EAU GUIDELINES ON UROLITHIASIS

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Aetiology and classification

Urinary stones can be classified according to size, location, X-ray characteristics, aetiology of formation, composition, and risk of recurrence. The recurrence risk is basically determined by the disease or disorder causing the stone formation.

Risk groups for stone formation

The risk status of stone formers is of particular interest because it defines the probability of recurrence or regrowth and is imperative for pharmacological treatment (Table 1).

Table 1: High-risk stone formers

General factors
Early onset of urolithiasis (especially children and teenagers)
Familial stone formation
Recurrent stone formers
Short time since last stone episode
Brushite-containing stones ($CaHPO_4.2H_2O$)
Uric acid and urate-containing stones
Infection stones

Solitary kidney (the kidney itself does not particularly increase the risk of stone formation, but prevention of stone recurrence is of crucial importance to avoid acute renal failure)
Chronic Kidney Disease (CKD)
Diseases associated with stone formation
Hyperparathyroidism
Metabolic syndrome
Mineral Bone Disorder (MBD)
Nephrocalcinosis
Polycystic kidney disease (PKD)
Intestinal disorders and surgery (Intestinal urinary diversions and enteric hyperoxaluria caused by ileal resection, short bowel, pancreatic insufficiency, malabsorptive bariatric surgery, etc.).
Increased levels of vitamin D
Sarcoidosis
Spinal cord injury, neurogenic bladder
Genetically determined stone formation
Cystinuria (type A, B and AB)
Primary hyperoxaluria (PH)
Renal tubular acidosis (RTA) type I
2,8-Dihydroxyadeninuria
Xanthinuria
Lesch-Nyhan syndrome
Cystic fibrosis
Drug-induced stone formation
Anatomical abnormalities associated with stone formation
Medullary sponge kidney (tubular ectasia)
Ureteropelvic junction (UPJ) obstruction
Calyceal diverticulum, calyceal cyst
Ureteral stricture

Vesico-uretero-renal reflux
Horseshoe kidney
Ureterocele
Environmental and professional factors
High ambient temperatures
Chronic lead and cadmium exposure

Diagnostic Evaluation

Diagnostic imaging

Standard evaluation of a patient includes a detailed medical history and physical examination. The clinical diagnosis should be supported by appropriate imaging. Ultrasound (US) should be used as the primary diagnostic imaging tool, although pain relief, or any other emergency measures, should not be delayed by imaging assessments. Non-contrast-enhanced computed tomography (NCCT) has become the gold standard for diagnosing acute flank pain and has replaced intravenous urography (IVU). Kidney-ureter-bladder (KUB) urography should not be performed if NCCT is being considered.

Recommendations	Strength rating
Immediate imaging is indicated with fever or solitary kidney, and when diagnosis is uncertain.	Strong
Use non-contrast-enhanced computed tomography to confirm stone diagnosis in patients with acute flank pain following initial ultrasound assessment.	Strong

Diagnostics: Metabolism-related

Each emergency patient with urolithiasis needs a succinct biochemical work-up of urine and blood; no difference is made between high- and low-risk patients for stone formation. Subsequent risk stratification and metabolic evaluation should be performed after the acute episode.

Recommendations: basic laboratory analysis - emergency stone patients	Strength rating
Urine	
Dipstick test of spot urine sample: • red cells; • white cells; • nitrites; • approximate urine pH; • urine microscopy and/or culture.	Weak
Blood	
Serum blood sample: • creatinine; • uric acid; • (ionised) calcium; • sodium; • potassium; • blood cell count; • C-reactive protein.	Strong
Perform a coagulation test (partial thromboplastin time and international normalised ratio) if intervention is likely or planned.	Strong

Examination of sodium, potassium, C-reactive protein (CRP), and blood coagulation time can be omitted if no intervention is planned in non-emergency stone patients. Patients at high risk for stone recurrence should undergo a more specific analytical programme (see section on Metabolic Evaluation).

Recommendations related to non-emergency stone analysis	Strength rating
Perform stone analysis in first-time stone formers using a valid procedure (X-ray diffraction or infrared spectroscopy).	Strong
Repeat stone analysis in patients presenting with: • recurrent stones despite drug therapy; • early recurrence after complete stone clearance; • late recurrence after a long stone-free period because stone composition may change.	Strong

Diagnosis for special groups/conditions – Pregnancy and Children

Recommendations	Strength rating
Pregnancy	
Use ultrasound (US) as the preferred method of imaging in pregnant women.	Strong
Use magnetic resonance imaging as a second-line imaging modality in pregnant women.	Strong
Use low-dose computed tomography (CT) as a last-line option in pregnant women.	Strong

Children	
Complete a metabolic evaluation based on stone analysis in all children, based on stone composition when this is available.	Strong
Collect stone material for analysis to classify the stone type.	Strong
Perform US as first-line imaging modality in children when a stone is suspected; it should include the kidney, fluid-filled bladder, and the ureter.	Strong
Perform a kidney-ureter-bladder radiography (or low-dose non-contrast-enhanced CT) if US will not provide the required information.	Strong

In children, the most common non-metabolic disorders facilitating stone formation are vesico-ureteral reflux, UPJ, neurogenic bladder, and other voiding difficulties. The radiation dose for IVU is comparable to that for voiding cysto-urethrography, but the need for contrast medium injection is a major drawback.

Disease Management

Acute treatment of a patient with renal colic

Pain relief is the first therapeutic step in patients with an acute stone episode.

Recommendations	Strength rating
Offer a non-steroidal anti-inflammatory as the first drug of choice; depending on cardiovascular risk factors and side effects.	Strong
Offer opioids (hydromorphone, pentazocine or tramadol) or ketamine in the acute setting as a second choice.	Weak

Offer renal decompression or ureteroscopic stone removal in case of analgesia refractory colic pain.	Strong

Administration of daily α-blockers may reduce colic episodes, but clinicians should be aware that the evidence in support of this is conflicting. If analgesia cannot be achieved medically then drainage (either ureteric stent or percutaneous nephrostomy) or stone removal is indicated.

