RENAL and URETERIC STONES

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- November 2023

To the CHI Original Renal and Ureteric Stones Clinical Guidance- Issued May 2020

Contents

Related Documents

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Abbreviations

ACP	American College of Physicians
ASIR	Age-Standardized Incidence Rate
BOO	Bladder Outlet Obstruction
CHI	Council of Health Insurance
CT	Computed Tomography
DALY	Disability-Adjusted Life Years
dRTA	Distal Renal Tubular Acidosis
ECIRS	Endoscopic Combined Intrarenal Surgery
EMA	European Medicines Agency
FDA	Food and Drug Administration
FRAX	World Health Organization's Fracture Risk Assessment
GIO	Glucocorticoid-induced Renal and Ureteric Stones
HR	Heart Rate
HRT	Hormone Replacement Therapy
LE	Level of Evidence
MET	Medical Expulsion Therapy
MOF	Major Osteoporotic Fracture
MRI	Magnetic Resonance Imaging
NCCT	Non-Contrast Computed Tomography
NICE	National Institute for Health and Care Excellence
NSAID	Non-Steroidal Anti-Inflammatory Drug
PCNL	Percutaneous Nephrolithotomy
PCNL	Percutaneous Nephrolithotripsy
PMDA	Pharmaceuticals and Medical Devices Agency
PNL	Percutaneous Nephrolithotomy
RIRS	Retrograde Intrarenal Surgery
SC	Subcutaneous

SDI	Socio-Demographic Index
SFDA	Saudi Food and Drug Authority
SFR	Stone-Free Rates
SOGC	Society of Obstetricians and Gynecologists of Canada
SWL	Shock Wave Lithotripsy
URS	Ureteroscopy/Ureterorenoscopy
US	Ultrasonography

Executive Summary

Nephrolithiasis specifically refers to calculi in the kidneys, but renal calculi and ureteral calculi (ureterolithiasis) are often discussed in conjunction. Ureteral calculi almost always originate in the kidneys, although they may continue to grow once, they lodge in the ureter. The pain generated by renal colic is primarily caused by dilation, stretching, and spasm because of the acute ureteral obstruction[1].

The classic presentation for a patient with acute renal colic is the sudden onset of severe pain originating in the flank and radiating inferiorly and anteriorly; at least 50% of patients will also have nausea and vomiting. Patients with urinary calculi may report pain, infection, or hematuria. Patients with small, non-obstructing stones or those with staghorn calculi may be asymptomatic or experience moderate and easily controlled symptoms[1].

The location and characteristics of pain in nephrolithiasis include the following[1]:

- Stones obstructing ureteropelvic junction: Mild to severe deep flank pain without radiation to the groin; irritative voiding symptoms (e.g., frequency, dysuria); suprapubic pain, urinary frequency/urgency, dysuria, stranguria, bowel symptoms.
- Stones within ureter: Abrupt onset of severe, colicky pain in the flank and ipsilateral lower abdomen; radiation to testicles or vulvar area; intense nausea with or without vomiting
- Upper ureteral stones: Pain radiates to flank or lumbar areas.
- Midureteral calculi: Pain radiates anteriorly and caudally.
- Distal ureteral stones: Pain radiates into groin or testicle (men) or labia majora (women)
- Stones passed into bladder: Mostly asymptomatic; rarely, positional urinary retention.
- Inadequate fluid intake, resulting in reduced urine production, leads to the accumulation of substances that can form kidney stones in the urine. This environmental factor plays a crucial role, perhaps the most significant one, in the development of kidney stones. The specific mechanisms responsible for tubular damage or dysfunction leading to stone formation have not yet been fully understood. Most research on the causes and prevention of urinary tract stone disease has focused on the impact of elevated levels of calcium, oxalate, and uric acid in urine, as well as reduced levels of citrate.
- Hypercalciuria is the most common metabolic abnormality seen in kidney stone formation. Some cases of hypercalciuria are linked to increased calcium

absorption in the intestines, often associated with excessive dietary calcium intake and/or overactive calcium absorption processes, leading to an imbalance between calcium and oxalate absorption in the small intestine. Others are related to excessive calcium resorption from bone, such as in cases of hyperparathyroidism. There are also instances where the renal tubules are unable to effectively reabsorb calcium from the glomerular filtrate, known as renal leak hypercalciuria.

- Magnesium and citrate, particularly citrate, play crucial roles in inhibiting the formation of stones in the urinary tract. Reduced levels of these substances in the urine increase the likelihood of stone formation.

The four main chemical types of renal calculi, which together are associated with more than 20 underlying etiologies include calcium stones, struvite (magnesium ammonium phosphate) stones, uric acid stones, and cystine stones[1].

Most patients with nephrolithiasis form calcium stones (80%), most of which are composed primarily of calcium oxalate or calcium phosphate. The other main types include uric acid, struvite (magnesium ammonium phosphate), and cystine stones. Of note, one patient may have a stone that contains more than one type of crystal[1].

Risk Factors - Influenced by certain diseases, habits, composition of urine: Personal history of prior kidney stones increases the risk of kidney stones by 15% within the first year, and 50% within the next ten years, A family history of kidney stones increases the risk by 2.5 times, Increased enteric oxalate absorption, typically due to malabsorption, leads to increased formation of calcium oxalate crystals, urinary tract infections alter urinary pH in the setting of urease-producing bacteria, producing struvite crystals, low fluid intake, history of diabetes, obesity, gout, and hypertension, acidic urine (pH < 5.5), which promotes uric acid formation in the setting of chronic diarrhea and gout[1].

