CDI QUALITY INSTITUTE

Provider Led Entity

CDI Quality Institute PLE
Renal, Adrenal, & Urinary Tract AUC
2020 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 & Ureteral 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 protocols may be useful to improve imaging of the urinary system. **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, such as those with renal insufficiency or contrast allergy. 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 protocols may be useful to improve imaging of the urinary system (kidneys, ureters, bladder, and surrounding structures).
- **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**, while not defined as an advanced imaging modality, can be useful to identify stones, or for follow-up of patients being treated for renal or ureteral calculus. Ultrasound can also evaluate hydronephrosis in patients with renal insufficiency or allergy to iodinated contrast. Ultrasound expertise may be limited and/or not available in some practice settings.

Hematuria not due to an identified benign cause:

- 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 – **CT abdomen/pelvis with IV contrast (urography protocols preferred)**
  [*further evaluate findings on recent ultrasound or non-contrast imaging*]
- Red – **Scintigraphy; PET; PET-CT**

* If urography protocols are not used, consider urology consult for retrograde pyelogram.
** Consider urology consult for retrograde pyelogram

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

Notes concerning applicability and/or patient preferences: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (42 C.F.R. § 414.94. 2015):

- Emergency services when provided to individuals with emergency medical conditions (including major trauma).
- For an inpatient and for which payment is made under Medicare Part A.

Guideline and PLE expert panel consensus opinion summary:
Overview:
Patients with gross hematuria and patients with significant risk factors for malignancy should undergo a hematuria work-up (Davis et al [*AUA*] 2012, evidence strength: C; Wolfman et al [*ACR*] 2020; PLE expert panel consensus opinion). Significant risk factors for urinary tract malignancy include male gender, age > 35 years, past or current smoker, occupational exposure to chemicals, analgesic abuse, urologic disorder or disease, irritative voiding symptoms, chronic urinary tract infection, history of pelvic irradiation and exposure to known carcinogenic agents or chemotherapy (Davis et al [*AUA*] 2012; Wolfman et al [*ACR*] 2020). Microscopic hematuria patients with an identified benign cause, such as vigorous exercise, infection, trauma, menstruation or a recent urologic procedure are unlikely to benefit from advanced imaging (Davis et al [*AUA*] 2012; PLE expert panel consensus opinion). Patients without a known cause of microscopic hematuria are candidates for advanced imaging, however, 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).

CT without and with IV contrast (urography protocols preferred):
Multiphasic CT urography without and with intravenous contrast is the imaging procedure of choice for asymptomatic hematuria because it has the highest sensitivity (91-100%) and specificity (94-97%) for

imaging the upper tracts (Davis et al [*AUA*] 2012, Evidence Strength/Grade C; Wolfman et al [*ACR*] 2020). It is also preferred for its ability to provide excellent diagnostic information in a single imaging session (Davis et al [AUA] 2012; Sharp et al [*AAFP*] 2013). Multiphasic CT urography should include a non-contrast CT to evaluate for calculi, a contrast phase to evaluate for a renal mass, and an excretory phase to evaluate the urothelium of the upper and lower urinary tracts (Davis et al [*AUA*] 2012; PLE expert panel consensus opinion).

MR abdomen or abdomen/pelvis without and with IV contrast (urography protocols preferred):
For patients with contraindications that prevent use of multiphasic CT (such as renal insufficiency or contrast allergy), MR urography without and with IV contrast can be used as an alternative imaging approach (Davis et al [*AUA*] 2012, Evidence Strength: Grade C). However, MRU is poor at detecting stone disease, which is a common etiology of microscopic hematuria (Sharp et al [*AAFP*] 2013).

MRI abdomen or abdomen/pelvis without IV contrast (urography protocols preferred):
When collecting system detail is important, but the patient has contraindications to both multiphasic CT (such as renal insufficiency or contrast allergy) and MRI contrast, MR urography without IV contrast, or combining non-contrast MRI with retrograde pyelogram (RPG) provides an alternative evaluation of the entire upper tract (Davis et al [*AUA*] 2012, Expert Opinion; PLE expert panel consensus opinion).

CT abdomen/pelvis without IV contrast:
For patients with contraindications prohibiting use of multiphasic CT (such as renal insufficiency or contrast allergy) and also MRI (such as presence of metal in the body) and where collecting system detail is also important, combining a non-contrast CT with retrograde pyelogram provides alternative evaluation of the entire upper tracts (Davis et al [*AUA*] 2012, Expert Opinion; PLE expert panel consensus opinion).

CT abdomen/pelvis with IV contrast (urography protocols preferred):
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).

Ultrasound:
Ultrasound is not considered to be an advanced imaging modality, and is not typically used as a first-line imaging modality for the evaluation of hematuria (Wolfman et al [*ACR*] 2020). However, a recent large prospective study suggests that kidney and bladder ultrasound may be adequate for the initial evaluation of microscopic hematuria (Wolfman et al [*ACR*] 2020; Tan et al 2018). Combining a renal ultrasound with retrograde pyelogram provides alternative evaluation of the entire upper tracts (Davis et al [*AUA*] 2012, Expert Opinion; PLE expert panel consensus opinion).

<u>Clinical notes:</u>

- Patients with gross hematuria have a high incidence of malignancy (up to 30-40%) (Sharp et al [*AAFP*] 2013; Wolfman et al [*ACR*] 2020).
- Patients with microscopic hematuria have a low risk of malignancy (2-4%). 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).
- Assessment of atraumatic microscopic hematuria should include a careful history, physical examination, and laboratory examination to rule out benign causes (Davis et al [*AUA*] 2012; Wolfman et al [*ACR*] 2020).

