"
- Bosniak II: "Benign Bosniak II renal cyst requiring no follow-up" or "Likely benign Bosniak II renal mass requiring no follow-up"
- Bosniak IIF: "Bosniak IIF cystic renal mass. The large majority of Bosniak IIF masses are benign. When malignant, nearly all are indolent. Generally, Bosniak IIF masses are followed by imaging at 6 months and 12 months, then annually for a total of 5 years to assess for morphologic change."
- Bosniak III: "Bosniak III cystic renal mass. Bosniak III masses have an intermediate probability of being malignant. If not already obtained, consider urology consultation."

- Bosniak IV: "Bosniak IV cystic renal mass. The large majority of Bosniak IV masses are malignant. If not already obtained, consider urology consultation."

Unless there are contraindications to iodinated CT contrast or gadolinium-based MR IV contrast, characterization of a cyst should be performed without and with IV contrast using a dedicated renal mass protocol (Herts et al [*ACR*] 2018). In general, any mass with density > 20 Hounsfield units (HU) and < 70 HU on unenhanced CT, as well as any heterogeneous mass, is considered indeterminate and warrants further evaluation (Wang et al [*ACR*] 2020).

CT abdomen:
CT is the most commonly used modality for evaluating indeterminate renal masses (Wang et al [*ACR*] 2020). CT without and with IV contrast is optimal for the evaluation of indeterminate renal masses, but CT without IV contrast can also be useful in certain instances, such as in the detection of macroscopic fat, a feature consistent with an angiomyolipoma, a benign lesion (Richard et al [CUA] 2022; Wang et al [ACR] 2020; PLE expert panel consensus opinion). Non-contrast CT can also be used for first-line imaging in patients who cannot receive CT contrast and are also unable to undergo MRI (Richard et al [CUA] 2022; PLE expert panel consensus opinion). A CT with IV contrast should only be used to further characterize a renal mass that has been identified with non-contrast CT in the past six months (PLE expert panel consensus opinion).

MRI abdomen:
MRI of the abdomen is also frequently used to characterize renal lesions (Wang et al [*ACR*] 2020). MRI is more sensitive to contrast enhancement and is recommended for renal masses with inconclusive enhancement, or for depicting enhancing nodules (Herts et al [ACR] 2018). Additionally, MRI better detects and characterizes small renal cysts by their T2 hyperintensity, better detects enhancement in small renal lesions, and is not subject to pseudoenhancement like CT (Herts et al [ACR] 2018). However, MRI also depicts more septa or thickened walls in complex cystic masses, which may result in a higher Bosniak classification (Herts et al [ACR] 2018). MRI without and with IV contrast is optional for renal lesion characterization, but a non-contrast MRI can be useful in patients who are unable to receive contrast (Wang et al [*ACR*] 2020; PLE expert panel consensus opinion).

Ultrasound:
When expertise is available, ultrasound can play an important role in detecting and characterizing renal masses, such as in patients who cannot receive iodinated contrast (Wang et al [*ACR*] 2020). Ultrasound has also been shown to be useful in further characterizing hyperattenuating cysts presenting as indeterminate hyperattenuating renal lesions on CT (Wang et al [ACR] 2020).

<u>Clinical notes:</u>

- For patients with suspected renal malignancy, a baseline chest x-ray is suggested to assess for pulmonary metastases (Richard et al [CUA] 2022). If any abnormalities are detected on the chest x-ray, a chest CT should be performed (Richard et al [CUA] 2022).

<u>Evidence update (2016-present):</u>
Low Level of Evidence
Hu et al (2018), in a retrospective study, aimed to determine frequency and clinical significance of homogeneous renal masses measuring 21-39 Hounsfield units (HU) on contrast-enhanced CT. A total of 1,387 patients (age 40-69 years) were included. Images were reviewed by three radiologists to identify all masses ≥ 10 mm and 21-39 HU. Cases of known renal cancer or imaging performed for a renal

indication were excluded. The primary outcome (reference standard) was subsequent characterization of the renal mass as clinically significant, defined as a solid mass (unequivocal enhancement on renal mass protocol CT or MRI, Doppler flow on ultrasound), a Bosniak IIF-IV cystic mass on subsequent renal mass protocol CT, MRI, or renal ultrasound, or clinical progression within 5 years of follow-up, defined as metastatic renal cancer or extirpative therapy. Results found that eligible masses (n = 74) were found in 5% (n = 63) subjects. Of those with a reference standard (n = 42), none (0% [95% CI: 0.0%-8.4%]) were determined to be clinically significant. The authors conclude that incidental renal masses on contrast-enhanced CT that are homogeneous and display attenuation of 21-39 HU are uncommon in patients 40-69 years, unlikely to be clinically significant, and may not need further imaging evaluation. They encouraged replication of results in an independent and larger population.