Management of sepsis and anuria in the obstructed kidney

The obstructed kidney with all signs of urinary tract infection and/or anuria is a urological emergency. Urgent decompression is often necessary to prevent further complications in infected hydronephrosis secondary to stone-induced unilateral, or bilateral, renal obstruction.

Recommendations	**Strength rating**
Urgently decompress the collecting system in case of sepsis with obstructing stones, using percutaneous drainage or ureteral stenting.	Strong
Delay definitive treatment of the stone until sepsis is resolved.	Strong
Further measures	
Collect (again) urine for antibiogram test following decompression.	Strong
Start antibiotics immediately (+ intensive care, if necessary).	Strong
Re-evaluate antibiotic regimen following antibiogram findings.	Strong

Medical expulsive therapy (MET)

Several drug classes including α-blockers, B3 adrenergic receptor agonists, calcium channel inhibitors and phosphodiesterase type 5 inhibitors (PDEI-5) are used for MET. A class effect of α-blockers in MET has been demonstrated in both adults and children although this is an off-label indication and there is contradictory evidence as to its benefit, besides some advantage for distal ureteral stones > 5 mm. Most recent studies show efficacy for MET for stones between 5-10mm.

Recommendation	Strength rating
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm*.	Strong

**α-blockers are an off-label treatment.*

Chemolytic dissolution of stones

Oral chemolysis of stones or their fragments can be useful in uric acid stones. It is based on alkalinisation of urine by application of alkaline citrate or sodium bicarbonate. The pH should be adjusted to 7.0-7.2. Percutaneous irrigation chemolysis is rarely used any more.

Recommendations (oral chemolysis of uric acid stones)	Strength rating
Inform the patient how to monitor urine-pH by dipstick and to modify the dosage of alkalising medication according to urine pH, as changes in urine pH are a direct consequence of such medication.	Strong
Carefully monitor patients during/after oral chemolysis of uric acid stones.	Strong

Combine oral chemolysis with tamsulosin in case of (larger) ureteral stones (if active intervention is not indicated).	Weak

Shock Wave lithotripsy (SWL)

The success rate for SWL will depend on the efficacy of the lithotripter and on:

- size, location (ureteral, pelvic or calyceal), and composition (hardness) of the stone(s);
- patient's habitus;
- performance of SWL.

Contraindications of SWL

Contraindications are limited, but include:

- pregnancy;
- bleeding disorders (which should be compensated for at least 24 hours before and 48 hours after treatment);
- uncontrolled urinary tract infections (UTIs);
- severe skeletal malformations and severe obesity, which prevent targeting of the stone;
- arterial aneurysm in the vicinity of the stone;
- anatomical obstruction distal to the stone.

Best clinical practice in SWL

Stenting prior to SWL

Routine use of internal stents before SWL does not improve stone-free rates (SFRs), or lower the number of auxiliary treatments; however, it may reduce formation of steinstrasse.

Pacemaker

Patients with a pacemaker can be treated with SWL. Patients with implanted cardioverter defibrillators must be managed with special care (firing mode temporarily reprogrammed during SWL treatment). However, this might not be necessary with new-generation lithotripters.

Shock waves, energy setting and repeat treatment sessions

- The number of shock waves that can be delivered at each session depends on the type of lithotripter and shock wave power.
- Starting SWL on a lower energy setting with stepwise power ramping prevents renal injury.
- Optimal shock wave frequency is 1.0 to 1.5 Hz.
- Clinical experience has shown that repeat sessions are feasible (within one day for ureteral stones).

Antibiotic prophylaxis

No standard prophylaxis prior to SWL is recommended in patients with pre-operative sterile urine, even if a ureteral catheter or nephrostomy tube is present.

Recommendations	**Strength rating**
Ensure correct use of the coupling agent because this is crucial for effective shock wave transmission.	Strong
Maintain careful fluoroscopic and/or ultrasonographic monitoring during shock wave lithotripsy (SWL).	Strong
Use proper analgesia because it improves treatment results by limiting pain-induced movements and excessive respiratory excursions.	Strong
Do not use antibiotic prophylaxis for extracorporeal shockwave lithotripsy in patients with sterile urine. Prescribe antibiotic prophylaxis only in the case of suspected or diagnosed infected stones or bacteriuria.	Strong

Ureteroscopy (URS) (rigid and flexible, including RIRS)

Apart from general problems, for example, with general anaesthesia or untreated UTIs, URS can be performed in all patients without any specific contraindications. If ureteral access is not possible, insertion of a JJ stent followed by URS after several days is an alternative. During URS, placement of a safety wire is recommended, even though some groups have demonstrated that URS can be performed without it. Routine use is therefore recommended, while omission may be acceptable in selected cases in experienced hands. Ureteral access sheaths allow repeated access to the upper urinary tract and may improve visibility and irrigation outflow; however, their insertion may be associated with ureteral injury and should be performed with caution.

Recommendations	Strength rating
Use holmium:yttrium-aluminium-garnet (Ho:YAG) or Thulium fiber laser (TFL) laser lithotripsy for (flexible) ureteroscopy (URS).	Strong
Perform stone extraction only under direct endoscopic visualisation of the stone.	Strong
Do not insert a stent in uncomplicated cases.	Strong
Offer medical expulsive therapy for patients suffering from stent-related symptoms and after laser lithotripsy to facilitate the passage of fragments.	Strong
Use flexible URS (even for stones > 2 cm) in cases where percutaneous nephrolithotomy or SWL are not options. However, in this case, there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed.	Strong

Percutaneous nephrolithotomy (PCNL)

Percutaneous nephrolithotomy is the standard procedure for large renal calculi. Different rigid and flexible endoscopes are available.

Contraindications to PCNL include:

- untreated UTI;
- tumour in the presumptive access tract area;
- potential malignant kidney tumour;
- pregnancy.