- The presence of microscopic hematuria and dysmorphic red blood cells (RBCs), cellular casts, proteinuria, elevated creatinine level, or hypertension should raise suspicion for medical renal etiologies, such as immunoglobulin A nephropathy, Alport syndrome, benign familial hematuria, or other nephropathy (Sharp et al [*AAFP*] 2013).
- If asymptomatic microscopic hematuria persists on follow-up urinalysis, a full repeat evaluation should be considered within three to five years of the initial evaluation. Patients' risk factors for urologic malignancy should guide clinical decision making about reevaluation (Sharp et al [*AAFP*] 2013; Davis et al [*AUA*] 2012).
- Changes in the clinical scenario, such as a substantial increase in the degree of microscopic hematuria, detection of dysmorphic RBCs with concomitant hypertension and/or proteinuria, development of gross hematuria, pain, or other new symptoms, may warrant earlier re-evaluation and/or referral to other practitioners, such as nephrologists (Davis et al [*AUA*] 2012).
- 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 (Wolfman et al [*ACR*] 2019).
- MR urography (MRU) 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. IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones (Wolfman et al [ACR] 2019).
- Patient undergoing MR urography (MRU) should have a low likelihood for renal calculus disease. If a patient undergoes MRU for the work-up of atraumatic hematuria, consideration should be given to cystoscopy with cytology for bladder evaluation (PLE expert panel consensus opinion).
- For microscopic hematuria, the use of ultrasound (US) and intravenous urography (IVU) does not exclude the need for additional imaging studies. In addition, the sensitivities and specificities of US and IVU are such that the possibility of missed diagnoses is significant. Both of these issues are avoided with the use of CT urography and MR urography (Davis et al [*AUA*] 2012).
- 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).

<u>Technical notes:</u>

- Split bolus technique should be considered in patients at low risk for cancer undergoing multiphasic CT or CT with IV contrast in order to limit radiation dose to the patient. The split bolus technique aims to combine the nephrographic and urographic phases of imaging into one acquisition (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*] 2019).
- Premedication (e.g., corticosteroids) may be appropriate in patients with a history of moderate or severe allergic reaction to IV contrast prior to undergoing retrograde pyelography (PLE expert panel consensus opinion).

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

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 patients. 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 (low level of evidence).

Tan et al (2018), in a prospective, multicenter, observational study, reported incidence of upper tract disease and bladder cancer in patients with macroscopic/microscopic hematuria. Based on diagnostic ability of CT urography (CTU) and renal and bladder ultrasound (RBUS) to identify upper tract cancer, the authors also sought to determine whether CTU can be safely replaced by 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 (moderate level of evidence).

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 (moderate level of evidence).

Bretlau et al (2015), in a retrospective study, identified 771 patients undergoing CTU for either visible (gross) hematuria without symptoms, visible hematuria with symptoms, nonvisible (microscopic) hematuria without symptoms, or nonvisible hematuria with symptoms. In total, 18% of patients had a tumor or complex cyst, 9% a calculus, and another disease (infection or anomaly) in 15%. 58% had no abnormality found. Lesions were found more frequently in patients with visible hematuria (48%) than in patients with non-visible hematuria (29%). Authors conclude that "CTU with its low dose of contrast medium and radiation is a useful diagnostic imaging test for investigating patients with hematuria" (low level of evidence).

Mullen et al (2015) in a retrospective study, evaluated the yield of repeat CT urography (CTU) in detecting urinary tract malignancies in 5,525 patients with hematuria. A total of 751 (13.6%) patients underwent repeat CTU at 1-3 years. Initial CTU showed no findings suspicious for malignancy in 103

(70%) of 148 patients. Of these, none had malignancy identified on repeat CTU. 45 patients (30%) had findings suspicious of malignancy on the initial CT. Malignancy was found in four patients (8.9%) on repeat CTU in this group. The authors conclude that in patients with hematuria, repeat CTU within 3 years is unlikely to show urinary tract malignancy (low level of evidence).

Aguilar-Davidov et al (2013), in a retrospective study, reviewed the utility of CT urography for detection of bladder tumors in patients with microscopic hematuria. Sensitivity of CT urography was 29%, specificity 99%, PPV 67%, NPV 95%, and diagnostic accuracy 95%. Authors conclude that due to the low sensitivity of CT urography, “cystoscopy should be considered the standard for bladder evaluation of patients with microscopic hematuria” (low level of evidence).

Pichler et al (2013) in a retrospective study, evaluated the role of repeated urological evaluation after negative initial diagnostic work-up of asymptomatic microscopic hematuria (AMH) in 87 low-risk patients (56 women; mean age 52.4; range: 19-87). Patients had negative initial diagnostic assessment including ultrasound (US), cystoscopy, upper urinary tract (UUT) imaging using intravenous urography (IVU) or multiphasic computed tomography (CT), absence of risk factors and a follow-up period of ≥ 3 years. Three years after initial workup, cystoscopy confirmed no bladder carcinoma in any of the patients. Low-risk patients with persistent AMH after negative urological evaluation have a negligible risk of developing bladder cancer on follow-up (low level of evidence).

Song et al (2012), in a retrospective study of 1,209 patients (age range, 20–94), aimed to determine prevalence and characteristics of clinically important extraurinary findings on MDCT urography for hematuria evaluation. In 82 patients (6.8%), 85 clinically important incidental extraurinary findings were identified. Follow-up evaluation was available for 50.6% of findings by histologic diagnosis (n = 9), imaging evaluation (n = 31), or clinical information (n = 3). There were 11 (0.9%) examinations with acute findings, of which acute inflammation of the gastrointestinal tract and pancreaticobiliary system were most common. Seventy-two (5.9%) examinations revealed 74 nonacute but important findings. Lung nodules were most prevalent, followed by intraabdominal aneurysms and cystic ovarian masses. There were five (0.4%) histologically proven malignant neoplasms. The authors conclude prevalence of clinically important incidental extraurinary findings at MDCT urography performed for hematuria was 6.8% (low level of evidence).

