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Editorial by XXX on pp. x–y of this issue

EAU Guidelines on Diagnosis and Conservative Management of Urolithiasis

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Abstract

Context: Low-dose computed tomography (CT) has become the first choice for detection of ureteral calculi. Conservative observational management of renal stones is possible, although the availability of minimally invasive treatment often leads to active treatment. Acute renal colic due to ureteral stone obstruction is an emergency that requires immediate pain management. Medical expulsive therapy (MET) for ureteral stones can support spontaneous passage in the absence of complicating factors. These guidelines summarise current recommendations for imaging, pain management, conservative treatment, and MET for renal and ureteral stones. Oral chemolysis is an option for uric acid stones.

Objective: To evaluate the optimal measures for diagnosis and conservative and medical treatment of urolithiasis.

Evidence acquisition: Several databases were searched for studies on imaging, pain management, observation, and MET for urolithiasis, with particular attention to the level of evidence.

Evidence synthesis: Most patients with urolithiasis present with typical colic symptoms, but stones in the renal calices remain asymptomatic. Routine evaluation includes ultrasound imaging as the first-line modality. In acute disease, low-dose CT is the method of choice. Ureteral stones <6 mm can pass spontaneously in well-controlled patients. Sufficient pain management is mandatory in acute renal colic. MET, usually with α-receptor antagonists, facilitates stone passage and reduces the need for analgesia. Contrast imaging is advised for accurate determination of the renal anatomy. Asymptomatic calyceal stones may be observed via active surveillance.

Conclusions: Diagnosis, observational management, and medical treatment of urinary calculi are routine measures. Diagnosis is rapid using low-dose CT. However, radiation exposure is a limitation. Active treatment might not be necessary, especially for stones in the lower pole. MET is recommended to support spontaneous stone expulsion.

Patient summary: For stones in the lower pole of the kidney, treatment may be postponed if there are no complaints. Pharmacological treatment may promote spontaneous stone passage.

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1. Introduction

The latest print versions of the European Association of Urology (EAU) guidelines for the diagnosis and treatment of urolithiasis were published in 2001 for renal stones [1] and 2007 for ureteral stones [2], but online updates have been published annually [3]. The EAU guidelines on metabolic evaluation and prevention of urinary stones were published in 2015 [4]. Imaging modalities and choices have changed over the years and medical expulsive therapy (MET) has found its way into clinical practice [5]. This paper presents a summary of the comprehensive update of imaging and conservative treatment of urinary calculi as presented in the 2015 EAU urolithiasis guidelines [3]. Updates on interventional treatment and paediatric urolithiasis will be published separately.

2. Evidence acquisition

A professional research librarian carried out literature searches for all sections of the urolithiasis guidelines covering the period up to August 2014. Searches were carried out using the Cochrane Library Database of Systematic Reviews, the Cochrane Library of Controlled Clinical Trials, and Medline and Embase on the Dialog–Datastar platform. The searches used the controlled terminology of the respective databases. Both MesH and Emtree were analysed for relevant terms. In many cases, the use of free text ensured the sensitivity of the searches. The focus of the searches was identification of all level 1 scientific papers (systematic reviews and meta-analyses of randomised controlled trials [RCTs]). If sufficient data were identified to answer the clinical question, the search was not expanded to include lower-level literature. Level of evidence (LE) and/or grade of recommendation (GR) were determined according to the Oxford Centre for Evidence-based Medicine [6]. In some cases there is no direct link between LE and GR, and recommendations were upgraded or downgraded following expert panel discussion. These cases are clearly identifiable and marked in the recommendations with an asterisk.

3. Evidence synthesis

3.1. Prevalence, aetiology, and classification of stones

Stone recurrence depends on geographic, climatic, ethnic, dietary, and genetic factors. Prevalence varies from 1% to 20% [7,8]. Stone composition is the basis for further diagnostic and management decisions. Stones can be classified by cause (Table 1), aetiology of formation, composition, and risk of recurrence [9,10]. Further classifications are based on stone size and location or X-ray characteristics (plain X-ray appearance on kidney-ureter-bladder [KUB] radiography; Table 2) [11]. Non–contrast-enhanced CT (NCCT) can be used to classify stones according to density and composition [11,12].

Table 1 – Stone classification by aetiology

Non–infection stones
• Calcium oxalate
• Calcium phosphate including brushite and carbonate apatite
• Uric acid
Infection stones
• Magnesium ammonium phosphate
• Carbonate apatite
• Ammonium urate
Genetic causes
• Cystine
• Xanthine
• 2,8-Dihydroxyadenine
Drug stones

3.2. Diagnostic evaluation

Evaluation includes a detailed medical history, physical examination, appropriate imaging, and basic evaluation. Patients with ureteral stones usually present with loin pain, vomiting, and sometimes fever, whereas renal stones may be asymptomatic [13].