Best clinical practice

Both prone and supine positions are equally effective. Percutaneous nephrolithotomy performed with small instruments tends to be associated with significantly lower blood loss, but the duration of procedure tends to be significantly longer.

Recommendations	Strength rating
Perform pre-procedural computed tomography imaging, including contrast medium where indicated or retrograde study when starting the procedure, to assess stone comprehensiveness and anatomy of the collecting system to ensure safe access to the renal stone.	Strong
Perform a tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube and ureteral stent) percutaneous nephrolithotomy (PCNL) procedure, in uncomplicated cases.	Strong
Take a stone culture or urine culture directly from the renal pelvis at the time of PCNL, if possible.	Strong

General recommendations for stone removal

Recommendations	Strength rating
Obtain a urine culture or perform urinary microscopy before any treatment is planned.	Strong
Exclude or treat urinary tract infections prior to stone removal.	Strong
Offer peri-operative antibiotic prophylaxis to all patients undergoing endourological treatment.	Strong
Offer active surveillance to patients at high risk of thrombotic complications in the presence of an asymptomatic calyceal stone.	Weak
Decide on temporary discontinuation, or bridging of antithrombotic therapy in high-risk patients, in consultation with the physician.	Strong
Retrograde (flexible) ureteroscopy is the preferred intervention if stone removal is essential and antithrombotic therapy cannot be discontinued since it is associated with less morbidity.	Strong

Ureteral stones

Observation of ureteral stones is feasible in informed patients who develop no complications (infection, refractory pain, deterioration of renal function).

Recommendations	Strength rating
If active removal is not indicated in patients with newly diagnosed small* ureteral stones, initially observe patients and undertake periodic evaluation.	Strong
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm**.	Strong
Inform patients that ureteroscopy (URS) has a better chance of achieving stone-free status with a single procedure.	Strong
Inform patients that URS has higher complication rates when compared to shock wave lithotripsy.	Strong
Use URS as first-line therapy for ureteral (and renal) stones in cases of morbid obesity.	Strong

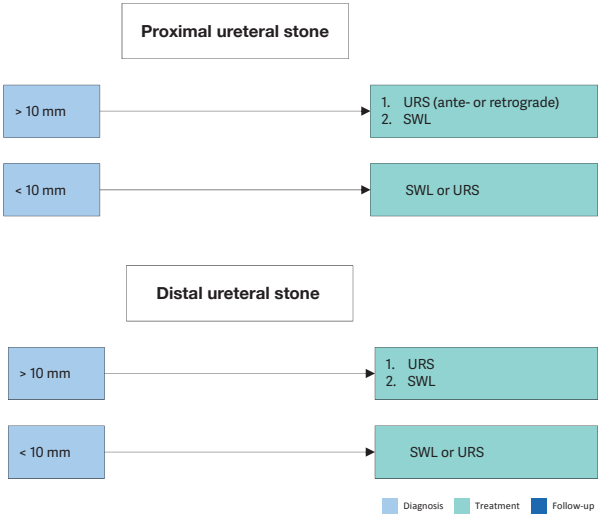
**See stratification data (J Urol, 2007. 178: 2418).*
***α-blockers are an off-label treatment for this indication*

Indication for active stone removal and selection of procedure in the ureter:

- stones with a low likelihood of spontaneous passage;
- persistent pain despite adequate analgesic medication;
- persistent obstruction;
- renal insufficiency (renal failure, bilateral obstruction, or single kidney).

The suspected stone composition might influence the choice of treatment modality.

Figure 1: Treatment algorithm for ureteral stones (if stone removal is indicated)



SWL = shock wave lithotripsy; URS = ureteroscopy.

Renal stones

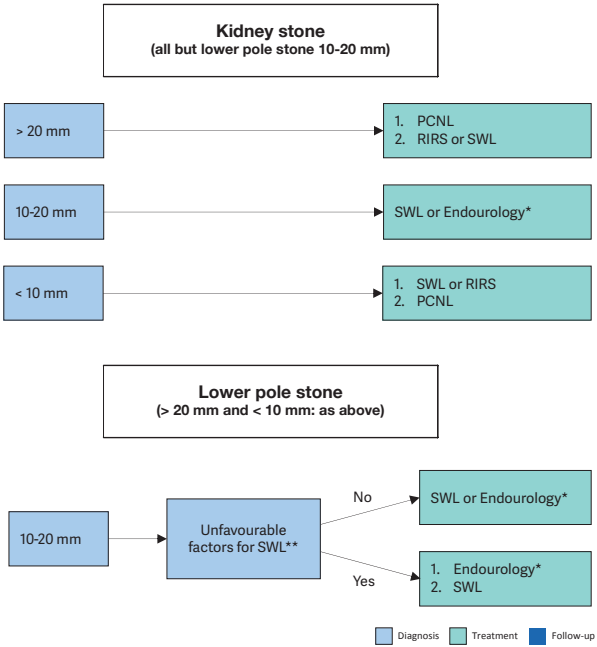
It is still debatable whether all renal stones should be treated, or whether annual follow-up is sufficient for asymptomatic calyceal stones that have remained stable for six months. Patients should be counselled appropriately as to the risks of observing asymptomatic calyceal stones.

Recommendations	Strength rating
Offer active treatment for renal stones in case of stone growth, *de novo* obstruction, associated infection, and acute and/or chronic pain.	Weak
Evaluate 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 computed tomography.	Strong
Perform percutaneous nephrolithotomy (PCNL) as first-line treatment of larger stones > 2 cm.	Strong
Treat larger stones (> 2 cm) with flexible ureteroscopy or shock wave lithotripsy (SWL), in cases where PCNL is not an option. However, in such instances there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed.	Strong
Perform PCNL or retrograde intrarenal surgery (RIRS) for the lower pole, even for stones > 1 cm, as the efficacy of SWL is limited (depending on favourable and unfavourable factors for SWL).	Strong

Indication for active stone removal and selection of procedure in the kidney

- stone growth;
- stones in high-risk patients for stone formation;
- obstruction caused by stones;
- infection;
- symptomatic stones (e.g., pain, haematuria);
- patient preference;
- comorbidity;
- social situation of the patient (e.g., profession or travelling).