Cauberg et al (2011), in a prospective study, sought to define the indications for imaging the upper urinary tract (UUT) with CT urography (CTU) in 456 patients presenting with hematuria. All patients (mean age 56.7 +/- 16.6 years) underwent standard evaluation with history, physical exam, ultrasound (US) of kidneys and bladder, cystoscopy, and cytology. CTU or MR urography (MRU) was performed in patients with abnormal findings on cystoscopy or US, and in high risk patients. KUB and US of the kidney/bladder were performed on the remaining patients. US findings (OR 7.7, 95% CI 4.0–14.9), P < 0.001) and type of hematuria (OR 2.6, 95% CI 1.3–5.1, P = 0.01) were significant predictors for abnormal cross-sectional urography result. 44/456 (9.6%) of patients with negative US results had positive findings on CTU/MRU, with most of these missed lesions being stones. The authors concluded that for patients who present with microscopic hematuria, US is sufficient to exclude significant UUT disease. For patients with macroscopic hematuria, the likelihood of finding UUT disease is higher, and a CTU as a first-line test seems justified (low level of evidence).

Suspected renal or ureteral calculus:

- Green – **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*]
- 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; 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:
Overview:
Diagnostic imaging is recommended in patients with acute flank pain and a suspicion for a renal or ureteral stone. CT of the abdomen and pelvis without IV contrast is the preferred advanced imaging modality (Moreno et al [*ACR*] 2015*; Turk et al [*EAU*] 2019). MRI can be used to evaluate for obstruction of the renal collecting system in patients who cannot undergo CT with IV contrast (PLE expert panel consensus opinion). Ultrasound, although not an advanced imaging modality, can also be used as the primary diagnostic imaging tool for stones when expertise is available however limited evidence has shown that it is not as sensitive for renal and ureteral calculi as non-contrast CT (Turk et al [*EAU*] 2019; *NICE* 2019).

CT KUB without IV contrast:
Non-contrast CT (NCCT) is the preferred initial imaging study for patients suspected of having a renal or ureteral stone (Fulgham et al [*AUA*] 2013; Level A Evidence; Moreno et al [*ACR*] 2015*), and should be considered in presentation of renal colic/acute flank pain (*NICE* 2019; Turk et al [*EAU*] 2019). Non-contrast CT has a reported median sensitivity and specificity for the detection of ureteral calculi of 98% and 97%, respectively, far superior to other imaging modalities (Fulgham et al [*AUA*] 2013; *NICE* 2019). In patients with acute flank pain who have had a previous ultrasound assessment, non-contrast CT can be used to confirm stone diagnosis (Turk et al [*EAU*] 2019 Level 1a/Grade A Evidence). If the patient has hydronephrosis on ultrasound or if the patient has persistent symptoms without hydronephrosis on ultrasound, CT can also be obtained for further evaluation (PLE expert panel consensus opinion).

CT abdomen/pelvis with IV contrast or **CT abdomen/pelvis without and with IV contrast**
In patients with unexplained pain, uncertainty, or when an abnormality is revealed on CT without contrast or ultrasound, intravenous contrast material can be administered and excretory phase images obtained for definitive diagnosis (Moreno et al [*ACR*] 2015*; PLE expert panel consensus opinion).

MRI abdomen or abdomen/pelvis (urography protocols preferred):
MR urography can be an excellent tool for the evaluation of hydronephrosis, and is also useful in the setting of an CT contrast allergy. However, MRI can be limited in its ability to detect smaller stones (Moreno et al [*ACR*] 2015*; Assimos et al [*AUA*] 2016).

Renal scintigraphy:
Renal scintigraphy may be indicated when further assessment of renal/urinary tract obstruction is necessary (Kim et al [*ACR-SPR*] 2017; PLE expert panel consensus opinion).

Ultrasound:
While not considered an advanced imaging modality, ultrasound can identify stones located in the calices, pelvis, and ureteropelvic and ureterovesical junctions, and can identify patients with upper urinary tract dilatation. US has a sensitivity of 45% and specificity of 94% for ureteric stones and a sensitivity of 45% and specificity of 88% for renal stones (Turk et al [*EAU*] 2019). Ultrasound is also useful for evaluation of hydronephrosis, particularly in patients with renal insufficiency or allergy to iodinated contrast (PLE expert panel consensus opinion). Additionally, it can be a viable option for a known stone former who has previously had radiolucent stones (PLE expert panel consensus opinion). However, ultrasound expertise may be limited and there is known to be widespread variation in the quality of ultrasound (*NICE* 2019; PLE expert panel consensus opinion).

Clinical notes:

- For suspected ureteral/renal stone with fever or solitary kidney, or when diagnosis is doubtful, immediate evaluation is indicated (Turk et al [*EAU*] 2019).
- The sensitivity and specificity of KUB radiography is 44-77% and 80-87%, respectively. KUB radiography should not be performed if non-contrast CT is considered, however, it is helpful in differentiating between radiolucent and radiopaque stones and for comparison during follow-up (Turk et al [*EAU*] 2019).
- The combination of renal ultrasonography and KUB is a viable option for a known stone former who has previously had radiopaque stones. Sensitivities of 58%-100% and specificities of 37.2%-100% have been reported for this combination of modalities (Fulgham et al [*AUA*] 2013).
- Unenhanced MR urography (MRU) relies upon heavily T2-weighted imaging of the intrinsic high signal intensity from urine for evaluation of the urinary tract. IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones (Wolfman et al [*ACR*] 2019).

Technical notes:

- If non-contrast CT is indicated in patients with BMI < 30, a low-dose technique can be used to reduce radiation risk. Low-dose CT has been shown to have a sensitivity of 86% for detecting ureteric stones < 3 mm and 100% for calculi > 3 mm. (Turk et al [*EAU*] 2019; Fulgham et al [*AUA*] 2013).
- In patients with a BMI > 30, US may be less effective at identifying renal and ureteral calculi, and CT may therefore be more efficacious (PLE expert panel consensus opinion).