3.2.1. Diagnostic imaging

Ultrasound (US) should be used as the primary diagnostic imaging tool, although pain relief and other emergency measures should not be delayed by imaging assessments (Table 3). US can identify stones located in the kidney and pyeloureteral and vesicoureteric junctions, but frequently fails to detect ureteral calculi. The upper urinary tract is usually dilated in patients with ureteral stones. For all stones, US has sensitivity of 19–93% and specificity of 84–100% [14].

The sensitivity and specificity of KUB radiography for stone identification are 44–77% and 80–87%, respectively [15]. KUB radiography may be helpful in differentiating between radiolucent and radiopaque stones and for comparison during follow-up. Magnetic resonance urography cannot be used to detect urinary stones [16]. NCCT has become the standard for diagnosing acute flank pain, and has replaced intravenous urography as it seems to be more accurate [17]. When stones are absent, the cause of abdominal pain should be identified.

NCCT can detect uric acid and xanthine stones, which are radiolucent on plain films, but not indinavir and matrix stones [18]. NCCT can determine stone density (Hounsfield units, HU) and skin-to-stone distance (Table 4), which affect extracorporeal shockwave lithotripsy (SWL) outcome [11,19,20]. The advantage of non-contrast imaging must be

Table 2 – X-ray characteristics of different stone types

Radiopaque	Poor radiopacity	Radiolucent
Calcium oxalate dihydrate	Magnesium ammonium phosphate	Uric acid
Calcium oxalate monohydrate	Apatite	Ammonium urate
Calcium phosphates	Cystine	Xanthine
		2,8-Dihydroxyadenine
		Drug-stones

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Table 3 – Recommendations for diagnostic imaging.

Recommendation	LE	GR
A contrast study is recommended if stone removal is planned and the anatomy of the collecting system needs to be assessed	3	A*
Enhanced CT is preferable because it enables 3D reconstruction of the collecting system. Intravenous urography may also be used		
With fever or a solitary kidney and when diagnosis is doubtful, immediate imaging is indicated	4	A*
Following initial US assessment, NCCT should be used to confirm stone diagnosis in patients with acute flank pain, because it is superior to IVU	1a	A

CT = computed tomography; LE = level of evidence; GR = grade of recommendation; US = ultrasound; NCCT = non–contrast-enhanced computed tomography.

Table 4 – The role of NCCT in diagnostic imaging.

Evidence summary	LE
If NCCT is indicated in patients with BMI <30 kg/m^2, use a low-dose technique	1b
NCCT allows measurement of stone density and skin-to-stone distance	

LE = level of evidence; NCCT = non–contrast-enhanced computed tomography; BMI = body mass index.

balanced against loss of information about renal function and anatomy of the urinary collecting system (Table 3). Radiation risk can be reduced by low-dose CT [21]. In patients with body mass index (BMI) <30 kg/m^2, low-dose CT has sensitivity of 86% for detecting ureteric stones <3 mm and 100% for calculi >3 mm [22]. A meta-analysis of low-dose CT accuracy revealed pooled sensitivity of 97% and specificity of 95% in patients with urolithiasis [23,24].

3.2.2. Basic laboratory analysis: non-emergency urolithiasis patients

Biochemical work-up is similar for all stone patients and includes blood cell count, electrolytes, creatinine, calcium, uric acid and, if UTI is present, C-reactive protein. Blood coagulation status should be assessed before intervention. Dipstick analysis is sufficient for routine screening, with urine culture in cases with signs of UTI. Patients at high-risk of stone recurrence should undergo more specific analysis according to the EAU guidelines on metabolic evaluation [4]. Stone analysis is fundamental for further metabolic evaluation (Table 5). Patients should be instructed to filter their urine to retrieve a stone for analysis. Stone passage and restoration of normal renal function should be confirmed. The preferred analytical procedure is infrared spectroscopy or X-ray diffraction [25]. Equivalent results can be obtained by polarisation microscopy. Chemical analysis (wet chemistry) is generally deemed to be obsolete [25].

Table 5 – Recommendations for stone analysis.

Recommendation	LE	GR
Stone analysis should be performed in all first-time formers using a valid method	2	A
Repeat stone analysis in patients	2	B
• Presenting with recurrent stones despite drug therapy		
• With early recurrence after complete stone clearance		
• With late recurrence after a long stone-free period because stone composition may change		

LE = level of evidence; GR = grade of recommendation.