Figure 2: Treatment algorithm for renal stones if active treatment is indicated



** The term 'endourology' encompasses all PCNL and URS interventions.*
*** See chapter 3.4.5 of full Urolithiasis guideline.*
PCNL = percutaneous nephrolithotomy; RIRS = retrograde renal surgery; SWL = shock wave lithotripsy; URS = ureteroscopy.

Open and laparoscopic surgery

Recommendation	Strength rating
Offer laparoscopic or open surgical stone removal in rare cases in which shock wave lithotripsy, retrograde or antegrade ureteroscopy and percutaneous nephrolithotomy fail, or are unlikely to be successful.	Strong

Steinstrasse

Steinstrasse occurs in 4% of cases of SWL. The main factor in steinstrasse formation after SWL is stone size. Medical expulsion therapy increases the stone expulsion rate of steinstrasse. When spontaneous passage is unlikely, further treatment of steinstrasse is indicated.

Recommendations	Strength rating
Treat steinstrasse associated with urinary tract infection (UTI)/fever preferably with percutaneous nephrostomy.	Weak
Treat steinstrasse when large stone fragments are present with shock wave lithotripsy or ureteroscopy (in absence of signs of UTI).	Weak

Management of patients with residual stones

Following initial treatment with SWL, URS or PNL residual fragments may remain and require additional intervention. The indications for active removal of residual stones and selection of the procedure are based on the same criteria as for primary stone treatment. For fragments > 4 mm, a large meta-analysis suggests low spontaneous passage rates and a high likelihood of subsequent intervention.

Recommendation	Strength rating
Treat residual fragments > 4mm.	Weak

Management of specific patient groups urinary stones

Pregnancy

If intervention becomes necessary, placement of a ureteral stent or a percutaneous nephrostomy tube are readily available primary options. Ureteroscopy is a reasonable alternative to avoid long-term stenting/drainage. There is a higher tendency for stent encrustation during pregnancy.

Urinary diversion

Patients with urinary diversion are at high risk for stone formation in the renal collecting system and ureter, or in the conduit or continent reservoir.

Neurogenic bladder

Patients with neurogenic bladder are more prone to development of urinary calculi. In myelomeningocele patients, latex allergy is common so appropriate measures need to be taken regardless of the treatment.

Transplanted kidneys

Transplanted patients are at additional risk due to their dependency on a solitary kidney, immunosuppression therapy and possible metabolic impairments. Conservative treatment for small asymptomatic stones is only possible under close surveillance and in absolutely compliant patients. Stones causing urinary stasis/obstruction require immediate intervention or drainage of the transplanted kidney.

Recommendation	Strength rating
Pregnancy	
Treat all uncomplicated cases of urolithiasis in pregnancy conservatively (except where there are clinical indications for intervention).	Strong
Urinary diversion	
Perform percutaneous lithotomy to remove large renal stones in patients with urinary diversion, as well as for ureteral stones that cannot be accessed via a retrograde approach, or that are not amenable to shock wave lithotripsy.	Strong
Transplanted kidneys	
Offer patients with transplanted kidneys, any of the contemporary management options, including shock wave lithotripsy, flexible ureteroscopy and percutaneous nephrolithotomy.	Strong

Special problems in stone removal

Calyceal diverticulum stones	• Shock wave lithotripsy, PCNL (if possible) or RIRS. • Can also be removed using laparoscopic retroperitoneal surgery. • Patients may become asymptomatic due to stone disintegration (SWL), whilst well-disintegrated stone material remains in the original position due to narrow calyceal neck.

Horseshoe kidneys	• Can be treated in line with the options described above. • Passage of fragments after SWL or fragmentation of stones might be poor. • Acceptable SFRs (up to 76%) with low major complication rates (2.4%) can be achieved with flexible ureteroscopy.
Stones in pelvic kidneys	• Shock wave lithotripsy, RIRS, PCNL or laparoscopic surgery.
Stones formed in a continent reservoir	• Each stone must be considered and treated individually.
Patients with obstruction of the UPJ	• When outflow abnormality requires correction, stones can be removed by PCNL together with percutaneous endopyelotomy or open/laparoscopic reconstructive surgery. • Ureteroscopy together with endopyelotomy with Ho:YAG laser.

Management of urolithiasis in children

In children, the indications for SWL and for PCNL is similar to those in adults. For endourological procedures, the smaller organs in children must be considered when selecting instruments for PCNL or URS. Children with renal stones of a diameter up to 20 mm (~300 mm^2) are ideal candidates for SWL.

Recommendations	Strength rating
Offer children with single ureteral stones less than 10 mm shock wave lithotripsy (SWL) if localisation is possible as first-line option.	Strong
Ureteroscopy is a feasible alternative for ureteral stones not amenable to SWL.	Strong
Offer children with renal stones with a diameter of up to 20 mm (~300 mm^2) SWL.	Strong
Offer children with renal pelvic or calyceal stones with a diameter > 20 mm (~300 mm^2) percutaneous nephrolithotomy.	Strong
Retrograde renal surgery is a feasible alternative for renal stones smaller than 20 mm in all locations.	Weak

Radiation exposure and protection during endourology

The diagnosis and treatment of nephrolithiasis is associated with high levels of ionising radiation exposure to patients. Currently, there are no studies performed estimating the lifetime radiation exposure of stone formers or the subsequent risk of malignancy development. Radiation exposure of patients is generally higher during PCNL, followed by SWL and URS. The EAU Urolithiasis Guidelines Panel's recommended protection methods to reduce radiation exposure to patients, surgical, anaesthesiologic and nursing staff are shown below.