de Silva et al (2017), in a retrospective study, evaluated what percentage of echogenic nonshadowing renal lesions > 4 mm found on US are angiomyolipomas (AMLs). Study data was obtained over 45 months, with follow-up data on 158 lesions (132 patients) available. A total of 98 (62%) lesions were AMLs, 8 (5.1%) were renal cell carcinomas, 3 (1.9%) were oncocytomas, 17 (10.8%) were artifacts, 7 (4.4%) were fat, 5 (3.2%) were calculi, 8 (5.1%) were scars, and 12 (7.6%) were complicated cysts. Mean age of patients with AML was significantly lower than those without (61.71 vs. 68.80 years; p = 0.005). There was also a female association with AMLs (p < 0.001). The authors conclude that echogenic nonshadowing renal lesions > 4 mm seen on US should not be assumed to represent an AML without follow-up because a percentage of renal cell carcinomas will be missed. Although certain US features can be useful in differentiating AML from renal cell carcinoma and CT is frequently diagnostic, an understanding of MRI is important for its potential to detect lipid-poor AMLs.

PICO 7: Evaluation of incidental/indeterminate adrenal mass or nodule (adrenal incidentaloma) $\geq$ 1 cm in size and/or with symptoms of adrenal hormone excess:

- Green – **CT abdomen without and/or with IV contrast**
- Green – **MRI abdomen without IV contrast**
- Yellow – **MRI abdomen without and with IV contrast**
- Yellow – **PET or PET-CT**
  [*history of malignancy*]
- Red – **Scintigraphy**
- Red **- Ultrasound**

Level of Evidence: CT: very low; MRI: very low; renal scintigraphy: insufficient; PET-CT: low

Notes concerning applicability and/or patient preferences:
Shared decision-making between patients and their clinicians should be used for the management of indeterminate non-functioning adrenal lesions, with management options including repeat imaging in 3-6 months vs. surgical resection (Rowe et al [CUA] 2023: clinical principle).

Notes concerning use of CT contrast: For the initial evaluation of an incidentally discovered adrenal mass, CT without IV contrast can be used, particularly if there are no suspicious imaging features. CT without and with IV contrast is indicated if a non-contrast CT is nondiagnostic or if there are concerning imaging features of malignancy. CT with IV contrast can be used to further characterize an adrenal lesion that has been identified with non-contrast CT in the past six months (PLE expert panel consensus opinion).

Guideline and PLE expert panel consensus opinion summary:
Overview:
Adrenal incidentalomas are adrenal masses greater than 1 cm in size that are detected on cross-sectional imaging performed for an unrelated indication (Rowe et al [CUA] 2023). These lesions are common, estimated to be present in 4% of patients (and up to 10% of the elderly population) and most of these lesions are benign nonfunctioning adrenocortical adenomas, with a minority being hormonally active or malignant (Rowe et al [CUA] 2023).

Many other criteria are involved in the assessment of incidental adrenal masses, including size, growth or stability, and endocrine function (Mody et al [ACR] 2021). Size is an important variable in predicting malignancy of an incidentally discovered adrenal mass; smaller lesions are usually benign, and incidental adrenal masses with <1 cm short axis measurement do not generally require further evaluation because of the overwhelming likelihood that these lesions are benign (Mody et al [ACR] 2021). Conversely, larger lesions have a greater likelihood of being malignant (Mody et al [ACR] 2021).

Initial Workup
It is recommended that all patients found to have an adrenal incidentaloma undergo clinical, biochemical, and imaging examinations to determine the presence/absence of symptoms and signs caused by an excess of adrenal hormone and to determine whether the tumor is homogenous and lipid-rich, and therefore benign (Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation; Fassnacht et al [*ESE & ENSAT* 2023). Computed tomography (CT) and magnetic resonance imaging (MRI)

are the primary imaging modalities performed to evaluate adrenal incidentalomas (Rowe et al [CUA] 2023). CT and MRI can identify benign lesions, therefore representing tools designed for the exclusion of adrenal malignancy, while FDG-PET/CT is mainly used for the detection of malignant disease (Fassnacht et al [*ESE & ENSAT*] 2023).