Table 6 – Radiation exposure of imaging modalities for stone detection [29–31]

Method	Radiation exposure (mSv)
Kidney-ureter-bladder radiography	0.5–1
Intravenous urography	1.3–3.5
Regular-dose noncontrast computed tomography	4.5–5
Low-dose noncontrast computed tomography	0.97–1.9
Enhanced computed tomography	25–35

3.2.3. Diagnosis of urolithiasis in pregnancy

Imaging in pregnant women is limited owing to the possible risk of foetal radiation exposure and potential induction of later malignancies in the child (Table 6). The risk depends on gestational age and the amount of radiation delivered. X-ray imaging during the first trimester should be reserved for diagnostic and therapeutic situations in which alternative imaging methods have failed [26]. US has therefore become the primary radiologic diagnostic tool, but has limitations in differentiating physiologic dilation from obstruction (Table 7) [27]. Low-dose CT reduces radiation exposure; however, because of potential radiation hazards it is restricted to selected cases [28]. Magnetic resonance imaging may define the level of urinary tract obstruction and visualise stones as a filling defect (Table 8).

3.3. Management of patients with renal or ureteral stones

3.3.1. Renal colic

Pain relief is the primary goal in patients with an acute stone episode (Table 9). Nonsteroidal anti-inflammatory

Table 7 – Limitations of ultrasound for stone evaluation in pregnancy.

Evidence summary	LE
Normal physiologic changes in pregnancy can mimic ureteral obstruction, so US may not help to differentiate dilation properly and has a limited role in acute obstruction	3

LE = level of evidence; US = ultrasound.

Table 8 – Recommendations for diagnostic imaging in pregnancy.

Recommendation	LE	GR
US is the method of choice for practical and safe evaluation of pregnant women	1a	A*
MRI may be used as a second-line imaging modality in pregnancy	3	C
In pregnant women, low-dose CT should be restricted to selected cases	3	C

LE = level of evidence; GR = grade of recommendation; US = ultrasound; MRI - magnetic resonance imaging; CT - computed tomography.

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Table 9 – Recommendations for pain relief in renal colic.

Recommendation	GR
In acute stone episodes, pain relief should be initiated immediately	A
Whenever possible, a nonsteroidal anti-inflammatory drug should be the first choice, such as diclofenac [a], indomethacin, or ibuprofen [b]	A
The second choice should be hydromorphine, pentazocine, or tramadol	C
Use α-blockers to reduce recurrent colic	A

GR = grade of recommendation.
[a] Affects the glomerular filtration rate in patients with reduced renal function (LE: 2a).
[b] Recommended to counteract recurrent pain after ureteral colic.

drugs are effective in patients with acute stone colic and have better analgesic efficacy than opioids [5,32]. Daily α-blockers reduce recurrent colic.

If medical analgesia is insufficient, drainage or stone removal should be performed (Table 10).

An obstructed kidney with signs of a UTI is a urologic emergency that requires urgent decompression to prevent further complications. Currently, there are two options for urgent decompression of obstructed collecting systems: placement of an indwelling ureteral catheter and percutaneous placement of a nephrostomy tube (Table 11). There is little evidence to support the superiority of one over the other [33,34]. Definitive stone removal should be delayed until the infection is cleared following a complete course of antimicrobial therapy (Table 12).

3.3.2. *Observation of renal stones*

The risk of a symptomatic episode or the need for intervention in patients with small nonobstructing stones is 10–25% per year [35,36]. However, a prospective RCT reported no advantage for prophylactic SWL for asymptomatic calyceal stones (Table 13) [35].

3.3.3. *Conservative management of ureteral calculi*

Some 95% of stones ≤4 mm pass within 40 d [37]. Observation is feasible in informed patients who develop no complications (infection, refractory pain, or deterioration of kidney function). Stones >6 mm are usually treated actively, although even such stones pass occasionally (Table 14).

Table 10 – Symptomatic ureteral stones.

Evidence summary	LE
For symptomatic ureteral stones, urgent stone removal as first-line treatment is a feasible option	1b

LE = level of evidence.

Table 11 – Placement of stents and catheters.

Evidence summary	LE
For decompression of the renal collecting system, ureteral stents and percutaneous nephrostomy catheters are equally effective	1b

LE = level of evidence.

Table 12 – Management of sepsis in obstructed kidneys.

Recommendation	LE	GR
For sepsis with obstructing stones, the collecting system should be urgently decompressed using percutaneous drainage or ureteral stenting	1b	A
Definitive treatment of the stone should be delayed until sepsis is resolved	1b	A
Collect urine for an antibiogram test following decompression	3	A*
Start antibiotics immediately thereafter (+ intensive care if necessary)	3	
Re-evaluate the antibiotic regimen following antibiogram findings	3	

LE = level of evidence; GR = grade of recommendation.

Table 13 – Recommendations for the treatment of kidney stones.

Recommendation	GR
Active surveillance with annual follow-up is an option for asymptomatic, nonobstructing calyceal stones, that have remained stable for 6 mo	C
Kidney stones should be treated in cases of growth, de novo obstruction, associated infection, and acute or chronic pain	A*
Comorbidity and patient preference need to be taken into consideration when making treatment decisions	C
If kidney stones are not treated, periodic evaluation is recommended (after 6 mo and yearly thereafter)	A*

GR = grade of recommendation.