Radiation protection measures
Limit studies or intervention involving radiation exposure to those that are strictly medically necessary.
Implement a patient electronic record of medical imaging.

Make use of imaging studies with lower radiation doses (US, KUB, digital tomosynthesis, low-dose and ultra-low dose CT scan).
Create and follow a precise radiation exposure protection protocol in your department.
Act in accordance with the as low as reasonably achievable (ALARA) principle.
Measure and report fluoroscopy time to the operative surgeon (use dosimeters and perform monthly calculations).
Technical measures to reduce radiation exposure include: • Reducing fluoroscopy time. • Limiting time adjacent to patient. • Using low-dose radiation. • Irradiating only to observe motion. • Intra-operative use of pulsed fluoroscopy. • Reduced fluoroscopy pulse rate. • Collimated fields. • Avoid digital image acquisition and rely on last image hold and instant replay technology.
Use radiation protection instruments (chest, pelvic and thyroid shields, lead or lead-free gloves, protective glasses, lead protection under the operating table between the X-ray source and the surgeon).
The radiation protection instruments must be cared for appropriately as any damage decreases effectiveness and increases exposure risk. They should be monitored and measured regularly to ensure integrity.
Proper surgeon and operating room setup should be observed (follow the inverse square law, use the X-ray source underneath the patient's body, decrease the X-ray source to patient distance, reduce magnification, avoid field overlap by not turning the C-arm in extreme angles, operate in the standing rather than the seated position).

Metabolic evaluation and recurrence prevention

After stone passage, every patient should be assigned to a low- or high-risk group for stone formation. For correct classification, two analyses are mandatory:

- reliable stone analysis by infrared spectroscopy or X-ray diffraction;
- basic analysis.

Only high-risk stone formers require specific metabolic evaluation. Stone type is the deciding factor for further diagnostic tests. For both groups, general preventive measures apply (see below).

General preventive measures	
Fluid intake (drinking advice)	Fluid amount: 2.5-3.0 L/day
	Water is the preferred fluid
	Diuresis: 2.0-2.5 L/day
	Specific weight of urine: < 1,010 g/day
Nutritional advice for a balanced diet	Balanced diet*
	Rich in vegetables and fibre
	Normal calcium content: 1-1.2 g/day
	Limited NaCl content: 4-5 g/day
	Limited animal protein content: 0.8-1.0 g/kg/day
Lifestyle advise to normalise general risk factors	Retain a normal BMI level
	Adequate physical activity
	Balancing of excessive fluid loss
	Reduce the intake of alcohol containing fluids
	Reduce the intake of sodas and calorie-containing fluids

Caution: Protein requirements are age dependent; therefore, protein restriction in childhood should be handled carefully.
** Avoid excessive consumption of vitamin supplements*

Calcium oxalate stones

Recommendations for pharmacological treatment of patients with specific abnormalities in urine composition	Strength rating
Prescribe thiazide and/or alkaline citrates in case of hypercalciuria*.	Strong
Advise oxalate restriction if hyperoxaluria is present.	Weak
Offer alkaline citrates in enteric hyperoxaluria.	Weak
Offer calcium supplement in enteric hyperoxaluria.	Strong
Advise reduced dietary fat and oxalate in enteric hyperoxaluria.	Weak
Prescribe alkaline citrates or sodium bicarbonate in case of hypocitraturia.	Strong
Prescribe allopurinol in case of hyperuricosuria.	Strong
Offer febuxostat as second-line treatment of hyperuricosuria.	Strong
Avoid excessive intake of animal protein in hyperuricosuria.	Strong
Advise restricted intake of salt if there is high urinary sodium excretion.	Strong

** Patients on hydrochlorothiazide should be advised to get their skin checked on a regular basis as they have a higher risk of developing an NMSC and some forms of melanoma. In patients with a history of skin cancer, the indication for treatment with hydrochlorothiazide should be thoroughly reviewed.*

Figure 3: Diagnostic algorithm for calcium oxalate stones

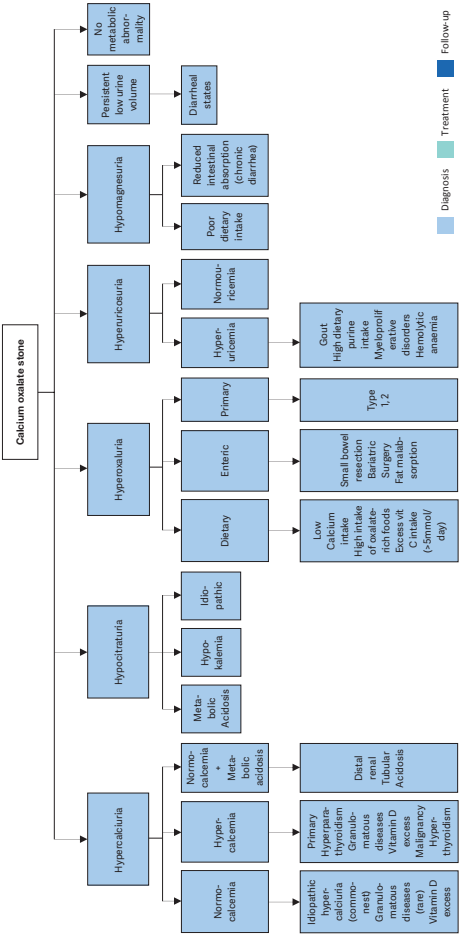
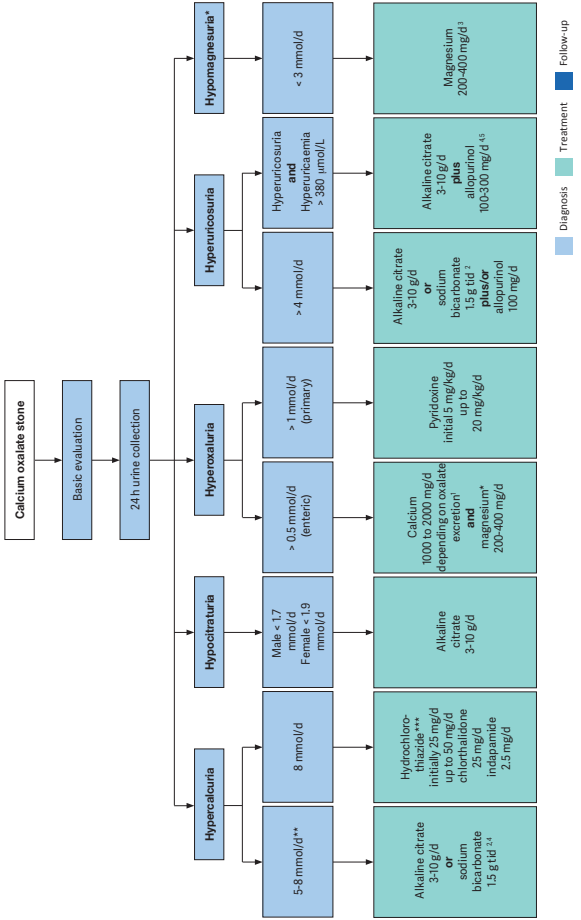