In general, an incidental adrenal mass that is < 1 cm in the short axis need not be pursued (Mayo Smith et al [ACR] 2017), unless clinical signs and symptoms suggestive of adrenal hormone excess are present (Fassnacht et al [*ESE & ENSAT*] 2023). For patients with no prior history of malignancy and an incidentally detected adrenal mass <1 cm without diagnostic benign imaging characteristics on initial study, the mass is most likely benign (Mody et al [ACR] 2021). Similarly, patients with benign non-functioning adenomas < 3 cm, myelolipomas, and other small masses containing macroscopic fat detected on the initial workup for an adrenal incidentaloma do not require further follow-up imaging or functional testing (Rowe et al [CUA] 2023: strong recommendation; moderate quality of evidence).

For patients with a history of malignancy and an adrenal mass > 1 cm and < 4 cm and no diagnostic benign imaging features on prior examinations or documented stability, adrenal-specific imaging should be performed. In this scenario, MRI abdomen without and with IV contrast or CT abdomen without and with IV contrast or FDG-PET/CT skull base to mid-thigh is usually appropriate (Mody et al [ACR] 2021).

In larger masses, imaging is usually not appropriate for patients with no prior history of malignancy and an incidentally detected indeterminate adrenal mass ≥ 4 cm without diagnostic benign imaging characteristics (Mody et al [ACR] 2021). Rather, after biochemical evaluation is performed, surgical resection (without biopsy) is recommended because of the increased likelihood of adrenocortical carcinoma (Mody et al [ACR] 2021). For lesions ≥ 4 cm in patients with a history of malignancy, there is no primary evidence supporting the use of adrenal CT for initial evaluation (Mody et al [ACR] 2021; Mayo-Smith et al [ACR] 2017). Rather, these patients should proceed with PET/CT or biopsy because the presumed diagnosis is metastatic disease (Mayo-Smith et al [ACR] 2017). While size is considered too unreliable to be used alone as a criterion for malignancy, a 4 cm cutoff is generally used to make decisions regarding surgery for lesions that do not have diagnostic benign imaging features (Mody et al [ACR] 2021).

Follow-Up
Interval growth of adrenal masses has been advocated as a potential indicator of malignancy; as a general principle, if prior imaging is available and a lesion has been stable for 1 year or more, it can typically be considered benign (Mody et al [ACR] 2021). No further imaging follow-up or functional testing is required for patients with adrenal lesions that grow < 3 mm/year on follow-up imaging (Rowe et al [CUA] 2023: weak recommendation; low quality of evidence). Additionally, no further imaging is needed in the following scenarios (Mayo-Smith et al [ACR] 2017):

- Adrenal mass has diagnostic features of a benign mass such as a myelolipoma, cyst, or hemorrhage
- Benign calcified mass, such as an old hematoma, or calcification from prior granulomatous infection is identified
- Mass with density of ≤ 10 HU on unenhanced CT or signal loss compared with the spleen between in- and opposed-phase imaging of a chemical-shift MRI (CS-MRI) examination, as these features are almost always diagnostic of a lipid-rich adenoma, regardless of size.

Stability of a lesion should be assessed by repeat imaging for nodules > 1 cm, but there is no literature supporting further evaluation of lesions <1 centimeter (Mody et al [ACR] 2021). If there are no diagnostic benign imaging features but the adrenal mass (≥ 1 to < 4 cm) has been stable for 1 year or longer, it is very likely benign, requiring no additional imaging. The American Association of Endocrine Surgeons do not recommend routine scheduled follow-up of a nonfunctional adrenal nodule (size < 4 cm) with benign imaging characteristics and noncontrast HU < 10 because the risk of developing malignancy is very low (Yip et al [AAES] 2022).

Nodules from 1-4 cm with indeterminate imaging characteristics (such as noncontrast CT with HU > 10) have a slightly increased risk of malignancy and should undergo at least 1 repeated image at 6 to 12 months to confirm stability (Yip et al [AAES] 2022: strong recommendation; low-quality evidence).

Patients with non-functioning adrenal lesions that are radiographically benign (< 10 HU) but > 4 cm should undergo repeat imaging in 6-12 months (Rowe et al [CUA] 2023: weak recommendation; low quality of evidence). Similarly, in patients with an indeterminate adrenal mass opting not to undergo adrenalectomy following initial assessment, a non-contrast CT or MRI after 6-12 months is suggested to exclude significant growth (Fassnacht et al [*ESE & ENSAT*] 2023).

A new or enlarging mass raises suspicion for malignancy (Mayo-Smith et al [ACR] 2017).