- 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).
- 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).

<u>Evidence update (2014-present):</u>
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 (low level of evidence).

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 $\geq$ 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 (low level of evidence).

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 (low level of evidence).

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 (low 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 (moderate level of evidence).

Daniels et al (2016), in a 2016 prospective study of 835 ED patients with suspected nephrolithiasis, examined rates of symptomatic stone disease or other acute diagnosis and rate of 90-day urological intervention after point of care limited ultrasound (PLUS) was added to results of STONE score. Presence of hydronephrosis increased sensitivity in low/moderate STONE score categories, from 3.2% to 64% and from 41% to 60%, respectively. The presence of moderate or greater hydronephrosis improved specificity from 67% to 98%, and from 42% to 92% in low- and moderate-risk patients, with likelihood ratios of 22 and 4.9, respectively. Of the 59 patients with high STONE score who received intervention within 90 days of ED visit, 48 (81%) had some degree of hydronephrosis, and hydronephrosis was overall 66% sensitive for predicting need for intervention in all groups. 54 acutely important alternate findings were identified on CT in 8.3%, 9.0%, and 1.8% of patients in low, moderate, and high risk STONE score groups, respectively. Presence of hydronephrosis further reduced risk of alternate diagnosis being identified (OR 0.31; 95% CI 0.16-0.60). The authors conclude hydronephrosis on renal PLUS modestly improved risk stratification in low- and moderate-risk STONE score patients. The presence or absence of hydronephrosis in high-risk patients did not significantly alter likelihood of symptomatic stone, but may aid in identifying patients more likely to require urologic intervention (high level of evidence). *The expert committee thought that the primary significance of this study was that patients with a low STONE score and no hydronephrosis on ultrasound had a low incidence of renal calculi on CT. The referring provider should consult the abdominal pain AUC recommendations when considering advanced imaging in these patients* (PLE expert panel consensus opinion*).*

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 (moderate level of evidence).

Yan et al (2015), in a prospective cohort study, studied the negative predictive value of normal renal ultrasound (US) in 610 patients presenting to the ER with suspected renal colic. Of 341 patients receiving US as initial imaging modality, 30.8% were normal. At 90-day follow-up, 0 patients received urological intervention, and no significant abdominal pathology was identified in this cohort. The authors conclude "although US has less diagnostic accuracy compared to CT, patients with a clinical diagnosis of renal colic and a normal renal sonogram are unlikely to require urologic intervention within 90 days of initial ED visit and can confidently be managed conservatively with appropriate analgesia and clinical follow-up" (moderate level of evidence).

Fields et al (2015), in a prospective study of 77 patients with symptoms of acute renal colic undergoing sonographic evaluation of the affected kidney, sought to define variables on ultrasound (US) that significantly predicted need for hospitalization within 30 days. It found those patients with moderate hydronephrosis on US had higher admission rate (36%) than those with mild or no hydronephrosis ($p < 0.01$), and concluded that information from bedside US may help clinicians determine which patients may benefit from hospital admission (moderate level of evidence).

Agarwal et al (2015), in a retrospective study, reviewed findings of 322 non-consecutive patients presenting to ED with flank pain who underwent CT for diagnosis of nephroureterolithiasis. All patients had initial non-contrast CT, while 154 had additional contrast-enhanced CT. Addition of contrast CT added information in 5.3% of cases but changed management in only 2%. Authors conclude that additional contrast-enhanced CT in patients with a strong clinical suspicion of nephrouterterolithiasis may not be indicated (low 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 (high level of evidence).

Samim et al (2015), in a retrospective study, evaluated prevalence, importance, and types of incidental findings (IF) in non-contrast CT scans performed for suspected renal colic, based on ACR white papers and other accepted radiographic recommendations. Review of 5,383 consecutive finalized reports of non-contrast CT using renal colic protocol was performed on adult ED patients over a 5.5-year period. Important IF were identified on 12.7% of scans. Prevalence of important IF increased with age: important IF in individuals age > 80 were 4 times more common than for those aged 18-30. Important IF occurred on 12.7% of non-contrast CT scans performed for suspected renal colic in the ED and are more common in older individuals (moderate level of evidence).

Moore et al (2014), in a prospective cohort study, sought to derive and validate a clinical prediction rule (STONE score) for the presence of uncomplicated ureteral stones in CT-eligible patients. Adult patients (mean age 44) with flank pain and suspected nephrolithiasis without history of trauma, evidence of infection, known active malignancy or renal disease, or previous urologic procedure were included. The derivation sample included 1,040 records, and found 5 factors to be most predictive of ureteral stone: male sex, short duration of pain, non-black race, presence of nausea/vomiting, and microscopic hematuria, yielding a (STONE) score 0-13. Prospective validation of 491 participants found that patients with low score (0-5) have < 10% probability of stones, moderate scores (6-9) have 50% probability, and high scores (10-13) have high (89%) probability. The authors conclude that "STONE score reliably predicts the presence of uncomplicated ureteral stone and lower likelihood of acutely important alternative findings" (high level of evidence).

Chan et al (2014), in a single-center retrospective cohort study, used blind reviews of 1,000 routine abdominopelvic CTs performed with delayed excretory phase imaging to determine the added value of the latter phase in routine imaging, excluding patients with primary indication of lesion characterization. Two patients demonstrated a finding on delayed phase imaging that would have significantly affected management (a renal mass and unknown contrast-nephropathy) that would otherwise have been missed on portal-venous phase imaging. Additional incidental findings were characterized in 2-3% of patients. Relative to the approximately 60% increase in radiation dose, the authors conclude that routine delayed phase imaging is not of clinical benefit to patients. (low level of evidence).

Dym et al (2014), in a cohort of 97 cases of non-contrast and contrast-enhanced CTs, demonstrated that the detection of nephrolithiasis of $\geq$ 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 (moderate level of evidence).

