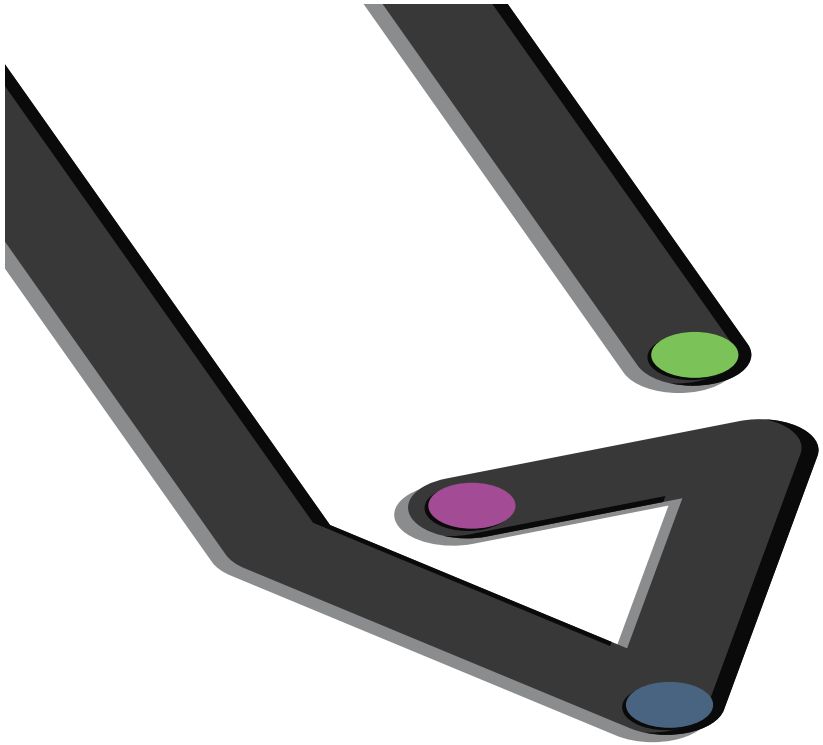

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ΠΑΘΗΣΕΩΝ

8ο

Ελληνικό
Διαδραστικό
Σχολείο

5 - 8 Μαρτίου | Πορταριά, Πήλιο

Διαδραστικό Σεμινάριο ΙΙ
Αμφισβητώντας τα guidelines της λιθίασης

Οι κατευθυντήριες οδηγίες της EAU

Ανδρέας Σκολαρίκος
Αναπληρωτής Καθηγητής Ουρολογίας ΕΚΠΑ

Δήλωση Συμφερόντων

- Κανένα

Table 1.1: Level of evidence (LE)*

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised controlled trials.
1b	Evidence obtained from at least one randomised trial.
2a	Evidence obtained from one well-designed controlled study without randomisation.
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study.
3	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports.
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities.

** Modified (1).*

Table 1.2: Grade of recommendation (GR)*

Grade	Nature of recommendations
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial.
B	Based on well-conducted clinical studies, but without RCTs.
C	Made despite the absence of directly applicable clinical studies of good quality.

**Modified from. (1).*

Guidelines on

Urolithiasis

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1.4 Publication history and summary of changes

1.4.1 Publication history

The EAU published its first guidelines on Urolithiasis in 2000. This 2015 document presents a limited update of the 2014 publication of the EAU Urolithiasis Guidelines.

1.4.2 Summary of changes

Key changes for the 2015 publication:

- The literature for the complete document has been assessed and updated, whenever relevant and 46 new references have been included.
- A new introductory section was added to Section 3.1(section Prevalence, aetiology, risk of recurrence), as well as a table. Additional data has been added to Table 1.2.
- Diagnostic imaging during pregnancy (section 3.3.3.1).

Recommendation	LE	GR
In pregnant women, ultrasound is the imaging method of choice.	1a	A*
In pregnant women, MRI should be used as a second-line imaging modality.	3	C
In pregnant women, low-dose CT should be considered as a last-line option. The exposure should be less than 0.05 Gy.	3	C

- In Section 3.4.1.2.1.1.1 - Conservative treatment (Observation) – a recommendation on the timing of patient follow-up has been included.

If renal stones are not treated, periodic evaluation is recommended (after 6 months and yearly thereafter).	A*

- In Section: 3.4.1.3 - Indication for active stone removal of kidney stones - a new recommendation has been added (stone composition section 3.4.1.4.4).

Recommendation	**LE**	**GR**
Radiolucent stones might be dissolvable (See Section 3.4.1.2.1.1.2.1.3).	2a	B

- In Section 3.4.2.2.1 - Stenting in ureteral stones - an additional recommendation has been included.

Recommendation	**LE**	**GR**
Alpha-blocker therapy is recommended in the case of stent-related symptoms.	1a	A

For ureterolithotomy, laparoscopy is recommended for large impacted stones when endoscopic lithotripsy or SWL has failed.	2	B

- In Section 3.4.2.5.1 - Antibiotic treatment – a new recommendation has been included.

Recommendations	**LE**	**GR**
UTIs must be excluded or treated prior to endourologic stone removal.	1b	A
In all patients undergoing endourologic treatment, perioperative antibiotic prophylaxis is recommended.	1b	A*

- A new Figure (3.4.2) - Recommended treatment options (if indicated for active stone removal) - has been included.

- In Section 3.4.5 - Management of stones in patients with neurogenic bladder – the recommendation has been expanded.

Recommendation	**GR**
In myelomeningocele patients, latex allergy is common so that appropriate measures need to be taken regardless of the treatment. For surgical interventions general anesthesia remains the only option.	B

- An additional recommendation was included in Table 3.4.6 - Special problems in stone removal.

Horseshoe kidneys	• Acceptable stone free rates can be achieved with flexible ureteroscopy [335].

- Figures 4.2 - Diagnostic and therapeutic algorithm for calcium oxalate stones - and 4.3 - Diagnostic and therapeutic algorithm for calcium phosphate stones - have updated reference values included.

- A new Section on Matrix stones has been added (4.12).

- In Table 4.6 - Pharmacological substances used for stone prevention - characteristics, specifics and dosage - Febuxostat for the treatment of hyperuricosuria and hyperuricaemia has been added.

- Section 4.4.4 - Recommendations for pharmacological treatment of patients with specific abnormalities in urine composition – a recommendation for Febustat has been added.

Hyperuricosuria	A llopurinol Febuxostat	1a 1b	A A

- In Table 4.8 - Pharmacological treatment of renal tubular acidosis – additional alternatives for the treatment of hypercalciuria have been included.

3. GUIDELINES

3.1 Prevalence, aetiology, risk of recurrence

*3.1.1 **Introduction***

Stone incidence depends on geographical, climatic, ethnic, dietary and genetic factors. The recurrence risk is basically dertermined by the disease or disorder causing the stone formation. Accordingly, the prevalence rates for urinary stones vary from 1% to 20% [4]. In countries with a high standard of life such as Sweden, Canada or the US renal stone prevalence is noteably high (> 10%). For some areas an increase of more than 37% over the last 20 years is reported [5] (Table 3.1.1).

Table 3.1.1: Prevalence and incidence of urolithiasis from two European countries [6, 7]

	Germany 2000 (%)	**Spain 2007 (%)**
Prevalence	4.7	5.06
Females	4.0	NA
Males	5.5	NA
Incidence	1.47	0.73
Females	0.63	NA
Males	0.84	NA

Table 3.1.2: Stones classified by aetiology*

Non-infection stones
• Calcium oxalate
• Calcium phosphate,
• Uric acid
Infection stones
• Magnesium ammonium phosphate
• Carbonate apatite
• Ammonium urate
Genetic causes
• Cystine
• Xanthine
• 2,8-dihydroxyadenine
Drug stones

**See Section 4.4.2*

Table 3.1.3: Stone composition

Chemical name	Mineral name	Chemical formula
Calcium oxalate monohydrate	Whewellite	$CaC_2O_4.H_2O$
Calcium oxalate dihydrate	Wheddelite	$CaC_2O_4.2H_2O$
Basic calcium phosphate	Apatite	$Ca_{10}(PO_4)_6.(OH)_2$
Calcium hydroxyl phosphate	Carbonite apatite	$Ca_5(PO_3)_3(OH)$
b-tricalcium phosphate	Whitlockite	$Ca_3(PO_4)_2$
Carbonate apatite phosphate	Dahllite	$Ca_5(PO_4)_3OH$
Calcium hydrogen phosphate	Brushite	$PO_4.2H_2O$
Calcium carbonate	Aragonite	CaCO3
Octacalcium phosphate		$Ca_8H2(PO_4)_6.5H_2O$
Uric acid	Uricite	$C_5H_4N_4O_3$
Uric acid dihydrate	Uricite	$C_5H_4O_3$-$2H_20$
Ammonium urate		$NH_4C_5H_3N_4O_3$
Sodium acid urate monohydrate		$NaC_5H_3N_4O_3.H_2O$
Magnesium ammonium phosphate	Struvite	$MgNH_4PO_4.6H_2O$
Magnesium acid phosphate trihydrate	Newberyite	$MgHPO_4.3H_2O$
Magnesium ammonium phosphate monohydrate	Dittmarite	$MgNH_4(PO_4).1H_2O$
Cystine		$[SCH_2CH(NH_2)COOH]_2$
Gypsum	Calcium sulphate dihydrate Zinc phosphate tetrahydrate	$CaSO_4.2H_2O$ $Zn_3(PO_4)_2.4H_2O$
Xanthine		
2,8-Dihydroxyadenine		
Proteins		
Cholesterol		
Calcite		
Potassium urate		
Trimagnesium phosphate		
Melamine		
Matrix		
Drug stones	• Active compounds crystallising in urine • Substances impairing urine composition (Section 4.11)	
Foreign body calculi		

Table 3.1.4: High-risk stone formers [10-17]

General factors
Early onset of urolithiasis (especially children and teenagers)
Familial stone formation
Brushite-containing stones ($CaHPO_4.2H_2O$)
Uric acid and urate-containing stones
Infection stones
Solitary kidney (the kidney itself does not particularly increase risk of stone formation, but prevention of stone recurrence is of more importance)
Diseases associated with stone formation
Hyperparathyroidism
Metabolic syndrome [17]
Nephrocalcinosis
Gastrointestinal diseases (i.e., jejuno-ileal bypass, intestinal resection, Crohn's disease, malabsorptive conditions, enteric hyperoxaluria after urinary diversion) and bariatric surgery [16]
Sarcoidosis
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
Drugs associated with 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

3.2 Classification of stones

- Stone size
- Stone location
- X-ray characteristics

Table 3.2.1: X-ray characteristics

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 (Section 4.11)

3.3 Diagnostic evaluation

3.3.1 ***Diagnostic imaging***

Table 3.3.1: Radiation exposure of imaging modalities [33-36]

Method	Radiation exposure (mSv)
KUB radiography	0.5-1
IVU	1.3-3.5
Regular-dose NCCT	4.5-5
Low-dose NCCT	0.97-1.9
Enhanced CT	25-35

Recommendation	LE	GR
If NCCT is indicated in patients with BMI < 30, use a low-dose technique.	1b	A

NCCT = non-contrast enhanced computed tomography.