Figure 4: Therapeutic algorithm for calcium oxalate stones

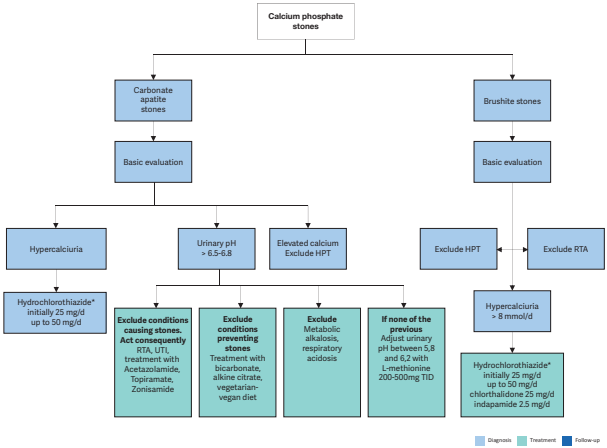


[1] Be aware of excess calcium excretion.
[2] tid = three times/day (24h).
[3] No magnesium therapy for patients with renal insufficiency.
[4] There is no evidence that combination therapy (thiazide + citrate or thiazide + allopurinol) is superior to thiazide therapy alone.
[5] Febuxostat 80 mg/d.
**Low evidence (see text)*
*** Calciuria is a continuous variable, and treatment may be adjusted to clinical need even when below the threshold indicated.*
****Patients on hydrochlorothiazides should be advised to get their skin checked on a regular basis as they have a higher risk of developing a NMSC and some forms of melanoma. In patients with history of skin cancer the indication for the intake of hydrochlorothiazides should be thoroughly reviewed.*

Calcium phosphate stones

Recommendation	Strength rating
Prescribe thiazide in case of hypercalciuria > 8 mmol/24 hours.	Strong

Figure 5: Diagnostic and therapeutic algorithm for calcium phosphate stones



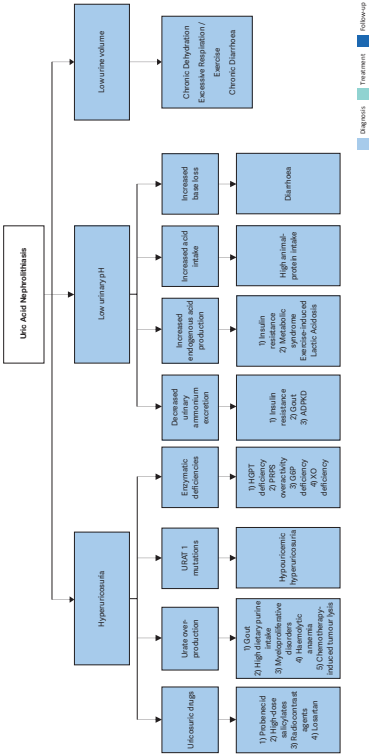
HPT = hyperparathyroidism; RTA = renal tubular acidosis; UTI = urinary tract infection.
** Patients on hydrochlorothiazide should be advised to get their skin checked on a regular basis as they have a higher risk of developing NMSC and some forms of melanoma. In patients with a history of skin cancer, the indication for treatment with hydrochlorothiazide should be thoroughly reviewed.*

Hyperparathyroidism

Elevated levels of ionised calcium in serum (or total calcium adjusted for albumin) require assessment of intact parathyroid hormone to confirm or exclude suspected hyperparathyroidism (HPT). Although the effect on stone relapses is uncertain if primary HPT is diagnosed, parathyroidectomy is generally suggested to prevent or cure other complications.

Management of uric acid, ammonium urate and cystine stones

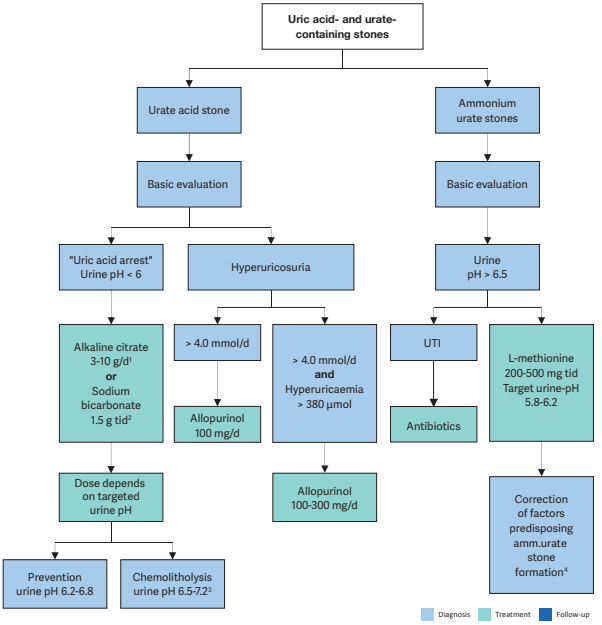
Figure 6: Diagnostic algorithm for uric acid stones