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 (Smith-Bindman et al 2014; high level of evidence).

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 – **PET; 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:

Overview:

Clinicians should offer reimaging to patients prior to surgery if passage of stones is suspected or if stone movement will change management. Reimaging 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. 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). 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 without and with IV contrast (urography protocols preferred):

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). A contrast study is recommended if stone removal is planned and the anatomy of the renal collecting system needs to be assessed (Turk et al [*EAU*]2019, Level 3/Grade A Evidence). Enhanced CT is preferable in complex cases because it enables 3D reconstruction of the collecting system, as well as measurement of stone density and skin-to-stone distance. (Turk et al [*EAU*] 2019, Level 4/Grade C Evidence).

CT abdomen/pelvis with IV contrast (urography protocols preferred):
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 (urography protocols preferred):
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 with nuclear renal scan or another 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:
Clinicians may obtain a functional imaging study (DTPA or MAG-3) if clinically significant loss of renal function in the involved kidney or kidneys is suspected (Assimos et al [*AUA*] 2016, Conditional Recommendation; Evidence Level Grade C).

<u>Clinical notes:</u>

- Consider the stone composition before deciding on the method of removal, based on patient history, former stone analysis of the patient, or Hounsfield unit (HU) on unenhanced CT (Turk et al [*EAU*] 2019).
- Renal stone attenuation of < 900-1000 HU and a skin-to-stone distance of < 10 cm can help predict success with SWL (Assimos et al [*AUA*] 2016)
- 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*] 2019).
- 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*] 2019).
- 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).
- 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):
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 concluded "ureteroscopic treatment of ureteral stones can be safely and effectively performed with no use of contrast study imaging, except in doubtful cases of anatomical abnormalities" (low level of evidence).

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

- **Green** – *
- **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, PET; PET-CT; Scintigraphy**

***Ultrasonography (US) with or without KUB radiography can be used for initial follow-up of patients being treated for renal or ureteral calculus (Fulgham et al [*AUA*] 2013; PLE expert panel consensus opinion).**

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:

After definitive surgical intervention for a ureteral calculus, follow-up imaging is obtained to assure complete stone removal and/or absence of obstruction (Fulgham et al [*AUA*] 2013). For patients who undergo ureteroscopy with stone fragmentation, follow-up imaging will document the presence of residual fragments and/or hydronephrosis (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). For patients undergoing MET in whom there is documented stone passage and resolution of symptoms, no further imaging is necessary (Fulgham et al [*AUA*] 2013).

Ultrasonography/KUB radiography:

Although not considered to be an advanced imaging modality, ultrasonography (US), with or without KUB radiography, 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 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. If the patient is asymptomatic and KUB/sonogram shows no stones or hydronephrosis, no further imaging is required. If follow-up KUB/sonogram 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 sonogram is sufficient to document resolution of hydronephrosis (Fulgham et al [*AUA*] 2013).

CT:
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>

- 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 SWL or ureteroscopy with lithotripsy is widely accepted (Fulgham et al [*AUA*] 2013).
- 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 the most common etiology (Fulgham et al [*AUA*] 2013).
- The need for follow up studies in asymptomatic patients following treatment is subject to debate. The incidence of postoperative obstruction in asymptomatic patients is low (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>:
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 (low level of evidence).

Akhavein et al (2015), in a retrospective cohort, evaluated 122 patients with renal calculi receiving pre- and post-operative STONE scoring through CT imaging to determine success of PCNL treatment. Nephrolithometry scores ranged from 5-13, and mean nephrolithometry scores for residual stone of 0-2, 3-4, and > 4 mm were 8.87, 9.73, and 10.79 respectively. The authors conclude that with use of strict CT imaging criteria for assessment of residual stone status, the STONE scoring system is reproducible and predictive of treatment success (low level of evidence).

Suspected infection in any of the following:

- **Immunocompromised patients,**
- **Patients with ≥ 48 hours of unsuccessful therapy, and/or**
- **Patients with progressive, recurrent, or atypical symptoms:**

  - Green – **CT abdomen/pelvis without and/or with IV contrast**
  - 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; PET-CT; 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: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (42 C.F.R. § 414.94. 2015):

- Emergency services when provided to individuals with emergency medical conditions (including major trauma).
- For an inpatient and for which payment is made under Medicare Part A.

Guideline and PLE expert panel consensus opinion summary:

Overview:

Advanced diagnostic imaging is usually not appropriate for initial evaluation of uncomplicated pyelonephritis (Bonkat et al [*EAU*] 2019; Nikolaidis et al [*ACR*] 2018). However, imaging should be performed without delay in atypical cases (e.g., suspicion for renal calculi, outflow obstruction, interstitial cystitis or urothelial cancer) (Bonkat et al [*EAU*] 2019) or in patients with history of diabetes or immune compromise, history of stones or obstruction, prior renal surgery, or lack of response to therapy (Nikolaidis et al [*ACR*] 2018). Imaging is also recommended in the patient who remains febrile after 48-72 hours of treatment (level of evidence: 4) or immediately if there is deterioration in clinical status (Bankat et al [*EAU*] 2019; PLE expert panel consensus opinion).

CT:

CT in the setting of acute pyelonephritis is indicated if the patient has complications or is immunocompromised, after 48-72 hours or unsuccessful therapy, and/or if the symptoms are atypical (Nikolaidis et al [*ACR*] 2018; Bonkat et al [*EAU*] 2019; PLE expert panel consensus opinion). In diabetic or immunocompromised patients who do not respond promptly to treatment, CT without and with IV contrast is recommended (PLE expert panel consensus opinion). Contrast-enhanced CT has high sensitivity in detecting parenchymal changes in acute pyelonephritis, including early in the course of disease (Nikolaidis et al [*ACR*] 2018). CT without IV contrast can be used if contrast is contraindicated and is useful in patients with known or suspected renal or ureteral calculi, and in patients with obstruction (PLE expert panel consensus opinion).