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

IVU = intravenous urography; NCCT = non-contrast enhanced computed tomography.

Upgraded following panel consensus.

3.3.1.2 Radiological evaluation of patients for whom further treatment of renal stones is planned

Recommendations	**LE**	**GR**
A contrast study is recommended if stone removal is planned and the anatomy of the renal collecting system needs to be assessed.	3	A*
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. IVU may also be used.	4	C

**Upgraded based on panel consensus.*

CT – computed tomograpy; IVU = intravenous urography.

3.3 Diagnostic evaluation

3.3.2 ***Diagnostics - metabolism-related***

Table 3.3.2: Recommendations: basic laboratory analysis - emergency urolithiasis patients [11, 12, 37, 38]

Urine	**GR**
Dipstick test of spot urine sample • red cells • white cells	A*
• nitrite • approximate urine pH Urine microscopy and/or culture	A
Blood	
Serum blood sample • creatinine • uric acid • (ionised) calcium • sodium • potassium	A*
• Blood cell count • CRP	A*
If intervention is likely or planned: Coagulation test (PTT and INR).	A*

**Upgraded based on panel consensus.*

CPR = C-reactive protein; INR = international normalised ratio; PTT = partial thromboplastin time.

Recommendations	LE	GR
Always perform stone analysis in first-time formers using a valid procedure (XRD or IRS).	2	A
Repeat stone analysis in patients: • presenting with reccurent 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 [38].	2	B

IRS = infrared spectroscopy; XRD = X-ray diffraction.

3.3 Diagnostic evaluation

3.3.3 ***Diagnosis in special groups and conditions***

3.3.3.1 Diagnostic imaging during pregnancy

Recommendations	LE	GR
In pregnant women, ultrasound is the imaging method of choice.	1a	A*
In pregnant women, MRI should be used as a second-line imaging modality.	3	C
In pregnant women, low-dose CT should be considered as a last-line option. The exposure should be less than 0.05 Gy.	3	C

**Upgraded following panel consensus.*

CT = computed tomograpy; MRI = magnetic resonance imaging.

3.3.3.2 Children

Statement	LE
In paediatric patients, the most common non-metabolic disorders are vesicoureteral reflux, ureteropelvic junction obstruction, neurogenic bladder, and other voiding difficulties [50].	4
Recommendations	**GR**
In children, US is the first-line imaging modality when a stone is suspected.	B
If US does not provide the required information, KUB radiography (or NCCT) should be performed.	B
All efforts should be made to collect stone material that then should be analysed to classify the stone type.	A*

US = ultrasound; KUB = kidney, ureter, bladder; NCCT = non-contrast enhanced computed tomography.

**Upgraded following panel consensus.*

3.4 Disease management

3.4 Disease management

3.4.1 Management of patients with renal or ureteral stones

3.4.1.1 General patient management

Treatment decisions for upper urinary tract calculi are based on several general aspects such as stone composition, stone size, and symptoms.

Statement and recommendations for analgesia during renal colic

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

Recommendations	**GR**
In acute stone episodes, pain relief should be initiated immediately.	A
Whenever possible, an NSAID should be the first drug of choice. e.g. diclofenac*, indomethacin or ibuprofen**.	A
Second choice: hydromorphine, pentazocine or tramadol.	C
Use α-blockers to reduce recurrent colics.	A

**Affects glomerular filtration rate (GFR) in patients with reduced renal function (LE: 2a).*

***Recommended to counteract recurrent pain after ureteral colic.*

Recommendations	LE	GR

Recommendations	GR
Collect urine for antibiogram test following decompression.	A*
Start antibiotics immediately thereafter (+ intensive care if necessary).	
Re-evaluate antibiotic regimen following antibiogram findings.	

**Upgraded based on panel consensus.*

3.4 Disease management

3.4.1.2 Specific stone management

3.4.1.2.1 Renal stones

3.4.1.2.1.1.1 Conservative treatment (Observation)

Statement	LE
It is still debatable whether renal stones should be treated, or whether annual follow-up is sufficient for asymptomatic caliceal stones that have remained stable for 6 months.	4

Recommendations	GR
If renal stones are not treated, periodic evaluation is recommended (after 6 months and yearly follow-up of symptoms and stone status [US, KUB or CT]).	A*

**Upgraded based on panel consensus.*

3.4.1.3 Indication for active stone removal of renal stones [181]

- Stone growth;
- Stones in high-risk patients for stone formation;
- Obstruction caused by stones;
- Infection;
- Symptomatic stones (e.g., pain or haematuria);
- Stones > 15 mm;
- Stones < 15 mm if observation is not the option of choice.
- Patient preference;
- Comorbidity;
- Social situation of the patient (e.g., profession or travelling);
- Choice of treatment.

Statement	LE
Although the question of whether caliceal stones should be treated is still unanswered, stone growth, de novo obstruction, associated infection, and acute and/or chronic pain are indications for treatment [181-183].	3

Recommendations	GR
Kidney stones should be treated in the case of growth, formation of 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

**Upgraded based on panel consensus.*

3.4.1.2.1.1.2 Pharmacological treatment

Recommendations	**GR**
The dosage of alkalising medication must be modified by the patient according to urine pH, which is a direct consequence of such medication.	A
Dipstick monitoring of urine pH by the patient is required three times a day (at regular intervals). Morning urine must be included.	A
Careful monitoring of radiolucent stones during/after therapy is imperative.	A*
The physician should clearly inform the patient of the significance of compliance.	A

**Upgraded based on panel consensus.*

3.4.1.2.1.1.3 Extracorporeal shock wave lithotripsy (SWL)

Success depends on the efficacy of the lithotripter and the following factors:

- size, location (ureteral, pelvic or calyceal), and composition (hardness) of the stones (Section 3.4.2.4);
- patient's habitus (Section 3.4.1.3);
- performance of SWL (best practice, see below).

Each of these factors has an important influence on retreatment rate and final outcome of SWL.

3.4.1.2.1.1.3 Extracorporeal shock wave lithotripsy (SWL)

3.4.1.2.1.1.3.1 Contraindications of extracorporeal shock wave lithotripsy

There are several contraindications to the use of extracorporeal SWL, including:

- pregnancy, due to the potential effects on the foetus [82];
- bleeding diatheses, which should be compensated for at least 24 h before and 48 h after treatment [83];
- uncontrolled UTIs;
- severe skeletal malformations and severe obesity, which prevent targeting of the stone;
- arterial aneurysm in the vicinity of the stone [84];
- anatomical obstruction distal to the stone.

3.4.1.2.1.1.3 Extracorporeal shock wave lithotripsy (SWL)

3.4.1.2.1.1.3.2 Best clinical practice

Recommendation	LE	GR
Ensure correct use of the coupling gel because this is crucial for effective shock wave transportation (28).	2a	B

3.4.1.2.1.1.3 Extracorporeal shock wave lithotripsy (SWL)

3.4.1.2.1.1.3.2 Best clinical practice

Recommendation	LE	GR
In case of infected stones or bacteriuria, antibiotics should be given prior to SWL.	4	C

** Upgraded based on panel consensus.*

3.4.1.2.1.1.3 Extracorporeal shock wave lithotripsy (SWL)

Table 3.4.1: SWL-related complications [124-138]

Complications			**%**	**Ref.**
Related to stone fragments	Steinstrasse		4 – 7	[124-126]
	Regrowth of residual fragments		21 - 59	[127, 128]
	Renal colic		2 - 4	[129]
Infectious	Bacteriuria in non-infection stones		7.7 - 23	[127, 130]
	Sepsis		1 - 2.7	[127, 130]
Tissue effect	Renal	Haematoma, symptomatic	< 1	[131]
		Haematoma, asymptomatic	4 - 19	[131]
	Cardiovascular	Dysrhythmia	11 - 59	[127, 132]
		Morbid cardiac events	Case reports	[127, 132]
	Gastrointestinal	Bowel perforation	Case reports	[133-135]
		Liver, spleen haematoma	Case reports	[135-138]

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

PNL remains the standard procedure for large renal calculi. Different rigid and flexible endoscopes are available and the selection is mainly based on the surgeon's own preference. Standard access tracts are 24-30 F. Smaller access sheaths, < 18 French, were initially introduced for paediatric use, but are now increasingly popular in adults.

The efficacy of miniaturized systems seems to be high, but longer OR times apply and benefit compared to standard PNL for selected patients has yet to be demonstrated [142]. There is some evidence that smaller tracts cause less bleeding complications, but further studies have to evaluate this issue [143-146].

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

3.4.1.2.1.1.4.1.1 Contraindications

Patients receiving anticoagulant therapy must be monitored carefully pre- and postoperatively. Anticoagulant therapy must be discontinued before PNL [147].

Other important contraindications include:

- untreated UTI;
- tumour in the presumptive access tract area;
- potential malignant kidney tumour;
- pregnancy (Section 3.4.3.1).

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

3.4.1.2.1.1.4.1.3 Best clinical practice

Recommendation	GR
Preprocedural imaging, including contrast medium where possible or retrograde study when starting the procedure, is mandatory to assess stone comprehensiveness, view the anatomy of the collecting system, and ensure safe access to the renal stone.	A*

Upgraded based on panel consensus.

*Upgraded based on panel consensus.

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

3.4.1.2.1.1.4.1.3 Best clinical practice

Positioning of the patient

Both positions prone and supine are equally safe.

Although the supine position confers some advantages, it depends on appropriate equipment being available to position the patient correctly, for example, X-ray devices and operating table. Most studies cannot demonstrate an advantage of supine PNL in terms of OR time. Prone position offers more options for puncture and is therefore preferred for upper pole or multiple access [152-154]. The Urolithiasis Guidelines Panel will be setting up a systematic review to assess this topic.

Dilatation

Dilatation of the percutaneous access tract can be achieved using a metallic telescope, single (serial) dilators or a balloon dilatator. The difference in outcomes is less related to the technology used than to the experience of the surgeon [155].

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

3.4.1.2.1.1.4.1.3 Best clinical practice

Nephrostomy and stents

The decision about whether or not to place a nephrostomy tube at the end of the PNL procedure depends on several factors, including:

- presence of residual stones;
- likelihood of a second-look procedure;
- significant intraoperative blood loss;
- urine extravasation;
- ureteral obstruction;
- potential persistent bacteriuria due to infected stones;
- solitary kidney;
- bleeding diathesis;
- planned percutaneous chemolitholysis.

Small bore nephrostomies seem to have advantages in terms of postoperative pain [157, 158].

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

3.4.1.2.1.1.4.1.3 Best clinical practice

Tubeless PNL is performed without a nephrostomy tube. When neither a nephrostomy tube nor a ureteral stent is introduced, the procedure is known as totally tubeless PNL. In uncomplicated cases, the latter procedure results in a shorter hospital stay, with no disadvantages reported [159-161].