ADPKD = autosomal dominant polycystic kidney disease; G6P = glucose-6 phosphate dehydrogenase;
HGPT = hypoxanthine guanine phosphorybosyl transferase;

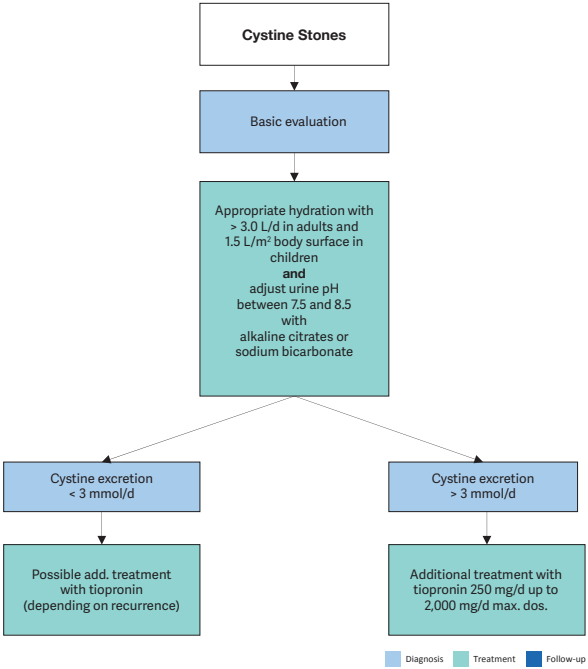
PRPS = phosphoribosyl-pyrophosphate synthetase superactivity; XO = xanthine oxidase.

Figure 7: Therapeutic algorithm for uric acid and ammonium urate stones



[1] d: day.
[2] tid: three times a day.
[3] A higher pH may lead to calcium phosphate stone formation.
[4] In patients with high uric acid excretion, allopurinol may be helpful.
UTI = urinary tract infection.

Figure 8: Metabolic management of cystine stones



Struvite/infection stones

Recommendations for therapeutic measures of infection stones	Strength rating
Surgically remove the stone material as completely as possible.	Strong
Prescribe antibiotics in case of persistent bacteriuria.	Strong

Prescribe ammonium chloride, 1 g, two or three times daily, to ensure urinary acidification.	Weak
Prescribe methionine, 200-500 mg, one to three times daily, as an alternative, to ensure urinary acidification.	Weak

2,8-Dihydroyadenine stones and xanthine stones

Both stone types are rare. Diagnosis and specific prevention is similar to that of uric acid stones.

Drug stones

Drug stones are induced by pharmacological treatment. Two types exist:

- stones formed by crystallised compounds of the drug;
- stones formed due to unfavourable changes in urine composition under drug therapy.

Treatment includes general preventive measures and the avoidance of the respective drugs

Unknown stone composition

Recommendations		
Investigation	**Rationale for investigation**	**Strength rating**
Take a medical history	• Stone history (former stone events, family history) • Dietary habits • Medication chart	Strong

Perform diagnostic imaging	• Ultrasound in the case of a suspected stone • Un-enhanced helical computed tomography • Determination of Hounsfield units provides information about the possible stone composition	Strong
Perform a blood analysis	• Creatinine • Calcium (ionised calcium or total calcium + albumin) • Uric acid	Strong
Perform a urinalysis	• pH measurement • Dipstick test: leukocytes, erythrocytes, nitrites • Protein, specific weight • Urine cultures • Microscopy of urinary sediment (morning urine) • Cyanide nitroprusside test (cystine exclusion)	Strong

Further examinations depend on the results of the investigations listed above.

Follow-Up of Urinary Stones

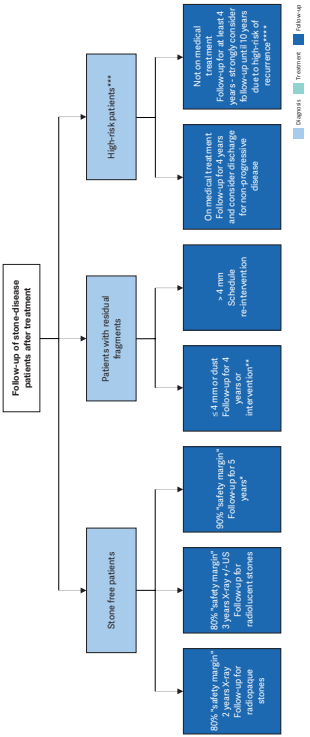
Patients suffering from urinary tract urolithiasis have a predisposition to develop symptoms, complications, and recurrence of stones. There is little information on how patients should be monitored after their treatment, with no general agreement on the frequency and duration of follow-up.

The EAU Urolithiasis Guidelines Panel performed a systematic review questioning the benefits and harms of scheduled imaging and metabolic follow-up for patients who underwent definitive treatment for upper urinary tract stone disease. Based on the results, a consensus was reached regarding the frequency of follow-up for stone-free patients (the general population and high-risk patients), patients with residual fragments ≤ 4 mm, and patients with residual fragments > 4 mm.

Stone-free patients could be discharged after two years (radiopaque stones) or after three years (radiolucent stones). Patients with small ≤ 4mm, asymptomatic fragments should be followed-up or scheduled for an intervention according to patient preference, while those with larger stones should primarily be offered re-intervention.