MRI:

MRI may be particularly useful for patients in whom the use of iodinated contrast material must be avoided (particularly those with contrast sensitivity) (Nikolaidis et al [*ACR*] 2018; PLE expert panel consensus opinion). In certain cases, MR urography (MRU) protocols may be useful and allow for a comprehensive assessment of the kidneys, ureters, bladder, and surrounding structures; most MRU protocols use IV contrast, but in certain cases, could be performed without contrast (Nikolaidis et al [*ACR*] 2018).

Ultrasound:

When 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). However, ultrasound can miss subtle changes of mild pyelonephritis and underestimate the severity of renal involvement or perinephric extension (Nikolaidis et al [*ACR*] 2018).

<u>Clinical notes:</u>

- Pyelonephritis is suggested by fever, chills, flank pain, nausea, vomiting, or costovertebral angle tenderness, with or without the typical symptoms of cystitis (Bankat et al [*EAU*] 2019).
- When the kidney itself is involved or when there is difficulty in differentiating lower UTI from renal parenchymal involvement, imaging studies are often requested, both for diagnosis and to plan management (Nikolaidis et al [*ACR*] 2018).
- Conditions thought to predispose a patient with lower UTI to renal involvement include vesicoureteral reflux, altered bladder function, congenital urinary tract anomalies, and the presence of renal calculi (Nikolaidis et al [*ACR*] 2018).
- Abdominal radiography is of very limited use in the setting of acute pyelonephritis, unless large coexisting staghorn or obstructing calculi are being followed (Nikolaidis et al [*ACR*] 2018).

<u>Evidence update (2014-present):</u>

El-Merhi et al (2018), in a retrospective study, evaluated non-contrast CT performance by reporting the difference in attenuation between normal and inflamed renal parenchyma in 74 patients with acute pyelonephritis (APN) and failure to respond after 48 hours of antibiotics treatment. Mean attenuation values in Hounsfield units (HU) were measured in the upper, middle, and lower segments of inflamed and normal kidney of the same patient. Results found mean attenuation in these segments of the inflamed renal cortex was 32%, 25%, and 29% lower than mean attenuation of corresponding cortical segments of the contralateral normal kidney, respectively ($p < 0.01$). Mean attenuation in these segments of the inflamed renal medulla was 48%, 21%, and 30% lower than the mean attenuation of corresponding medullary segments of contralateral normal kidney ($p < 0.02$). Mean attenuation between inflamed and non-inflamed renal cortex and medulla was 29% and 30% lower, respectively ($p < 0.001$). The authors conclude that non-contrast CT showed a significant decrease in parenchymal density of the kidney affected with APN in comparison to the contralateral normal kidney of the same patient (low level of evidence).

Millet et al (2017), in a prospective study, assessed the added-value of systematic unenhanced abdominal CT on emergency department (ED) diagnosis. The study included 401 consecutive patients 75 years of age or older, admitted to the ED with acute abdominal symptoms, and investigated by early systematic unenhanced abdominal CT scan. Systematic unenhanced CT significantly improved the accurate diagnosis (76.8% to 85%, p=1.1x10-6) and management (88.5% to 95.8%, p=2.6x10-6) rates compared to current practice. It allowed diagnosing 30.3% of acute unsuspected pathologies, 3.4% of which were unexpected surgical procedure requirement. Systematic unenhanced abdominal CT improves ED diagnosis accuracy and appropriate management in elderly patients presenting with acute abdominal symptoms compared to current practice (moderate level of evidence).

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 – 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; PET; 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:

Cystic renal lesions are typically identified incidentally on routine imaging (Richard et al [*CUA*] 2017), and cannot be diagnosed confidently as benign or malignant at the time of discovery (Wang et al [*ACR*] 2020). The Bosniak classification of cystic renal masses was originally described using CT imaging, but other modalities, such as MRI or ultrasound, are now also being used to help better delineate these lesions (Richard et al [*CUA*] 2017). 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:

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, such as in the detection of fat seen in angiomylipoma(s) (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 (PLE expert panel consensus opinion). A CT with IV contrast only can 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:

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).

Clinical notes:

- Bosniak category I lesions are simple cysts that are considered benign. Transformation into a more complex cyst is rare and has been reported in only a handful of cases. As this is rare in occurrence, these cysts do not require follow-up (Richard et al [*CUA*] 2017, Level of evidence: 3; Recommendation: B).
- Bosniak category II lesions are minimally complex cysts also generally considered to be benign, but there are reports in the literature of them being malignant. Similar to category I cysts, a follow-up for properly classified Bosniak II cysts is not warranted (Level of evidence: 3; Recommendation: C). When there is doubt as to their categorization based on imaging characteristics, these lesions should be considered as being Bosniak category IIF lesions and followed accordingly (Richard et al [*CUA*] 2017).
- Bosniak category IIF lesions have a higher risk (25%) of malignancy (Smith et al 2012) and require follow-up (Level of evidence: 3; Recommendation: B). In view of the low metastatic potential of these lesions (if malignant), it seems reasonable to follow these lesions with a contrast-enhanced CT scan or MRI every six months for the first year (Level of evidence: 4; Recommendation: D). Ultrasound in combination with CT or MRI may be used if the lesion is stable on follow-up. Cases without progression should be followed annually for at least five years (Richard et al [*CUA*] 2017, Level of evidence: 4; Recommendation: D).
- Bosniak category III lesions have thickened walls or septa with enhancement, and have been found to be malignant approximately 54% of the time. Surgical excision is generally suggested (Level of evidence: 3; Recommendation: B). Active surveillance and thermal-ablation therapies may also be considered as appropriate treatment alternatives in select cases (Level of evidence: 4; Recommendation: D). There is currently no evidence to dictate any specific follow-up scheme. However, if active surveillance is considered, it seems reasonable to follow these lesions with abdominal imaging every six months for the first two years, followed by yearly imaging thereafter, if the lesion is stable (Richard et al [*CUA*] 2017, Level of evidence: 4; Recommendation: D).
- Bosniak category IV lesions also contain distinct enhancing soft tissue components, and have been found to be malignant approximately 80-90% of the time. Surgical excision is generally suggested (Level of evidence: 3; Recommendation: B). Nevertheless, most of these malignant cysts are thought to have low metastatic potential and thus, more conservative management may be safely considered in select cases (Richard et al [*CUA*] 2017, Level of evidence: 4; Recommendation: D).