Recommendation	**LE**	**GR**
In uncomplicated cases, tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube and ureteral stent) PNL procedures provide a safe alternative.	1b	A

3.4.1.2.1.1.4.1 Percutaneous nephrolithotomy (PNL)

Table 3.4.2: Complications following PNL [162]

Complications	Transfusion	Embolisation	Urinoma	Fever	Sepsis	Thoracic complication	Organ injury	Death	LE
(Range)	(0-20%)	(0-1.5%)	(0-1%)	(0-32.1%)	(0.3-1.1%)	(0-11.6%)	(0-1.7%)	(0-0.3%)	1a
N = 11,929	7%	0.4%	0.2%	10.8%	0.5%	1.5%	0.4%	0.05%	

Perioperative fever can occur, even with a sterile preoperative urinary culture and perioperative antibiotic prophylaxis, because the renal stones themselves may be a source of infection. Intraoperative renal stone culture may therefore help to select postoperative antibiotics [163, 164]. Intraoperative irrigation pressure < 30 mm Hg and unobstructed postoperative urinary drainage may be important factors in preventing postoperative sepsis. Bleeding after PNL may be treated by brief clamping of the nephrostomy tube. Super-selective embolic occlusion of the arterial branch may become necessary in case of severe bleeding.

3.4.1.2.1.1.5 Ureterorenoscopy for renal stones (RIRS)

3.4.1.2.1.1.5 Ureterorenoscopy for renal stones (RIRS)

Technical improvements including endoscope miniaturisation, improved deflection mechanism, enhanced optical quality and tools, and introduction of disposables have led to an increased use of URS for both, renal and ureteral stones. Major technological progress has been achieved for retrograde intrarenal surgery (RIRS), [165-167]. Initial experience with digital scopes demonstrated shorter operation times due to the improvement in image quality [166-168]. For best clinical practice see Section 3.4.2.3.1.2 (Ureteral stones-URS)

Stones that cannot be extracted directly must be disintegrated. If it is difficult to access stones that need disintegration within the lower renal pole, it may help to displace them into a more accessible calyx [169].

Recommendation	**GR**
In case PNL is not an option, larger stones, even larger than 2 cm, may be treated with flexible URS. However, in that case there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed. In complex stone cases, open or laparoscopic approaches are possible alternatives.	B

GR = grade of recommendation; PNL = percutaneous nephrolithotomy; URS = ureterorenoscopy.

3.4.1.2.1.1.6 Open and laparoscopic surgery for removal of renal stones

Recommendations	LE	GR
Laparoscopic or open surgical stone removal may be considered in rare cases in which SWL,URS, and percutaneous URS fail or are unlikely to be successful.	3	C
When expertise is available, laparoscopic surgery should be the preferred option before proceeding to open surgery, escpecially when the stone mass is centrally located.	3	C

3.4.1.4 General recommendations and precautions for renal stone removal

3.4.1.4.1 Antibiotic therapy

Recommendation	GR
Urine culture or urinary microscopy is mandatory before any treatment is planned.	A*

**Upgraded following panel consensus.*

Recommendations	LE	GR
UTIs must be excluded or treated prior to endourologic stone removal.	1b	A
In all patients, perioperative antibiotic prophylaxis is recommended.	1b	A*

UTI = urinary tract infection.

3.4.1.4 General recommendations and precautions for renal stone removal

3.4.1.4.2 Antithrombotic therapy and stone treatment

Recommendations	LE	GR
In patients at high-risk for complications (due to antithrombotic therapy) in the presence of an asymptomatic caliceal stone, active surveillance should be offered.		C
Temporary discontinuation, or bridging of antithrombotic therapy in high-risk patients, should be decided in consultation with the internist.	3	B
Antithrombotic therapy should be stopped before stone removal after weighing the thrombotic risk.	3	B
If stone removal is essential and antithrombotic therapy cannot be discontinued, retrograde (flexible) ureterorenoscopy is the preferred approach since it is associated with less morbidity.	2a	A*

**Upgraded based on panel consensus.*

3.4.1.4 General recommendations and precautions for renal stone removal

3.4.1.4.4 Stone composition

Stones composed of brushite, calcium oxalate monohydrate, or cystine are particularly hard [27]. Percutaneous nephrolithotomy or RIRS are alternatives for removal of large SWL-resistant stones.

3.4.1.4.3 Obesity

Recommendation	LE	GR
Consider the stone composition before deciding on the method of removal (based on patients history, former stone analysis of the patient or HU in unenhanced CT. Stones with medium density > 1,000 HU on NCCT are less likely to be disintegrated by SWL) [27].		
Radiolucent stones might be dissolvable (See Section 3.4.1.2.1.1.2.1.3).	2a	B

CT = computed tomography; HU = hounsfield unit; NCCT = non-contrast enhanced computed tomograpy; SWL = shockwave lithotripsy.

3.4.1.4 General recommendations and precautions for renal stone removal

3.4.1.5 Steinstrasse

Table 3.4.3: Treatment of steinstrasse

Recommendations	LE	GR
Percutaneous nephrostomy is indicated for steinstrasse associated with urinary tract infection/ fever.	4	C
Shockwave lithotripsy or ureteronoscopy are indicated for steinstrasse when large stone fragments are present.	4	C

obstruction with/without UTI.		1. [illegible]	[illegible]			
		2. Stent	3			

3.4.1.6 Selection of procedure for active removal of renal stones

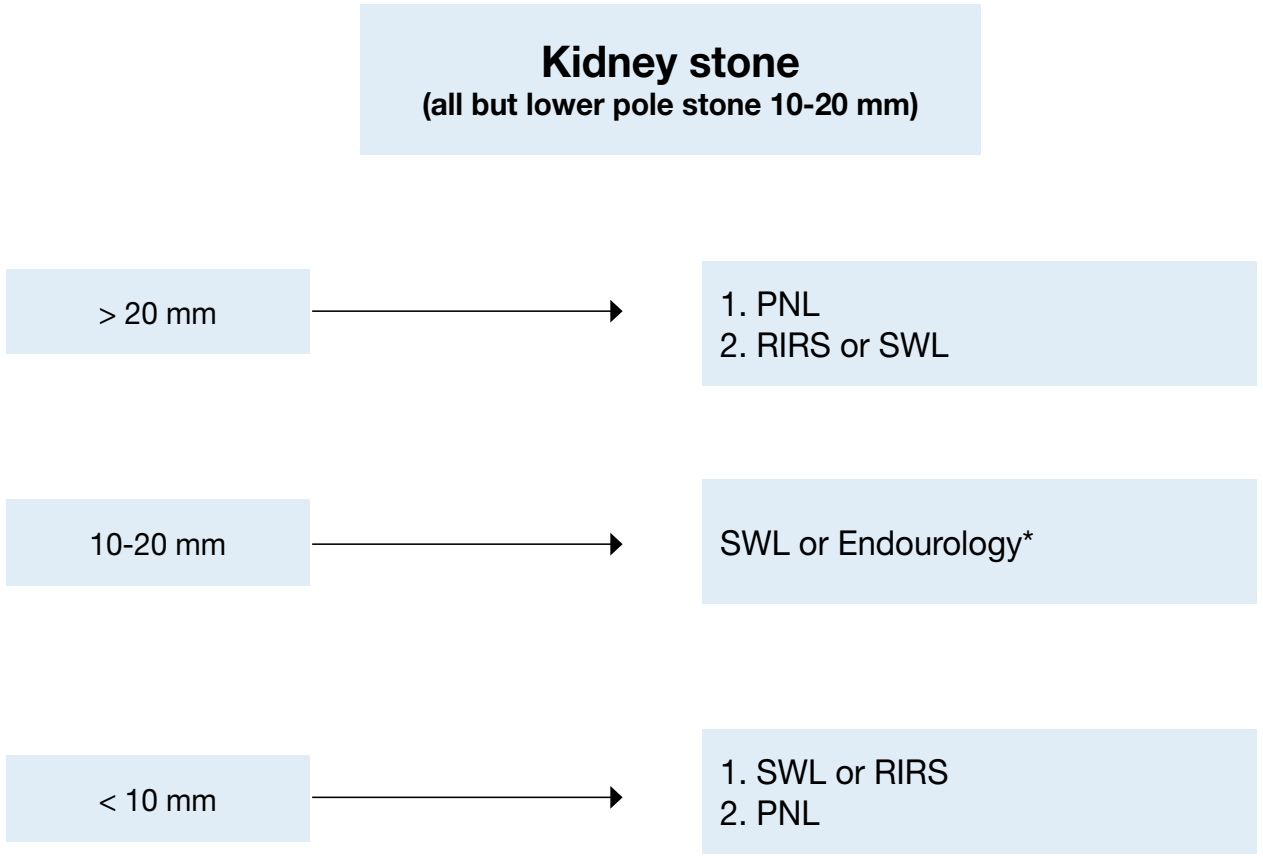
3.4.1.6.3 Recommendations for the selection of procedure for active removal of renal stones

Recommendations	**GR**
SWL and endourology (PNL, RIRS) are treatment options for stones < 2 cm within the renal pelvis and upper or middle calices.	B
PNL should be used as first-line treatment of larger stones > 2 cm.	B
In case PNL is not an option, larger stones (> 2 cm) may be treated with flexible URS. However, in that case there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed.	B
For the lower pole, PNL or RIRS is recommended, even for stones > 1.5 cm, because the efficacy of SWL is limited (depending on favourable and unfavourable factors for SWL).	B

PNL = percutaneous nephrolithotomy; RIRS = retrograde renal surgery; SWL = shock wave lithotripsy; URS = ureterorenoscopy.

3.4.1.6 Selection of procedure for active removal of renal stones

Figure 3.4.1: Treatment algorithm for renal calculi



3.4.1.6 Selection of procedure for active removal of renal stones

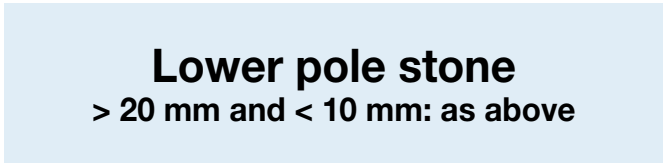
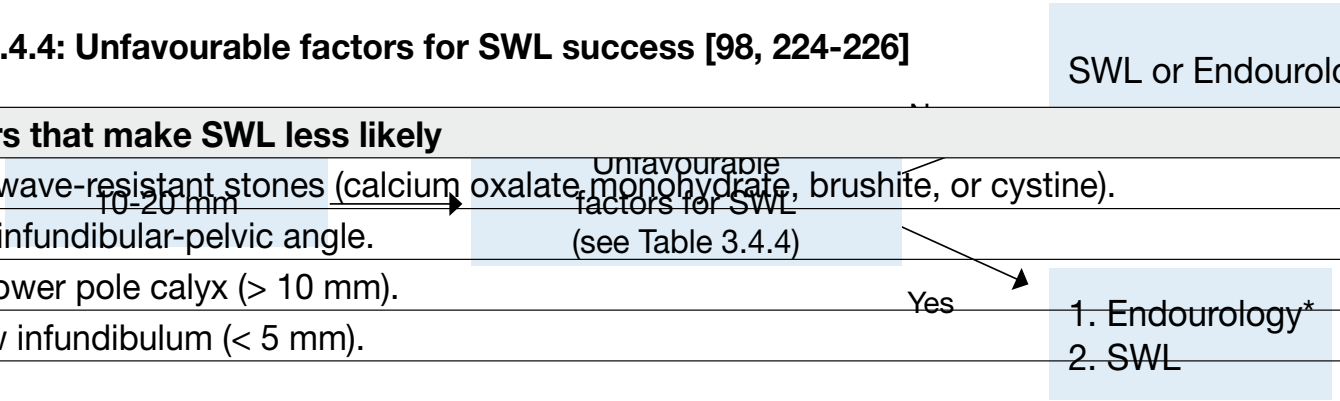


Table 3.4.4: Unfavourable factors for SWL success [98, 224-226]

Factors that make SWL less likely
Shockwave-resistant stones (calcium oxalate monohydrate, brushite, or cystine).
Steep infundibular-pelvic angle.
Long lower pole calyx (> 10 mm).
Narrow infundibulum (< 5 mm).