3.3.4. *MET*

The aim of MET is to facilitate spontaneous passage of ureteral (Table 15). The treatment should be discontinued in the case of complications (infection, refractory pain, or deterioration of kidney function). Owing to the high likelihood of spontaneous passage of stones <6 mm, MET is less likely to increase the stone-free rate (SFR) (LE: 1b) but reduces pain episodes (LE 1a) [5,38]. Meta-analyses have shown that patients with ureteral stones treated with α-blockers or calcium-channel inhibitors are more likely to pass stones with fewer colic episodes than those not receiving such therapy (Table 16) [5,38]. α-Blockers seem to be superior to calcium-channel inhibitors [39,40]. Even though tamsulosin is one of the most commonly used α-blockers [5,38], other studies evaluating different α blockers have demonstrated similar effects, indicating a

Table 14 – Recommendation for the conservative management of ureteral calculi.

Recommendation	LE	GR
In patients with newly diagnosed ureteral stones <6 mm [a], if active removal is not indicated, observation with periodic evaluation is an optional initial treatment	1a	A
Such patients may be offered appropriate medical therapy to facilitate stone passage during observation		

LE = level of evidence; GR = grade of recommendation, MET = medical expulsive therapy.
[a] The exact cutoff size for ureteral stones cannot be determined from the literature, but the panel suggests <6 mm.

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Table 15 – The role of MET in the treatment of urinary calculi.

Evidence summary	LE
There is good evidence that MET accelerates spontaneous passage of ureteral stones and fragments generated with SWL, and limits pain	1a
Several trials have demonstrated an α-blocker class effect on stone expulsion rates	1b
There is no evidence to support the use of corticosteroids as monotherapy for MET. Insufficient data exist to support the use of corticosteroids in combination with α-blockers as an accelerating adjunct	1b

LE = level of evidence; MET = medical expulsive therapy; SWL = shockwave lithotripsy.

Table 16 – Recommendations on MET to facilitate spontaneous passage of urinary calculi.

Recommendation	LE	GR
For MET, α-blockers are recommended	1a	A
Patients should be counselled about the attendant risks of MET, including associated drug side effects, and should be informed that it is administered off-label [a]	4	A*
Patients who elect for an attempt at spontaneous passage or MET should have well-controlled pain, no clinical evidence of sepsis, and adequate renal functional reserve	4	A
Patients should be followed once between 1 and 14 d to monitor stone position and be assessed for hydronephrosis	4	A*

LE = level of evidence; GR = grade of recommendation; MET = medical expulsive therapy.
[a] It is not known if tamsulosin harms the human foetus or if it is found in breast milk.

possible class effect [41–43]. No recommendation for the use of corticosteroids in combination with α-blockers in MET can be made [44,45].

3.3.5. Chemolytic dissolution of stones

Oral chemolysis of uric acid stones is based on alkalisation (pH 7.0–7.2) with citrate or sodium bicarbonate (Table 17) [46,47]. A combination of alkalisation and tamsulosin seems to achieve the highest SFRs for distal ureteral stones [48].

Table 17 – Recommendations for chemolysis of uric acid stones.

Recommendation	GR
The dose of alkalising medication should be modified by the patient according to urine pH, which is a direct consequence of such medication	A
Dipstick monitoring of urine pH by patients is required at regular intervals during the day (minimum three times daily). Morning urine should be included	A
Regular monitoring of radiolucent stones during/after US therapy is recommended	A*
Physicians should clearly inform patients of the significance of compliance	A

GR = grade of recommendation; US = ultrasound.
* Upgraded based on panel consensus.

4. Conclusions

Most patients with ureteral stones present with typical symptoms, although many stones in the renal calices remain asymptomatic. Routine evaluation includes imaging with US as the first-line modality. Low-dose CT has become the method of choice in the acute setting and when intervention is planned. In these cases, contrast imaging is advisable to achieve accurate anatomic assessment of the renal unit. Asymptomatic calyceal stones may be observed but there is a higher risk of symptoms and a need for intervention within 5 yr. Ureteral stones <6 mm can pass spontaneously in well-controlled patients, while MET supports the chance of successful passage and reduces the need for analgesics. Furthermore, oral chemolysis might be an efficient primary approach for treatment of radiolucent uric acid stones.

Author contributions: Thomas Knoll had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Türk, Knoll, Petřík, Sarica, Skolarikos, Seitz, Straub.
Acquisition of data: Türk, Knoll, Petřík, Sarica, Skolarikos, Seitz, Straub.
Analysis and interpretation of data: Türk, Knoll, Petrik, Sarica, Seitz, Skolarikos, Straub.
Drafting of the manuscript: Knoll.
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