Evidence update (2016-present):
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 $\geq$ 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 (low level of evidence).

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 (low level of evidence).

Itani et al (2016), in a retrospective study, reviewed 13,600 reports of abdominal sonographic examinations, and identified 120 small uncomplicated echogenic renal lesions in patients without known malignancy of any kind, tuberous sclerosis, or lesions > 1.0 cm. Advanced imaging (CT, MRI) and/or long term follow up was used as reference standard. None of the masses developed malignancy. The authors conclude that “small echogenic renal masses up to 1 cm in size that fulfill our study criteria are so likely to be benign that they can be safely ignored” (low level of evidence).

Evaluation of incidental/indeterminate adrenal mass or nodule (adrenal incidentaloma):

- 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**
  [*known PET-sensitive primary neoplasm*]
- Red – **Scintigraphy**

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

Notes concerning applicability and/or patient preferences: none

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 (Remer et al [*ACR*] 2012*). 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:
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* 2016; very low quality of evidence). CT and MRI are techniques to identify benign lesions, therefore representing tools designed for the exclusion of adrenal malignancy. Conversely, FDG-PET/CT is mainly used for the detection of malignant disease (Fassnacht et al [*ESE & ENSAT*] 2016). 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*] 2016).

CT:
Non-contrast computed tomography (CT) is recommended as an initial imaging study to determine whether the adrenal tumor is benign (Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation; Fassnacht et al [*ESE & ENSAT*] 2016; very low quality of evidence). If the non-contrast CT is consistent with a benign adrenal mass (Hounsfield units $\leq$ 10) that is homogeneous and < 4 cm, no further imaging is required (Fassnacht et al [*ESE & ENSAT*] 2016; very low quality of evidence). 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). In patients with a history of extra-adrenal malignancy, adrenal lesions, characterized as benign by non-contrast CT, require no further specific adrenal imaging follow-up (Fassnacht et al [*ESE & ENSAT*] 2016; Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation). 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*] 2016).

MRI:
Advantages of MRI over CT are its lack of radiation exposure, lack of iodine-based contrast media, and its superior tissue contrast resolution (Fassnacht et al [*ESE & ENSAT*] 2016). Use of MRI instead of CT is generally suggested in younger adults if dedicated adrenal imaging is required (Fassnacht et al [*ESE & ENSAT*] 2016; Lee et al Korean Endocrine Society 2017; E Level Recommendation). It is also indicated when nonenhanced CT is equivocal, for patients with iodinated contrast allergy, or when there are suspicious imaging features (Remer et al [*ACR*] 2012*; PLE expert panel consensus opinion).

PET or PET-CT:
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). 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 (Fassnacht et al [*ESE & ENSAT*] 2016; Lee et al [*Korean Endocrine Society*] 2017; C Level Recommendation).

* This guideline did not pass the AGREE II cutoff score of 90 or the rigor of development scaled domain score cutoff of 50%. It was included, however, because of its direct relevance to this clinical scenario.

<u>Clinical notes:</u>

- It is recommended that additional diagnostic work-up be conducted only in lesions $\geq$ 1 cm unless clinical signs and symptoms suggestive of adrenal hormone excess are present (Fassnacht et al [*ESE & ENSAT*] 2016).
- A size greater than 4-6 cm on a CT scan, a tumor with an irregular margin or heterogeneity, an attenuation coefficient of $\geq$ 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).
- The most useful tool to determine whether an adrenal tumor is malignant is a CT scan. When the tumor is < 4 cm, the risk of adrenal cancer is less than 2%, but when the size is $\geq$ 6 cm, the risk increases to 25% (Lee et al [*Korean Endocrine Society*] 2017).
- Ultrasonography (US) does not detect adrenal masses with the same sensitivity as CT or MRI (Terzolo et al [*Italian Association of Clinical Endocrinologists* (*AME*)] 2011).

<u>Technical notes:</u>

- In many adenomas, more than 50% of the contrast agent disappears 10 to 15 minutes after its administration. Adrenal cancer, pheochromocytoma, and metastatic cancer all show less than a 50% loss. This finding has very high sensitivity and specificity (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).

Evidence update (2011-present):
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 (low level of evidence).

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. The authors conclude "regardless of size, when interpreted as benign on CT scan, laparoscopic adrenalectomy, if technically feasible, should be the technique used when surgery is offered, or close surveillance may be a safe alternative" (low level evidence).

Young et al (2016) conducted a retrospective study of adrenal carcinoma incidence within incidentally discovered adrenal nodules on 653 patients (mean age 66 years) undergoing CT scans for other indications. After 3 years of follow-up in 392 patients, no nodules < 4 cm were malignant. The authors conclude that "in patients without pre-existing cancer, additional imaging for small incidental adrenal nodules is unnecessary" (low-level of evidence).