SWL = shockwave lithotripsy; PNL = percutaneous nephrolithotomy; URS = ureterorenoscopy; SFR = stone-free rate; RIRS = retrograde renal surgery

3.4.2 Ureteral stones

3.4.2.1.1 Conservative treatment / observation

There are only limited data about spontaneous stone passage according to stone size [230]. It is estimated that 95% of stones up to 4 mm pass within 40 days [3].

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

Recommendations	**LE**	**GR**
In patients with newly diagnosed small**ureteral stones if active removal is not indicated (Section 3.4.1.3), observation with periodic evaluation is an optional initial treatment.	1a	A
Appropriate medical therapy should be offered to these patients to facilitate stone passage during observation.*		

**See Section 3.4.2.1.2.1, Medical expulsive therapy (MET).*

3.4.2 Ureteral stones

3.4.2.1.2.1 Medical expulsive therapy (MET)

Statement	LE
There is good evidence that MET accelerates spontaneous passage of ureteral stones and fragments generated with SWL, and limits pain [72, 216, 231-237].	1a

Statement	LE
Several trials have demonstrated an α-blocker class effect on stone expulsion rates.	1b

Statement	LE
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 [238, 252, 253].	1b

3.4.2 Ureteral stones

3.4.2.1.2.1 Medical expulsive therapy (MET)

Recommendations for MET	LE	GR
For MET, α-blockers are recommended.	1a	A
Patients should be counseled regarding the attendant risks of MET, including associated drug side effects, and should be informed that it is administered off-label†*.		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.		A
Patients should be followed once between 1 and 14 days to monitor stone position and assessed for hydronephrosis.	4	A*

† *It is not known if tamsulosin harms the human foetus or if it is found in breast milk.*

**Upgraded based on panel consensus.*

***MET in children cannot be recommended due to the limited data in this specific population.*

MET = medical expulsion therapy.

3.4.2 Ureteral stones

3.4.2.1.2.1 Medical expulsive therapy (MET)

3.4.2.1.2.1.2 Factors affecting success of medical expulsive therapy (tamsulosin)

Stone location

Stone size

The vast majority of trials have investigated distal ureteral stones [72]. Two RCT assessed the effect of tamsulosin on spontaneous passage of proximal ureteral calculi <10 mm demonstrating stone migration to a more distal part of the ureter [254] and a significantly higher stones expulsion rate and shorter expulsion time for stones < 6 mm [255].

Due to the high likelihood of spontaneous passage of stones up to ~5 mm, MET is less likely to increase the stone-free rate (SFR) [72, 232] (LE: 1b). However, MET does reduce the need for analgesics [72, 232] (LE: 1a).

*3.4.2 **Ureteral stones***

3.4.2.1.2.1 Medical expulsive therapy (MET)

3.4.2.1.2.1.3 Medical expulsive therapy after extracorporeal shock wave lithotripsy (SWL)

3.4.2.1.2.1.4 Medical expulsive therapy after ureteroscopy

One RCT and a meta-analyses have shown that MET after SWL for ureteral or renal stones can expedite expulsion and increase SFRs and reduce analgesic requirements [119, 237] (LE: 1a).

3.4.2.1.2.1.6 Duration of medical expulsive therapy treatment

Most studies have had a duration of 1 month. No data are currently available to support other time-intervals.

MET following holmium:YAG laser lithotripsy increases SFRs and reduces colic episodes [256] (LE: 1b).

3.4.2.1.2.1.7 Possible side-effects include retrograde ejaculation and hypotension [72].

3.4.2 ***Ureteral stones***

3.4.2.4 Indications for active removal of ureteral stones [3, 230, 282]

Indications for active removal of ureteral stones are:

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

3.4.2 Ureteral stones

3.4.2.2 SWL

Best clinical practice see Section 3.4.1.2.1.1.4.1.3 (renal stones).

Stenting

The 2007 AUA/EAU Guidelines on the management of ureteral calculi state that routine stenting is not recommended as part of SWL [3]. When the stent is inserted, patients often suffer from frequency, dysuria, urgency, and suprapubic pain [257].

Recommendation	LE	GR
Routine stenting is not recommended as part of SWL treatment of ureteral stones.	1b	A
Alpha-blocker therapy is recommended in the case of stent-related symptoms.	1a	A

SWL = shock wave lithotripsy.

3.4.2 ***Ureteral stones***

3.4.2.3 Endourology techniques

3.4.2.3.1 Ureteroscopy (URS)

The current standard for rigid ureterorenoscopes are tip diameters of < 8 F. Rigid URS can be used for the whole ureter [3]. However technical improvements , enhanced quality and tools as well as the availability of digital scopes also alow to favour the use of flexible ureteroscopes in the ureter [165].

3.4.2.3.1.1 Contraindications

Apart from general problems, for example, with general anaesthesia or untreated UTIs, URS can be performed in all patients without any specific contraindications.

3.4.2 Ureteral stones

3.4.2.3.1.2 Best clinical practice in ureterorenoscopy (URS)

Safety aspects

Access to the upper urinary tract

Most interventions are performed under general anaesthesia, although local or spinal anaesthesia is possible. Intravenous sedation is suitable for female patients with distal ureteral stones [258].

Antegrade URS is an option for large, impacted proximal ureteral calculi [259] (Section 3.4.2.6.1).

Recommendation	GR
Placement of a safety wire is recommended.	A*

**Upgraded based on panel consensus.*

3.4.2 Ureteral stones

Ureteral access sheaths

Hydrophilic-coated ureteral access sheaths, which are available in different calibres (inner diameter from 9 F upwards), can be inserted via a guide wire, with the tip placed in the proximal ureter.

Ureteral access sheaths allow easy multiple access to the upper urinary tract and therefore significantly facilitate URS. The use of ureteral access sheaths improves vision by establishing a continuous outflow, decreasing intrarenal pressure, and potentially reduces operating time [262, 263].

The insertion of ureteral access sheaths may lead to ureteral damage whereas the risk was lowest in pre-stented systems [264].No data on long-term consequences are available [264, 265]. Use of ureteral access sheaths depends on the surgeon's preference.

3.4.2 Ureteral stones

Stone extraction

The aim of URS is complete stone removal. “Dust and go” strategies should be limited to the treatment of large (renal) stones.

Stones can be extracted by endoscopic forceps or baskets. Only baskets made of nitinol can be used for flexible URS [266].

Recommendation	LE	GR
Stone extraction using a basket without endoscopic visualisation of the stone (blind basketing) should not be performed.	4	A*

**Upgraded based on panel consensus.*

3.4.2 Ureteral stones

3.4.2.3.1.3 Complications

Statements	LE	GR
Recommendation		
Overall complication rate after URS is 9-25% [3, 280, 281]. Most are minor and do not require intervention.	3	B
In uncomplicated URS, a stent need not be inserted.	1a	A
Ureteral avulsion and ureteric injuries are rare [282]. Previous procedures are the most important risk factor for ureteral injuries [283].	3	B
An α-blocker can reduce stent-related symptoms.	1a	A

Holmium:yttrium-aluminium-garnet (laser); US ultrasound.

3.4.2 Ureteral stones

Recommendation	GR
Percutaneous antegrade removal of ureteral stones is an alternative when SWL is not indicated or has failed, and when the upper urinary tract is not amenable to retrograde URS.	A

SWL = shock wave lithotripsy; URS ureterorenoscopy

For ureterolithotomy, laparoscopy is recommended for large impacted stones when endoscopic lithotripsy or SWL has failed.	2	B

SWL = shock wave lithotripsy.

3.4.2 Ureteral stones

3.4.2.5.2 Obesity

Obesity can cause a lower success rate after SWL and PNL.

The same considerations apply as in renal stone removal (Section 3.4.1.4.2).

Statement	LE
In case of severe obesity, URS is a more promising therapeutic option than SWL.	2b

3.4.2.5.3 Bleeding disorder

URS can be performed in patients with bleeding disorders, with a moderate increase in complications [147, 208]. Discontinuation of anticoagulant therapy should be weighed against the risk, in each individual patient.

3.4.2.5 General recommendations and precautions

3.4.2.5.1 Antibiotic treatment

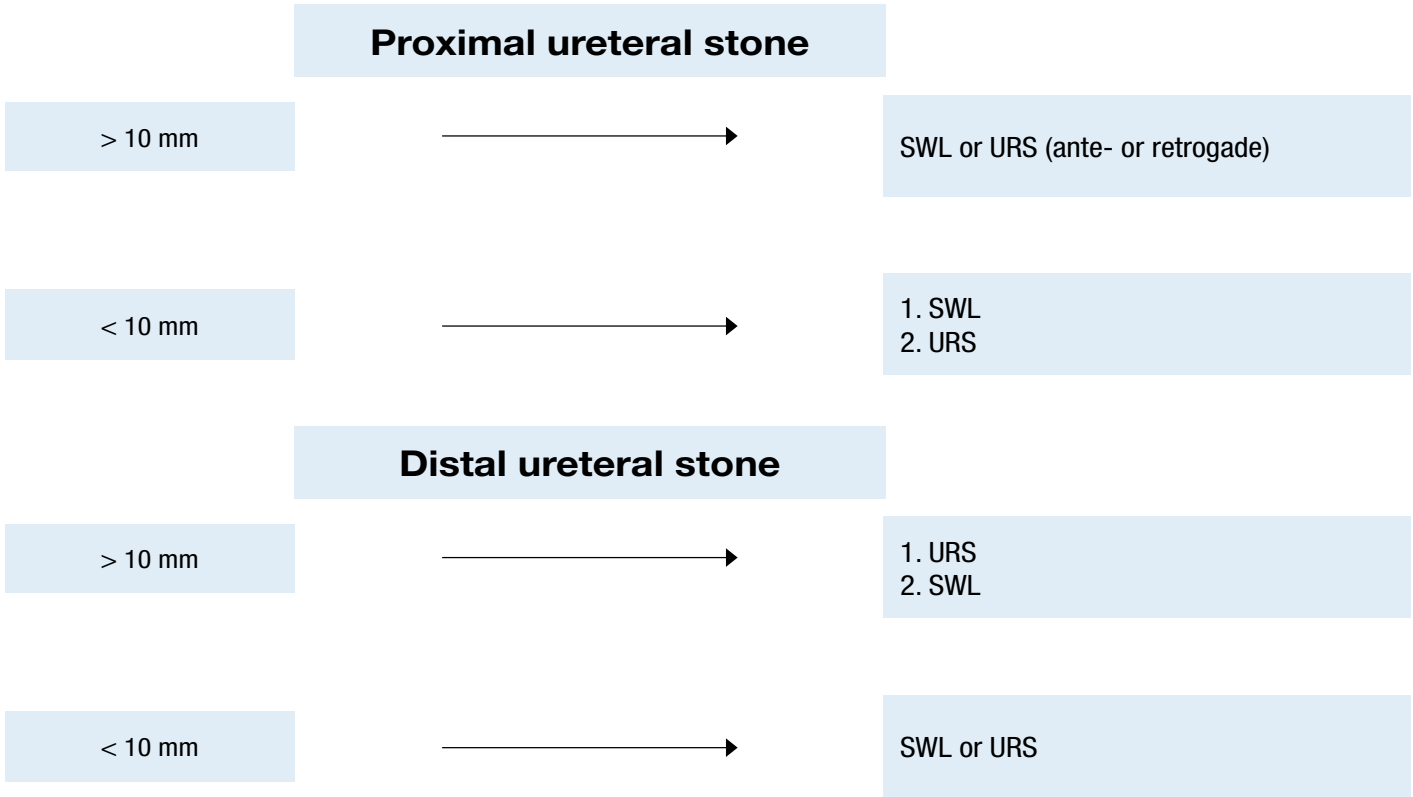
Single dose administration was found sufficient as perioperatice antibiotic prophylaxis [193, 194].