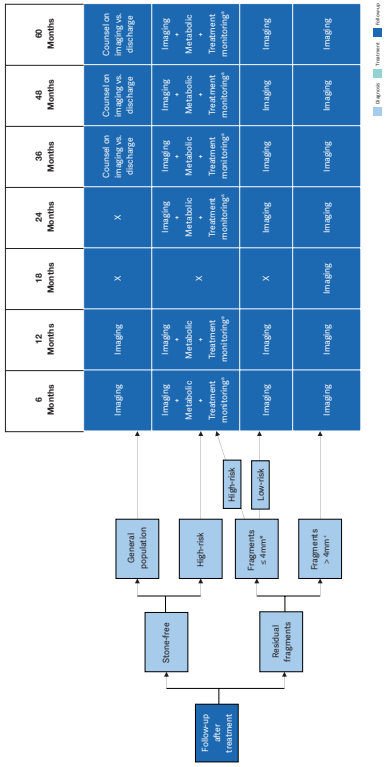
Proposed imaging consists of plain X-ray KUB and/or US, based on stone characteristics and clinician preference. Computed tomography scan should be offered in case of symptomatic disease or pre-operative imaging in order to avoid extensive radiation exposure.

Figure 9: Follow-up duration of urinary stone patients after treatment



** Not enough data about subgroup analysis of radiolucent and radiopaque stones.*
*** According to patient preference or symptomatic disease.*
**** Patients with diagnosed metabolic abnormalities.*
***** Lifelong follow-up is advised but data are available up to 10 years.*

Figure 10: Consensus on follow-up frequency and imaging modality to use after treatment



Stone free = No stone fragments on post-operative imaging (i.e., no stone fragments on CT/KUB/US).

High-Risk = Known biochemical abnormality (i.e. hypercalciuria, hypocitraturia, hyperuricosuria, RTA or high-risk stone type such as struvite).
Imaging = plain film KUB &/or kidney ultrasonography (KUS) based on clinicians' preference and stone characteristics. Consider CT if patient is symptomatic or if intervention is planned.
** Clinicians may choose the imaging-only pathway in patients with fragments < 2 mm.*
[a] Treatment monitoring for side effects, intolerance, and compliance.
+ Panel recommends re-intervention, however close follow-up may be considered for some patients at high risk for reintervention based on clinicians' preference.

Bladder Stones

Prevalence and stratification

The prevalence of bladder stones is higher in males. The age distribution is bimodal: incidence peaks at three years in children in developing countries and 60 years in adulthood.

Primary or endemic bladder stones occur in the absence of other urinary tract pathology, typically seen in children in areas with poor hydration, recurrent diarrhoea, and a diet deficient in animal protein. Secondary bladder stones occur in the presence of other urinary tract abnormalities, which include bladder outlet obstruction (BOO), neurogenic bladder dysfunction, chronic bacteriuria, foreign bodies (including catheters), bladder diverticula, and bladder augmentation or urinary diversion. Migratory bladder stones are those which have passed from the upper urinary tract where they formed and may then serve as a nidus for bladder stone growth.

Diagnostic imaging

Plain X-ray of KUB has a reported sensitivity of 21-78% for cystoscopically detected bladder stones in adults. Computed tomography and cystoscopy have a higher sensitivity for detecting bladder stones than US or X-ray in adults. There is a paucity of evidence for the investigation of bladder stones, particularly in children.

Disease management

Asymptomatic migratory bladder stones in adults may be left untreated. Primary and secondary bladder stones are usually symptomatic and are unlikely to pass spontaneously; active treatment is usually indicated. Uric acid stones can be dissolved by oral urinary alkalinisation when a pH > 6.5 is consistently achieved, typically using alkaline citrate or sodium bicarbonate. Regular monitoring is required during therapy. For further details see chapter 3.4.4 in the extended EAU Guidelines on Urolithiasis. Bladder stones can be treated with open, laparoscopic, or robotic assisted laparoscopic or endoscopic (transurethral or percutaneous) surgery, or extracorporeal SWL.

Recommendations	Strength rating
Use ultrasound (US) as first-line imaging with symptoms suggestive of a bladder stone.	Strong
Use cystoscopy or computed tomography (CT), or kidney-ureter-bladder X-Ray (KUB) to investigate adults with persistent symptoms suggestive of a bladder stone if US is negative.	Strong
All patients with bladder stones should be examined and investigated for the cause of bladder stone formation, including: • uroflowmetry and post-void residual; • urine dipstick, pH, ± culture; • metabolic assessment and stone analysis (see sections 3.3.2.3 and 4.1 of the Urolithiasis Guidelines for further details). In selected patients, consider: • upper tract imaging (in patients with a history of urolithiasis or loin pain); • cysto-urethroscopy or urethrogram.	Weak
Offer oral chemolitholysis for radiolucent or known uric acid bladder stones in adults.	Weak
Offer adults with bladder stones transurethral cystolithotripsy where possible.	Strong
Perform transurethral cystolithotripsy with a continuous flow instrument in adults (e.g., nephroscope or resectoscope) where possible.	Weak

Offer adults percutaneous cystolithotripsy where transurethral cystolithotripsy is not possible or advisable.	Strong
Suggest open cystolithotomy as an option for very large bladder stones in adults and children.	Weak
Offer children with bladder stones transurethral cystolithotripsy where possible.	Weak
Offer children percutaneous cystolithotripsy where transurethral cystolithotripsy is not possible or is associated with a high risk of urethral stricture (e.g., young children, previous urethral reconstruction, and spinal cord injury).	Weak
Open, laparoscopic, and extracorporeal shock wave lithotripsy are alternative treatments where endoscopic treatment is not advisable in adults and children.	Weak
Prefer "tubeless" procedure (without placing a catheter or drain) for children with primary bladder stones and no prior infection, surgery, or bladder dysfunction where open cystolithotomy is indicated.	Weak
Individualise imaging follow up for each patient as there is a paucity of evidence. Factors affecting follow up will include: • whether the underlying functional predisposition to stone formation can be treated (e.g., TURP); • metabolic risk.	Weak

Recommend regular irrigation therapy with saline solution to adults and children with bladder augmentation, continent cutaneous urinary reservoir or neuropathic bladder dysfunction, and no history of autonomic dysreflexia, to reduce the risk of stone recurrence.	Weak

This short booklet text is based on the more comprehensive EAU Guidelines accessible on the website: http://www.uroweb.org/guidelines/.