Patrova et al (2015), in a retrospective study of 647 patients (mean age 62.7), investigated outcomes of adrenal incidentaloma (AI). Patients had radiologic (CT or MRI) and hormonal evaluation performed at baseline; mean AI size was 25.3 ± 17.0 mm. 91.4% of adrenal lesions were hormonally normal. Hormonally active tumors were larger than nonfunctional ones (39.3 ± 24.3 mm vs. 23.9 ± 15.6 mm; P < .001). Bilateral adrenal tumors were discovered in 11% of patients. Four cases of adrenal cortical carcinoma (ACC) were detected, with mean tumor size 91 ± 34 mm; in 2 cases, tumors were hormonally active. Fourteen patients (2.2%) were diagnosed with adrenal gland metastasis, with mean tumor size 39.1 ± 23.0 mm. A total of 593 patients (93%) were followed $\geq$ 24 mo. In 86.3%, the size of tumor was unchanged by time of last follow-up. Almost all (99.6%) nonfunctioning AIs remained hormonally inactive during follow-up period. The authors conclude most AIs were benign, but a small number were functional and malignant. The prognosis of patients with adrenal metastasis was extremely poor, but otherwise, mortality rate was similar to that of general population. Follow-up of AIs < 4 cm with initial nonfunctional profile and benign radiologic appearance appears unwarranted (low level of evidence).

Nogueria et al (2015), in a retrospective study, examined imaging characteristics of adrenal tumors preceding the diagnosis of adrenocortical cancer (ACC). 20 patients with a diagnosis of ACC and a prior adrenal tumor were identified among 422 patients. Chart and image review for patient characteristics and initial, interval, and diagnostic imaging characteristics (size, homogeneity, borders, density, growth rate) were conducted. Of the initial tumors, 25% were < 2cm in size. Surveillance led to diagnosis of ACC within 24 months in 50% of patients. The growth pattern was variable, with some lesions showing long-term stability (up to 8 years) in size. Antecedent lesions in patients with a diagnosis of ACC are often indeterminate by imaging criteria and can be small. The authors conclude that, given the rarity of ACC, the increased risk of additional evaluation may not be warranted (low level of evidence).

Lou et al (2014) conducted a retrospective chart review aimed to determine the incidence of a secondary imaging modality (SIM) in the workup of adrenal masses and the usefulness of this additional imaging in changing surgical management among adult patients who underwent at least one imaging study prior to surgery. A multivariate logistic regression model was constructed to identify patient factors that predisposed SIM. A total of 264 cases met inclusion criteria, of which 98 (37%) were identified to have SIM. Patients with cancer, incidentaloma, and pheochromocytoma were more likely to undergo additional imaging. MRI was the most commonly obtained SIM. The authors conclude that the high incidence of unnecessary additional imaging performed in patients undergoing adrenalectomy is counter-productive to efforts towards high quality healthcare (low level of evidence).

Takanami et al (2014), in a retrospective study, analyzed 29 lipid-rich adrenal adenomas in 28 adult patients to determine the diagnostic accuracy of FDG PET-CT in predicting the hormone-secretion status of lipid-rich adenomas. Based on a modest sensitivity (0.69), specificity (0.81), and PPV (0.76) of the SUV ratio on FDG PET-CT for detecting hormone-secreting adenomas, the authors concluded that additional endocrinologic investigations are strongly recommended when an FDG-avid lipid-rich incidentaloma is detected on FDG PET-CT (low level of evidence).

Cho et al (2013) conducted a retrospective cohort study of 282 adrenal incidentalomas on routine abdominal CT, and found that a majority of tumors are nonfunctional and benign, with a small number of tumors (13.8%; more common in women and among those with HU > 10) being functional adrenal tumors, with even fewer representing malignancy. Few changes were observed over a mean 23 month follow-up period, and the authors conclude that initial imaging characteristics and biochemical workup are of significantly greater diagnostic value than follow-up examinations. No discussion was made of initial diagnostic accuracy at first imaging (low level of evidence).

Song et al (2013) conducted a retrospective study on 188 patients (age range 23- 95 years) with adrenal masses 1-4 cm to determine whether morphologic features of adrenal masses detected at initial contrast-enhanced MDCT differentiate benign from malignant disease. There were 171 (81%) benign and 40 (19%) malignant adrenal masses (all metastases diagnosed in patients with known extraadrenal malignancy). For individual morphologic features in diagnosing malignancy, irregular margins had 30–

33% sensitivity and 95–96% specificity and an enhancing rim had 5–13% sensitivity and 98–99% specificity. No imaging features were reliable in predicting benignity. When an adrenal mass was deemed suspicious, sensitivities for malignancy ranged from 54%-74% and specificities from 96%-97%. No malignant lesions occurred in patients without a known history of cancer. Authors concluded that when an adrenal mass has malignant morphologic features it likely represents a malignant lesion. The remaining morphologic features, (e.g., smooth margin and homogeneous density) can be seen in both benign and malignant disease, and are not sufficient for characterization of adrenal masses, particularly in patients with a known history of malignancy (low level of evidence).

Muth et al (2011), in a prospective cohort study, investigated the incidence, clinical features, and natural history of incidentally discovered adrenal mass lesions (adrenal incidentaloma [AI]) in patients undergoing radiological exam over an 18-month period. Inclusion criteria was incidentally discovered adrenal enlargement or mass lesion in patients without extra-adrenal malignancy on detection. Of 534 patients assessed for eligibility, 226 (mean age 67 years, 62.4% women; mean lesion diameter 23.9 mm, 22.6% bilateral) were included. Mean follow-up was 19.0 months. No primary adrenal malignancy was found. A total of 6.6% of patients with an AI had surgery, and benign hormone-producing tumors were verified in 3.1%. Repeat CT and hormone evaluation after 2 years did not increase the sensitivity for diagnosis of malignant or hormone-producing tumors (moderate level of evidence).

Guideline exclusions:

- Emergency services when provided to individuals with emergency medical conditions,
- Inpatients for which payment is made under Medicare Part A,
- Cancer staging or follow-up,
- Renal failure,
- Vascular imaging,
- Pregnant patients,
- Pediatric patients, and
- Dual energy CT

AUC Revision History:

Revision Date:	New AUC Clinical Scenario(s):	Posting Date:	Approved By:
07/28/2020	n/a	08/03/2020	CDI 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.mycdi.com/ple**