Recommendations	LE	GR
UTIs must be excluded or treated prior to endourologic stone removal.	1b	A
In all patients undergoing endourologic treatment, perioperative antibiotic prophylaxis is recommended.	1b	A*

UTI = Urinary tract infection.

3.4.2 Ureteral stones

Figure 3.4.2: Recommended treatment options (if indicated for active stone removal) (GR: A*)



**Upgraded following panel consensus.*
SWL = shockwave lithotripsy; URS = ureterorenoscopy.

3.4.2.7 Management of patients with residual stones

Recommendations	LE	GR
Statement		
Identification of biochemical risk factors and appropriate stone prevention is mandatory.	1b	1A
For well disintegrated stone material in the lower calix, an inversion therapy with simultaneous mechanical percussion maneuver under enforced diuresis may facilitate stone clearance [297].	1b	1b

Residual fragments, stones (largest diameter)	Symptomatic residuals	Asymptomatic residuals	LE	GR

Recommendations	LE	GR
After SWL and URS, and in the presence of residual fragments, MET is recommended using an α-blocker to improve fragment clearance.	1a	A

SWL = shockwave lithotripsy; URS = ureteronoscopy; MET = medical expulsive therapy

3.4.3 Management of Specific patient groups

3.4.3.1 Management of urinary stones and related problems during pregnancy

Statements	LE
If intervention becomes necessary, placement of a ureteral stent or a percutaneous nephrostomy tube are readily available primary options.	3
Ureteroscopy is a reasonable alternative to avoid long-term stenting/drainage.	1a
Regular follow-up until final stone removal is necessary due to the higher encrustation tendency of stents during pregnancy.	

Recommendation	GR
Conservative management should be the first-line treatment for all non-complicated cases of urolithiasis in pregnancy (except those that have clinical indications for intervention).	A

3.4.3 Management of Specific patient groups

3.4.4 Management of stones in patients with urinary diversion

Statement	LE
The choice of access depends on the feasibility of orifice identification in the conduit or bowel reservoir. Whenever a retrograde approach is impossible, percutaneous access with antegrade URS is the alternative.	4

Recommendation	GR
PNL is the preferred treatment for removal of 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 SWL.	A*

PNL = percutaneous nephrolithotomy; SWL = shockwave lithotripsy.

3.4.3 Management of Specific patient groups

3.4.5 Management of stones in patients with neurogenic bladder

Statement	LE
Patients undergoing urinary diversion and/or suffering from neurogenic bladder dysfunction are at risk for recurrent stone formation.	3

Recommendation	GR
In myelomeningocele patients, latex allergy is common so that appropriate measures need to be taken regardless of the treatment. For surgical interventions general, anesthesia remains the only option.	B

3.4.3 *Management of Specific patient groups*

3.4.6 *Management of stones in transplanted kidneys*

Recommendation	LE	GR
In patients with transplanted kidneys, unexplained fever, or unexplained failure to thrive (particularly in children), US or NCCT should be performed to rule out calculi [322].	4	B

Statements	LE
Conservative treatment for small asymptomatic stones is only possible under close surveillance and in absolutely compliant patients.	
SWL for small calyceal stones is an option with minimal complication risk but localisation of the stone can be challenging and SFRs are poor [333, 334].	4

Recommendation	GR
In patients with transplanted kidneys, all contemporary treatment modalities, including shockwave therapy, (flexible) ureteroscopy, and percutaneous nephrolithotomy are management options.	B
Metabolic evaluation should be completed after stone removal.	A*

**Upgraded following panel consensus.*

3.4.3 Management of Specific patient groups

Table 3.4.6: Special problems in stone removal

Caliceal diverticulum stones	• SWL, PNL (if possible) or RIRS. • Can be treated in line with the options described above [335-339] • Patients may become asymptomatic due to stone disintegration (SWL) but residual disintegrated stone material remains in the original position due to narrow caliceal neck. • URS together with endopyelotomy with Ho:YAG.
Horseshoe kidneys	• Can be treated in line with the options described above [340] • Passage of fragments after SWL might be poor • Access to the stone can be hindered with flexible ureteroscopy [341].
Stones in pelvic kidneys	• SWL, RIRS, PNL or laparoscopic surgery • For lower pole stones the URS versus RIRS, PNL or open surgery
Stones formed in a continent reservoir	• Section 3.4.4 • Each stone problem must be considered and treated individually

SWL = shockwave lithotripsy; PNL = percutaneous nephrolithotomy; URS = ureterorenoscopy; RIRS = retrograde renal surgery

3.4.3 Management of Specific patient groups

3.4.8 Management of urolithiasis in children

Statement	LE
Spontaneous passage of a stone is more likely in children than in adults [50].	4

Statements	LE
In children, the indications for SWL are similar to those in adults, however, they pass fragments more easily.	3
Children with renal stones of a diameter up to 20 mm (~ 300 mm^2) are ideal candidates for SWL.	1b

3.4.3 Management of Specific patient groups

3.4.8 Management of urolithiasis in children

Statements	LE
For paediatric patients, the indications for PNL are similar to those in adults.	1a

Recommendation	GR
In children, PNL is recommended for treatment of renal pelvic or caliceal stones with a diameter > 20 mm (~ 300 mm^2).	C

PNL = percutaneous nephrolithotomy.

3.4.3 *Management of Specific patient groups*

3.4.8 *Management of urolithiasis in children*

Recommendation	LE	GR
For intracorporeal lithotripsy, the same devices as in adults can be used (Ho:Yag laser, pneumatic- and US lithotripters).	3	C

4. FOLLOW UP
METABOLIC EVALUATION AND RECURRENCE PREVENTION

4.1 General metabolic considerations for patient work-up

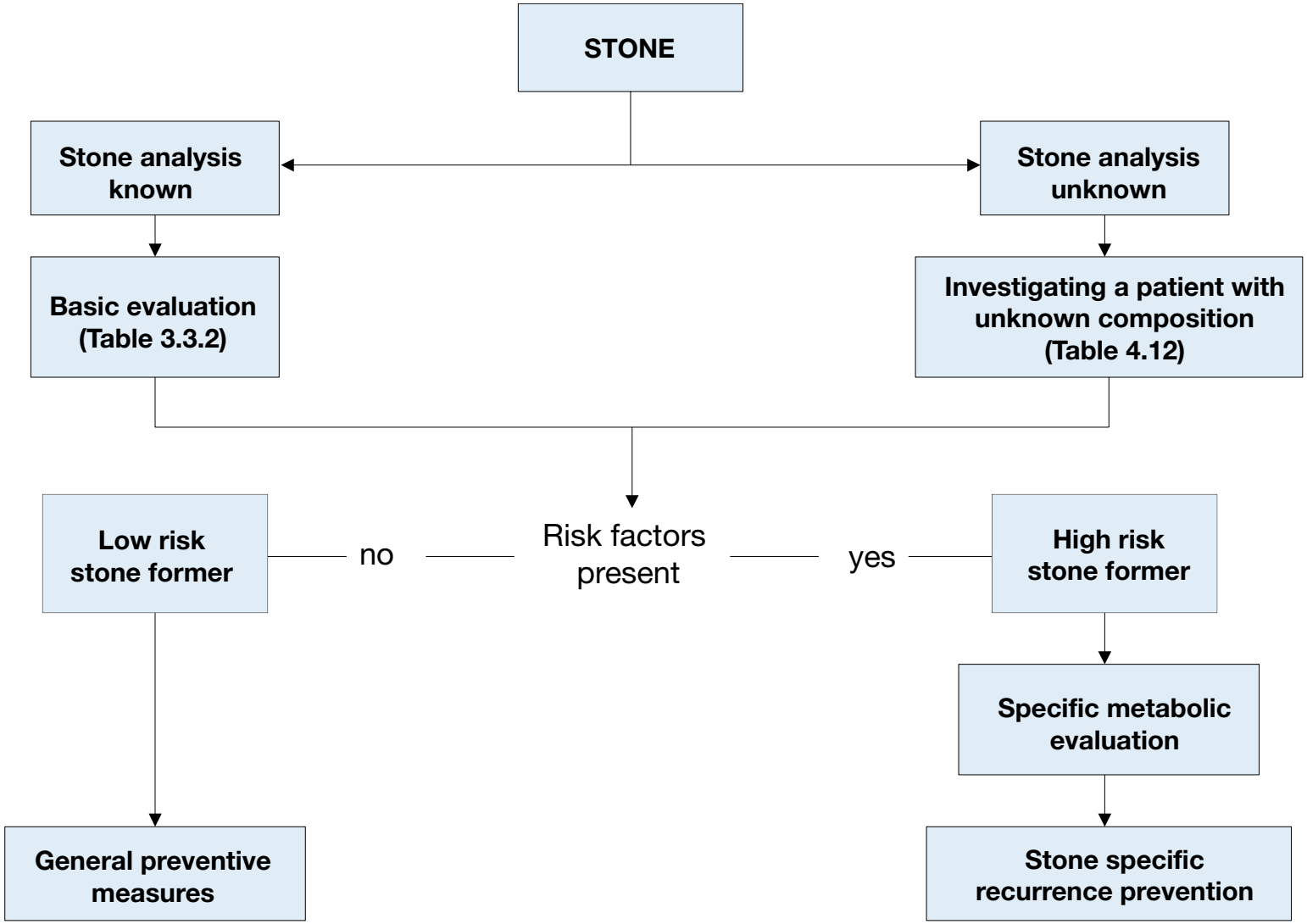
4.1.1 ***Evaluation of patient risk***

After stone passage, every patient should be assigned to a low- or high-risk group for stone formation (Figure 4.1).

For correct classification, two items are mandatory:

- reliable stone analysis by infrared spectroscopy or X-ray diffraction;
- basic analysis (Section 3.3.2).