CT abdomen:
Adrenal CT using a dedicated adrenal CT protocol remains the primary tool in the workup of an adrenal mass, using both density and washout to characterize an adenoma (Mody et al [ACR] 2021; Mayo-Smith et al [ACR] 2017; Rowe et al [CUA] 2023: strong recommendation; moderate quality of evidence; Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation; Fassnacht et al [*ESE & ENSAT*] 2023). Although there are some data to suggest that CS-MRI may be slightly more sensitive for detecting intracellular lipid than unenhanced CT, high-density adenomas may remain indeterminate on CS-MRI, and adrenal CT with washout has been shown to outperform CS-MRI (Mayo-Smith et al [ACR] 2017).

A mass that is homogeneous, well-circumscribed, and measures <10 Hounsfield Units (HU) in attenuation can be confidently diagnosed as benign, these overwhelmingly represent lipid-rich adrenal cortical adenomas (Rowe et al [CUA] 2023). If the non-contrast CT is consistent with a benign adrenal mass (Hounsfield units ≤ 10; homogeneous appearance), no further imaging is required (Fassnacht et al [*ESE & ENSAT*] 2023). When the noncontrast HU are > 10 and other clinical risk factors are not present, it is recommended that washout characteristics on an adrenal protocol CT be used to stratify the risk of malignancy for adrenal nodules (Yip et al [AAES] 2022: weak recommendation; low-quality evidence; Mody et al [ACR] 2021; Rowe et al [CUA] 2023: weak recommendation; moderate quality of evidence; Mayo-Smith et al [ACR] 2017). After administration of IV contrast, both lipid-rich and lipid-poor adenomas tend to wash out faster than malignant lesions. Studies have shown that a delay of 15 minutes after the administration of IV contrast greatly improves the sensitivity and specificity of CT for detecting adenomas (Mody et al [ACR] 2021). The adapted low-dose unenhanced CT protocols can limit radiation exposure and can be considered as an alternative to MRI (especially if the availability of MRI is limited) (Fassnacht et al [*ESE & ENSAT*] 2023). When a non-contrast CT is used, if possible, the scan should be checked with the patient on the table and if the lesion measures > 10 HU, contrast should be administered in order to assess the washout (PLE expert panel consensus opinion).

MRI abdomen:
In general, MRI of the abdomen is appropriate for the adrenal-specific imaging of patients with no prior history of malignancy and an incidentally detected indeterminate adrenal mass measuring > 1 cm without benign imaging characteristics (Mody et al [ACR] 2021). MRI can be a particularly important tool

for diagnosing an adenoma in patients with allergies to iodinated contrast (Mayo-Smith et al 2017). Other advantages of MRI over CT are its lack of radiation exposure and its superior tissue contrast resolution (Fassnacht et al [*ESE & ENSAT*] 2023). Use of MRI instead of CT is also generally suggested in younger adults if dedicated adrenal imaging is required (Fassnacht et al [*ESE & ENSAT*] 2023; Lee et al Korean Endocrine Society 2017; E Level Recommendation).

PET or PET-CT:
FDG-PET is sensitive to metabolically active lesions, with metastases usually showing greater uptake than benign lesions (Mody et al [ACR] 2021). In patients with a history of a PET sensitive extra-adrenal malignancy, FDG-PET/CT, performed as part of investigations for the underlying malignancy, can replace other adrenal imaging techniques, particularly when an enlarging lesion is detected (Fassnacht et al [*ESE & ENSAT*] 2023; Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation; Mayo-Smith et al [ACR] 2017). If a malignant adrenal tumor is suspected, but CT results are uncertain, positron emission tomography using F-FDG-PET or PET/CT can be performed selectively (Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation).

For lesions measuring 1 to 2 cm and no history of malignancy, there is no primary evidence supporting the use of FDG-PET/CT for initial evaluation (Mody et al [ACR] 2021).

FDG-PET/CT skull base to mid-thigh (or alternatively, image-guided biopsy) is usually appropriate for the adrenal-specific imaging of patients with a history of malignancy and an indeterminate adrenal mass ≥4 cm without diagnostic benign imaging characteristics on initial images (Mody et al [ACR] 2021).

<u>Clinical notes:</u>

- To determine the stability of an adrenal mass, available prior imaging examinations should be referred to whenever possible. Even if not of the same examination type, prior imaging studies of the adrenal glands can be helpful (Mayo-Smith et al [ACR] 2017).
- A size greater than 4-6 cm on a CT scan, a tumor with an irregular margin or heterogeneity, an attenuation coefficient of ≥ 10 HU on non-contrast CT, washout of the contrast agent after 10-15 minutes of < 40%, calcification, and/or invasion into surrounding tissue all suggest malignancy (Lee et al [*Korean Endocrine Society*] 2017).
- On CT, when the tumor is < 4 cm, the risk of adrenal cancer is less than 2%, but when the size is ≥ 6 cm, the risk increases to 25% (Lee et al [*Korean Endocrine Society*] 2017).
- The virtual unenhanced density of an adrenal mass, obtained from contrast-enhanced dual-energy CT, has been shown to approximate its true unenhanced density and can be used to diagnose an adenoma, potentially reducing the need for additional studies (Mayo-Smith et al [ACR] 2017).