Figure 4.1 Assignment of patients to low- or high-risk groups for stone formation



*4.1.3 **Timing of specific metabolic work-up***

For the initial specific metabolic work-up, the patient should stay on a self-determined diet under normal daily conditions and should ideally be stone free for at least 20 days [390

Follow-up studies are necessary in patients taking medication for recurrence prevention [391]. The first follow-up 24-h urine measurement is suggested 8-12 weeks after starting pharmacological prevention of stone recurrence. This enables drug dosage to be adjusted if urinary risk factors have not normalised, with further 24-h urine measurements if necessary. Once urinary parameters have been normalised, it is sufficient to perform 24-h urine evaluation every 12 months. The panel realise that on this issue there is only very limited published evidence. The Urolithiasis Guidelines Panel aim to set up a systematic review on the ideal timing of the 24-hour urine collection.

Table 4.5: General preventive measures

Fluid intake (drinking advice)	Fluid amount: 2.5-3.0 L/day Circadian drinking Neutral pH beverages Diuresis: 2.0-2.5 L/day Specific weight of urine: < 1010
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 advice to normalise general risk factors	BMI: retain a normal BMI level Adequate physical activity Balancing of excessive fluid loss

Caution: The protein need is age-group dependent, therefore protein restriction in childhood should be handled carefully.

**Avoid excessive consumption of vitamin supplements.*

4.2.4 ***Recommendations for recurrence prevention***

Recommendations		**LE**	**GR**
The aim should be to obtain a 24-h urine volume ≥ 2.5 L.		1b	A
Hyperoxaluria	Oxalate restriction	2b	B
High sodium excretion	Restricted intake of salt	1b	A
Small urine volume	Increased fluid intake	1b	A
Urea level indicating a high intake of animal protein	Avoid excessive intake of animal protein.	1b	A

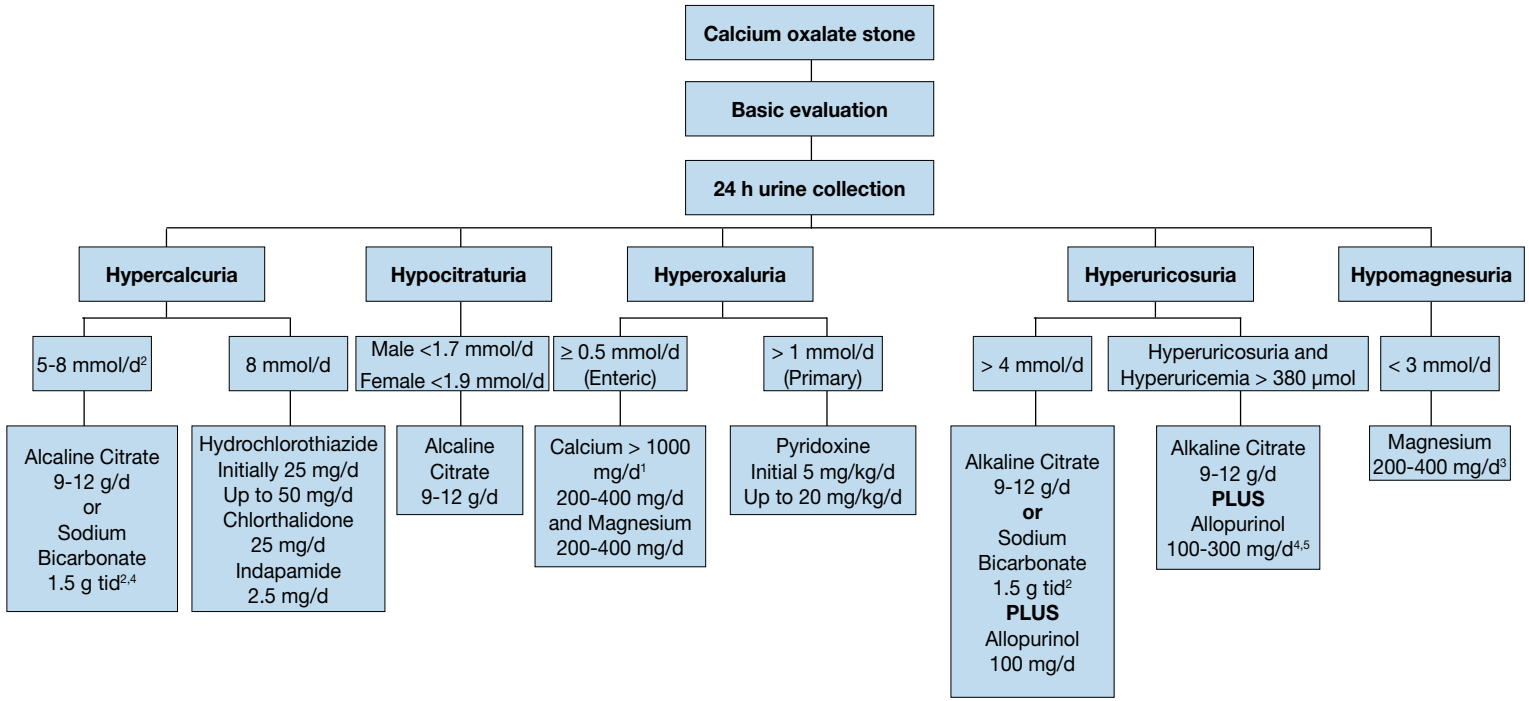
Table 4.6: Pharmacological substances used for stone prevention - characteristics, specifics and dosage

Agent	Rationale	Dose	Specifics and side effects	Stone type	Ref
Alkaline citrates	Alkalinisation Hypocitraturia Inhibition of calcium oxalate crystallisation	5-12 g/d (14-36 mmol/d) Children: 0.1-0.15 g/kg/d	Daily dose for alkalinisation depends on urine pH	Calcium oxalate Uric acid Cystine	[38, 399, 421-427]
Allopurinol	Hyperuricosuria Hyperuricaemia	100-300 mg/d Children: 1-3 mg/kg/d	100 mg in isolated hyperuricosuria Renal insufficiency demands dose correction	Calcium oxalate Uric acid Ammonium urate 2,8-Dihydroxyadenine	[428-432]
Calcium	Enteric hyperoxaluria	1000 mg/d	Intake 30 min before the meals	Calcium oxalate	[412-414]
Captopril	Cystinuria Active decrease of urinary cystine levels	75-150 mg	Second-line option due to significant side effects	Cystine	[433, 434]
Febuxostat	Hyperuricosuria Hyperuricaemia	80-120 mg/d	Acute gout contraindicated, pregnancy, xanthine stone formation	Calcium oxalate Uric acid	[435, 436]

			formation		
l-Methionine	Acidification	600-1500 mg/d	Hypercalciuria, bone demineralisation, systemic acidosis. No long-term therapy.	Infection stones Ammonium urate Calcium phosphate	[38, 437, 438]
Magnesium	Isolated hypomagnesiuria Enteric hyperoxaluria	200-400 mg/d Children: 6 mg/kg/d	Renal insufficiency demands dose correction. Diarrhoea, chronic alkali losses, hypocitraturia.	Calcium oxalate	[439, 440] low evidence
Sodium bicarbonate	Alkalinisation Hypocitraturia	4.5 g/d		Calcium oxalate Uric acid Cystine	[441]
Pyridoxine	Primary hyperoxaluria	Initial dose 5 mg/kg/d Max. 20 mg/kg/d	Polyneuropathia	Calcium oxalate	[442]

Thiazide (Hydrochloro-thiazide)	Hypercalciuria	25-50 mg/d Children: 0.5-1 mg/kg/d	Risk for agent-induced hypotonic blood pressure, diabetes, hyperuricaemia, hypokalaemia, followed by intracellular acidosis and hypocitraturia	Calcium oxalate Calcium phosphate	[38, 439, 443-451]
Tiopronin	Cystinuria Active decrease of urinary cystine levels	Initial dose 250 mg/d Max. 2000 mg/d	Risk for tachyphylaxis and proteinuria.	Cystine	[452-455]

Figure 4.2: Diagnostic and 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.

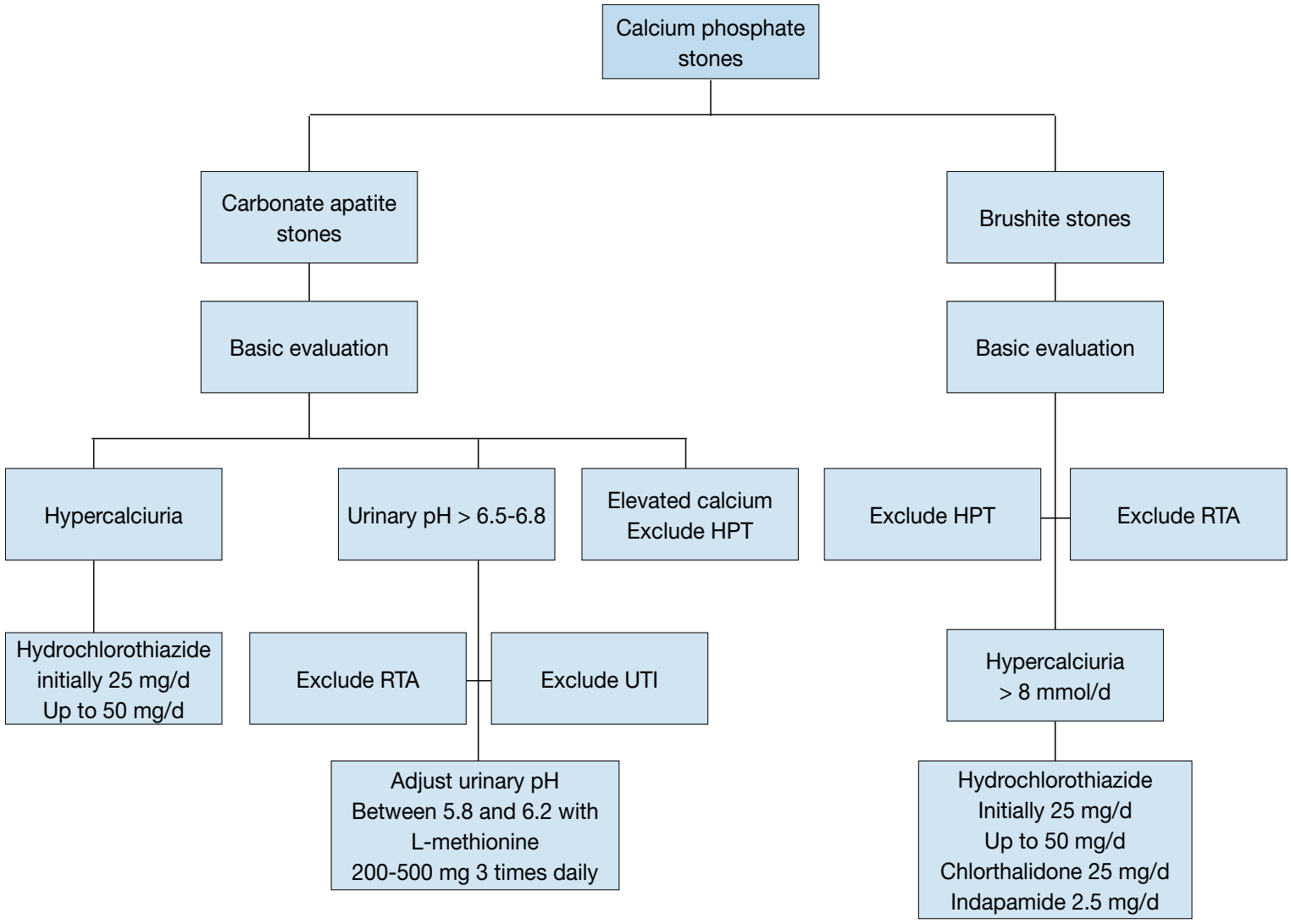
[4] There is no evidence that combination therapy (thiazide + citrate) (thiazide + allopurinol) is superior to thiazide therapy alone [443, 450].

[5] Febuxostat 80 mg/d.

4.4.4 *Recommendations for pharmacological treatment of patients with specific abnormalities in urine composition*

Urinary risk factor	**Suggested treatment**	**LE**	**GR**
Hypercalciuria	Thiazide + potassium citrate	1a	A
Hyperoxaluria	Oxalate restriction	2b	A
Enteric hyperoxaluria	Potassium citrate	3-4	C
	Calcium supplement	2	B
	Diet reduced in fat and oxalate	3	B
Hypocitraturia	Potassium citrate	1b	A
Hypocitraturia	Sodium bicarbonate if intolerant to potassium citrate	1b	A
Hyperuricosuria	Allopurinol Febuxostat	1a 1b	A A
High sodium excretion	Restricted intake of salt	1b	A
Small urine volume	Increased fluid intake	1b	A
Urea level indicating a high intake of animal protein	Avoid excessive intake of animal protein	1b	A
No abnormality identified	High fluid intake	2b	B

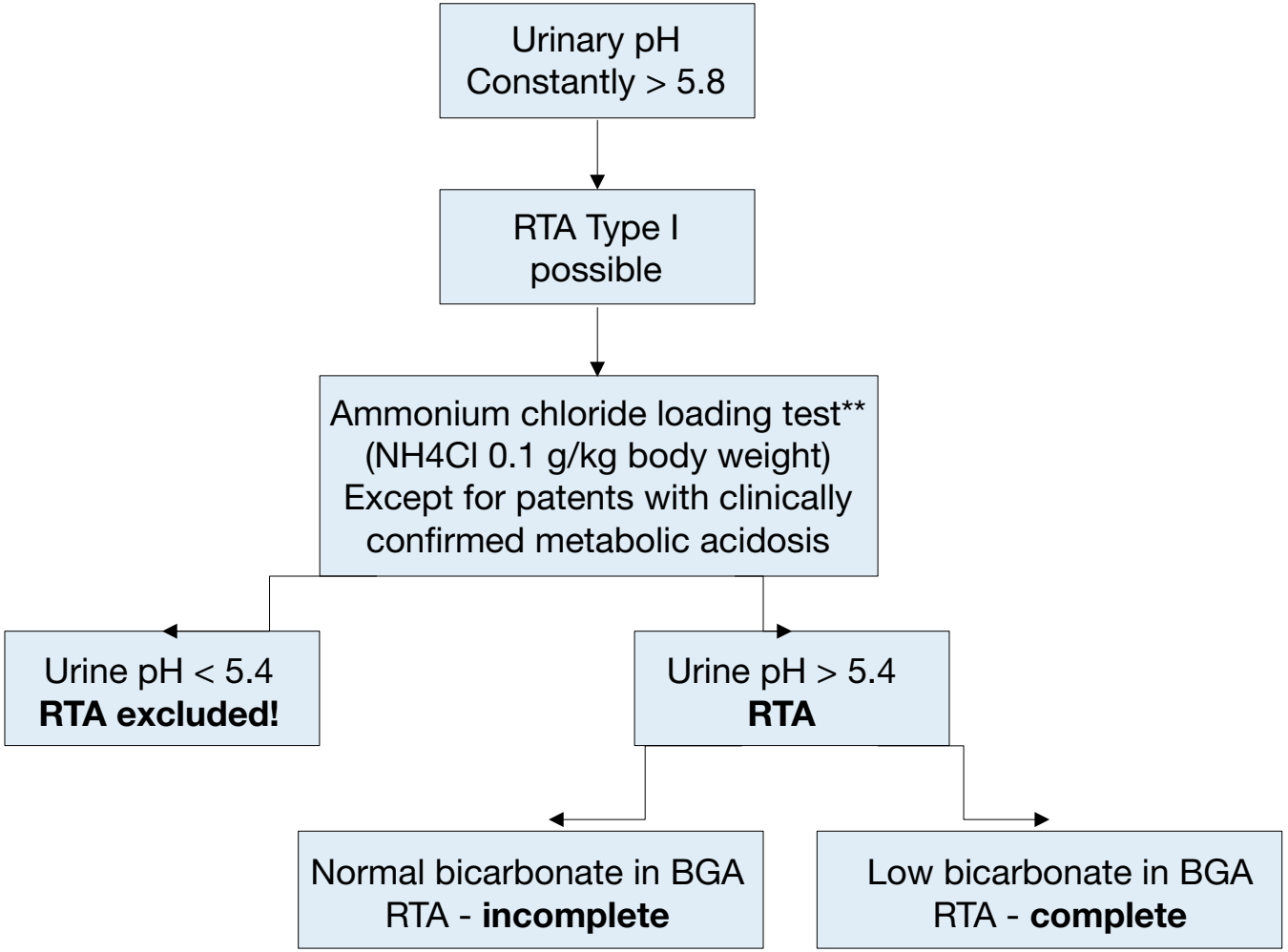
Figure 4.3: Diagnostic and therapeutic algorithm for calcium phosphate stones



4.5.4 Recommendations for the treatment of calcium phosphate stones

Urinary risk factor	Suggested treatment	LE	GR
Hypercalciuria	Thiazide	1a	A
Inadequate urine pH	Acidification	3-4	C
UTI	Antibiotics	3-4	C

Figure 4.4: Diagnosis of renal tubular acidosis



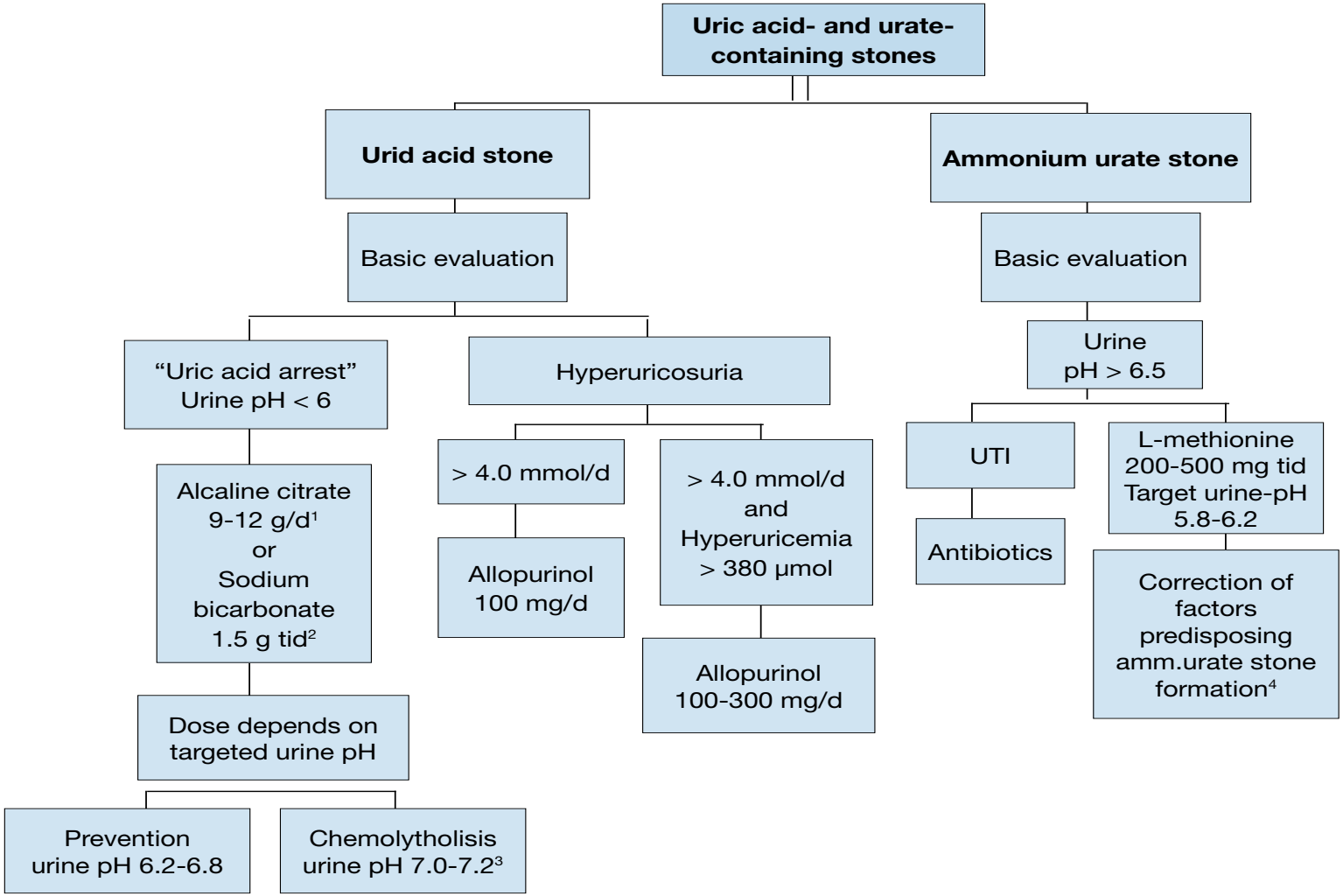
*** An alternative Ammonium Chloride loading test using NH4Cl load with 0.05 g/kg body weight over 3 days might provide similar results and may be better tolerated by the patient.And second alternative in these cases could be the furosemide acidification test.*

Table 4.8: Pharmacological treatment of renal tubular acidosis

Biochemical risk factor	Rationale for pharmacological therapy	Medication
Hypercalciuria	Calcium excretion > 8 mmol/day	Hydrochlorothiazide, - in adults: 25 mg/day initially, up to 50 mg/day - in children: 0.5-1 mg/kg/day Alternatives in adults: Chlorthalidone 25 mg/d Indapamide 2.5 mg/d
Inadequate urine pH	Intracellular acidosis in nephron	Alkaline citrate, 9-12 g/day divided in 3 doses OR Sodium bicarbonate, 1.5 g, 3 times daily

Urinary risk factor	Suggested treatment	LE	GR
Distal RTA	Potassium citrate	2b	B
Hypercalciuria	Thiazide + potassium citrate	1a	A

Figure 4.5: Diagnostic and 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.*