<u>Technical notes:</u>

- In many adenomas, more than 50% of the contrast agent disappears 10 to 15 minutes after its administration, while adrenal cancer, pheochromocytoma, and metastatic cancer all show less than a 50% loss (Lee et al [*Korean Endocrine Society*] 2017).
- The adrenal washout determination is based on the principle that adrenal adenomas rapidly wash out contrast material. Adrenal washout is calculated using CT scans through the adrenal gland and measuring Hounsfield Unit (HU) regions of interest (ROIs), ideally pre-IV contrast (A), post-IV contrast in the portal venous phase (B), and after a 15-minute delay post IV-contrast (C). When feasible, the ROI circle should cover at least half of the representative area of the adrenal

lesion where it is best seen. Images may be obtained through the adrenal glands only to reduce radiation dose (Dunnick & Korobkin 2002).

- The Percentage of Relative Washout is calculated by taking the HU measurement post-contrast in the portal venous phase (B), subtracting measurement post-delay (C), and then dividing by the measurement from the portal venous phase: (B-C)/B. If this number is > 0.40 (40%), the lesion has high likelihood of being an adenoma (benign) (Dunnick & Korobkin 2002).
- The Percentage of Enhancement Washout is calculated by taking the HU measurement from the portal venous phase (B) and subtracting the measurement in the delayed phase (C) and dividing this number by the subtraction of the non-contract HU measurement (A) from portal venous phase measurement (B): (B-C)/(B-A). If this number is greater than 0.6 (60%), the lesion has a high likelihood of being an adenoma (benign) (Dunnick & Korobkin 2002).

<u>Evidence update (2011-present):</u>

Low Level of Evidence

Marty et al (2018), in a retrospective study, assessed performance of CT and determined safe thresholds for diagnosis of adenomas and benign tumors among ‘true’ adrenal incidentalomas (AIs). A total of 233 consecutive patients were included: 183 adenomas, 33 pheochromocytomas, 23 adrenocortical carcinomas, 5 other malignant tumors and 9 other benign tumors. Reference standard was histopathology in 118 AIs, biological diagnosis of pheochromocytoma in 2 AIs and size stability after at least 1 year of follow-up in 133 AIs. Sensitivity, specificity and PPV/NPV were estimated for various thresholds of size, unenhanced attenuation (UA), and absolute/relative wash-out (RPW, APW) of contrast media. Results found combinations of size ≤ 30 mm + UA ≤ 20 HU and size ≤ 40 mm + UA ≤ 15 HU predicted the presence of an adenoma with 100% PPV. Non-adenomatous AIs with rapid contrast wash-out were exclusively benign pseudocysts and pheochromocytomas, suggesting that classical thresholds of 60% and 40% for APW and RPW, respectively, can be safely used for patients with normal metanephrine values. Inter-observer reproducibility of all parameters was excellent (intra-class correlation coefficients: 0.96–0.99). The authors conclude that their study suggests that combinations of CT criteria, namely size ≤ 40 mm and UA ≤ 15 HU, and APW and RPW > 60% and > 40%, respectively, are consistent with a diagnosis of adrenal adenoma and benign incidentaloma in patients with normal plasma or urinary metanephrines values.

Azoury et al (2017) conducted a retrospective observational study of 216 patients who underwent unilateral adrenalectomy for adrenal mass to characterize the predictive utility of CT findings on final surgical pathology. Malignant tumors were significantly larger in diameter (9.5 cm vs 2.7 cm) and all tumors that were identified as benign on CT imaging were also found to be benign on final surgical pathology.

Guideline exclusions:

- Cancer staging or follow-up,
- Renal failure,
- Vascular imaging,
- Pregnant patients,
- Pediatric patients, and
- Post processing algorithms or AI

AUC Revision History:

Revision Date:	New AUC Clinical Scenario(s):	Approved By:
07/28/2020	n/a	CDI Quality Institute's Multidisciplinary Committee
12/05/2023	n/a	RAYUS Quality Institute's Multidisciplinary Committee

Information on our evidence development process, including our conflicts of interest policy is available on our website at **https://www.rayusradiology.com/ple**

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Renal, Adrenal, & Urinary Tract AUC

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