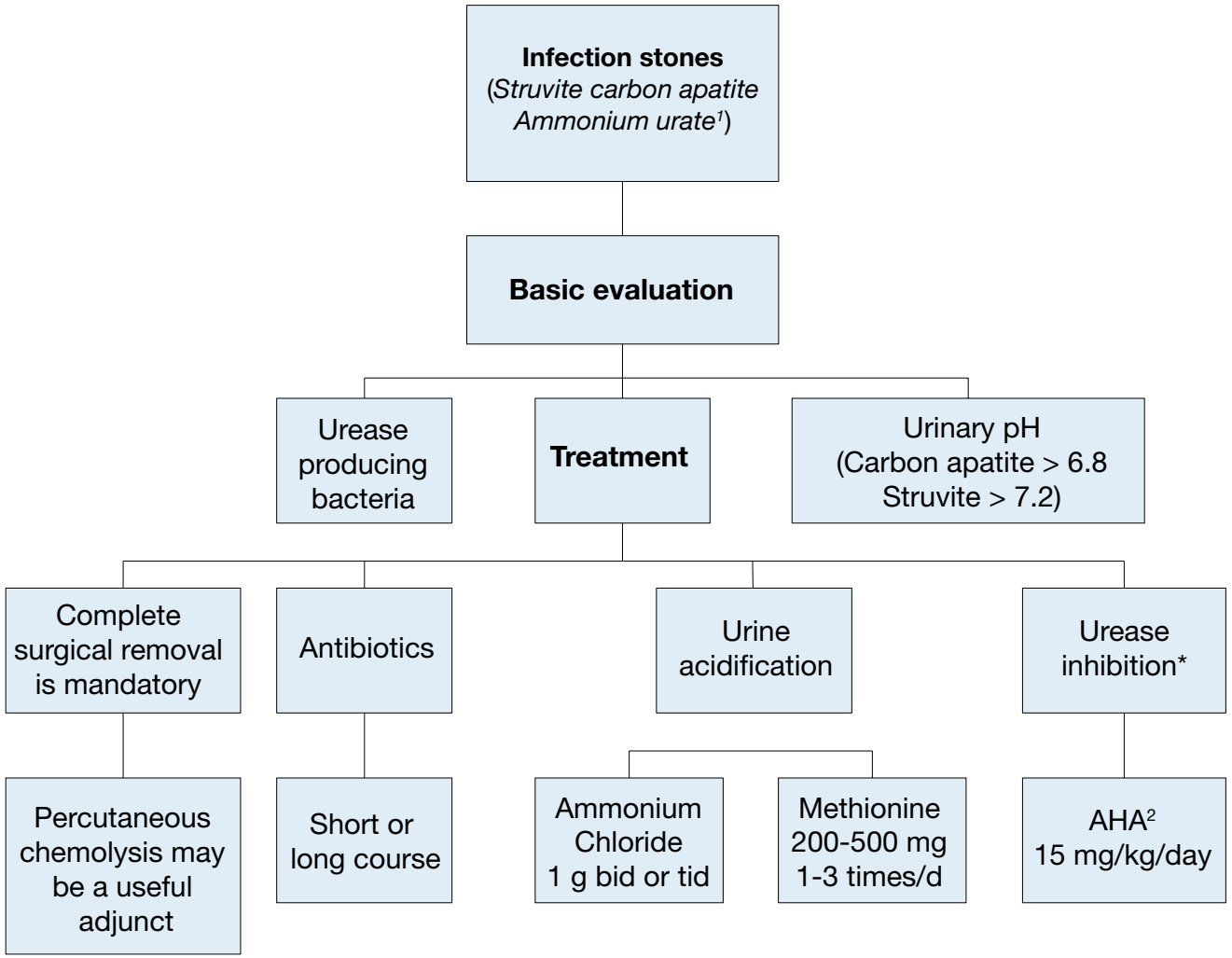
Table 4.9: Factors predisposing to struvite stone formation

Neurogenic bladder
Spinal cord injury/paralysis
Continent urinary diversion
Ileal conduit
Foreign body
Stone disease
Indwelling urinary catheter
Urethral stricture
Benign prostatic hyperplasia
Bladder diverticulum
Cystocele
Caliceal diverticulum
Ureteropelvic junction obstruction

Table 4.10: Most important species of urease-producing bacteria

Obligate urease-producing bacteria (> 98 %)
• *Proteus spp.* • *Providencia rettgeri* • *Morganella morganii* • *Corynebacterium urealyticum* • *Ureaplasma urealyticum*
Facultative urease-producing bacteria
• *Enterobacter gergoviae* • *Klebsiella spp.* • *Providencia stuartii* • *Serratia marcescens* • *Staphylococcus spp.*
CAUTION: 0-5% of *Escherichia coli, Enterococcus spp*. and *Pseudomonas aeruginosa* strains may produce urease.

Figure 4.6: Diagnostic and therapeutic algorithm for infection stones



[1] Discussed with uric acid stones,

[2] Acetohydroxamic acid

** When nationally available.*

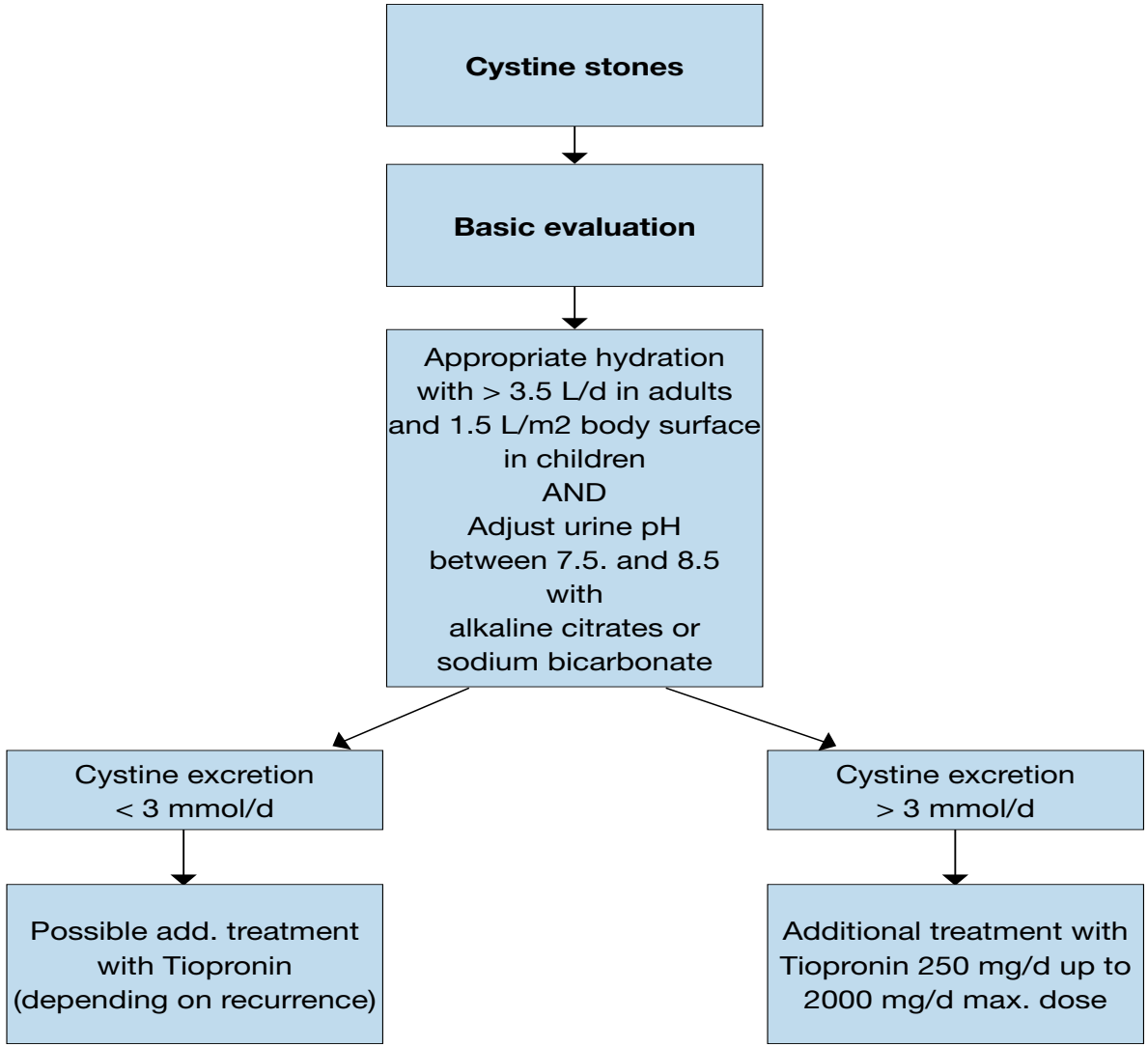
bid = twice a day; tid = three times a day.

4.8.3 Recommendations for therapeutic measures of infection stones

Recommendations for therapeutic measures	LE	GR
Surgical removal of the stone material as completely as possible	3-4	A*
Short-term antibiotic course	3	B
Long-term antibiotic course	3	B
Urinary acidification: ammonium chloride, 1 g, 2 or 3 times daily	3	B
Urinary acidification: methionine, 200-500 mg, 1-3 times daily	3	B
Urease inhibition	1b	A

**Upgraded following panel consensus.*

Figure 4.7: Metabolic management of cystine stones



4.9.3 Recommendations for the treatment of cystine stones

Therapeutic measures	LE	GR
Urine dilution High fluid intake recommended so that 24-h urine volume exceeds 3 L. Intake should be ≥ 150 mL/h.	3	B
Alkalinisation For cystine excretion < 3 mmol/day: potassium citrate 3-10 mmol 2 or 3 times daily, to achieve pH > 7.5.	3	B
Complex formation with cystine For patients with cystine excretion > 3 mmol/day, or when other measures are insufficient: tiopronin, 250-2000 mg/day.	3	B

Table 4.11: Compounds that cause drug stones

Active compounds crystallising in urine
• Allopurinol/oxypurinol
• Amoxicillin/ampicillin
• Ceftriaxone
• Quinolones
• Ephedrine
• Indinavir
• Magnesium trisilicate
• Sulphonamides
• Triamterene
• Zonisamide
Substances impairing urine composition
• Acetazolamide
• Allopurinol
• Aluminium magnesium hydroxide
• Ascorbic acid
• Calcium
• Furosemide
• Laxatives
• Methoxyflurane
• Vitamin D
• Topiramate

4.12 Matrix Stones

Pure matrix stones are extremely rare with less than 70 cases described in the literature. They are more prevalent in females. The main risk factors are recurrent urinary tract infections, especially due to *Proteous mirabilis* or *Escherichia coli*, previous surgery for stone disease, chronic renal failure and haemodialysis. Complete endourological removal, frequently via the percutaneous approach, is critical. Given the rarity of matrix calculi a specific prophylactic regimen to minimize recurrence cannot be recommended. Eliminating infections and prophylactic use of antibiotics are most commonly proposed [505].

Table 4.12: Investigating patients with stones of unknown composition

Investigation	Rationale for investigation
Medical history	• Stone history (former stone events, family history) • Dietary habits • Medication chart
Diagnostic imaging	• Ultrasound in the case of a suspected stone • Unenhanced helical CT • (Determination of Hounsfield units provides information about the possible stone composition)
Blood analysis	• Creatinine • Calcium (ionised calcium or total calcium + albumin) • Uric acid
Urinalysis	• Urine pH profile (measurement after each voiding, minimum 4 times daily) • Dipstick test: leukocytes, erythrocytes, nitrite, protein, urine pH, specific weight • Urine culture • Microscopy of urinary sediment (morning urine) • Cyanide nitroprusside test (cystine exclusion)