Several complications can arise due to kidney stones, and subsequently, stones that cause obstruction. These include Abscess formation, Urosepsis, Urinary fistula formation, Ureteral scarring and stenosis, Ureteral perforation, Renal function loss due to long-standing obstruction[2].

Laboratory tests to assess renal function, including either a basic or comprehensive metabolic panel, may be used. Additionally, a urinalysis, urine electrolytes, and urine pH can help direct towards a specific type of stone. A kidney-ureter-bladder (KUB) X-ray is also an option; however, uric acid stones are difficult to assess with this imaging. A CT of the abdomen and pelvis without contrast can also be performed and has higher sensitivity. Contrast medium is typically avoided when there is a concern for a kidney stone as enhancement of the vessels and ureters can obscure stone findings[2].

The medical management of acute stone attacks (renal colic) entails providing supportive care and administering various medications, including intravenous hydration, nonsteroidal anti-inflammatory drugs (NSAIDs), non-narcotic pain relievers, oral or intravenous narcotic pain medications, alpha blockers to aid in the passage of stones, antiemetic drugs, and antibiotics[1].

For the prevention and dissolution of stones, the following classes of medications are utilized: uricosuric agents, alkalinizing agents for uric acid and cysteine calculi, and thiazide diuretics, which are employed to address hypercalciuria[1].

In cases where stones are 7 mm or larger, they are unlikely to pass spontaneously and typically necessitate a surgical procedure, which may include: placement of a stent, percutaneous nephrostomy, extracorporeal shockwave lithotripsy (ESWL), ureteroscopy, percutaneous nephrostolithotomy (PCNL) or mini PCNL, open nephrostomy (although less invasive techniques are now preferred), and anatrophic nephrolithotomy, especially for large, intricate staghorn calculi that cannot be effectively cleared by a sufficient number of PCNL procedures; this procedure is commonly performed using laparoscopic or robotic methods[1].

Renal stone (nephrolithiasis) is a common disease, which is becoming widespread worldwide. It is common in developed and Industrialized countries, where its lifetime prevalence is approximately 14.0%, and this rate has been increasing. The lifetime risk of renal stones is 1.0%–5.0% in Asia, 5.0%–9.0% in Europe, and 10.0%–15.0% in the USA. Furthermore, it is a common disease in Saudi Arabia. Recent studies have shown that the prevalence of renal stones is as high as 20.0% among Saudi Arabians. Since it is a chronic and recurring health condition, its management involves a high burden of direct and indirect costs on patients[3].

In 2019, more than 115 million (95% uncertainty interval [95% UI] 93–140) incident cases of urolithiasis occurred worldwide, and the age-standardized incidence rate (ASIR) (per 100,000 population) decreased from 1696.2 (1358.1–2078.1) in 1990 to 1394 (1126.4–1688.2) in 2019. Nearly 13,279 (95% UI: 10616–16267) died of urolithiasis, contributing to 0.6 million (0.5– 0.7) disability-adjusted life years (DALYs) in 2019. The highest age-standardized DALY rates (33.33 per 100 000 population) in 2019 were observed in Armenia, whereas the largest negative estimated annual percentage changes of DALYs were seen in Poland[4].

At the global level, both the incident and DALY cases experienced substantial growth compared to the absolute cases in 1990. However, global age-standardized incidence and DALY rate of urolithiasis were observed to decline from 1990 to 2019. Males' ASIR was higher than females, while the gap narrowed over the years. A weakly positive correlation between ASIR of urolithiasis and SDI was also observed in this study[4].

CHI issued Renal and Ureteric Stones clinical guidance after thorough review of renowned international and national clinical guidelines in May 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Renal and Ureteric Stones clinical guidance and seeks to offer guidance for the effective management of Renal and Ureteric Stones. It provides an **update on the Renal and Ureteric Stones Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the issuance of updated versions of previously reviewed guidelines** namely European Association of Urology Guidelines on Urolithiasis [2023], Canadian Urological Association guideline: Evaluation and medical management of kidney stones [2022], Canadian Urological Association guideline: Management of ureteral calculi [2021].

Moreover, **new guidelines are added to the report** such as The Urological Association of Asia clinical guideline for urinary stone disease [2019], American Family Physician, Kidney Stones: Treatment and Prevention [2019].

There are no updated Saudi guidelines for the management of renal and ureteric stones. The last published guidelines by Saudi Medical Journal were in 2001 about the Current evaluation and management of renal and ureteral stones with a focus mainly on clinical presentation, evaluation, and surgical management so it will not be detailed in this report.

After carefully examining clinical guidelines and reviewing the SFDA drug list, there are no new SFDA registered drugs to include in the CHI formulary while removing Acemetacin, Metoclopramide Hydrochloride 10 mg suppository, Penicillamine and Tiaprofenic acid as they are no longer registered on the SFDA Drug List of September 2023. There have been no changes or updates made to any of the previously listed drugs in terms of drug information and prescribing edits since May 2020.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the Renal and Ureteric Stones therapeutic management.

Below is a table summarizing the major changes based on the different Renal and Ureteric Stones guidelines used to issue this report:

Table 1. General Recommendations for the Management of Renal and Ureteric Stones

Management of Renal and Ureteric Stones		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
<u>Role of lifestyle, metabolic components in urinary stone disease</u> 1. Fluid intake volume has been shown to be inversely related to urolithiasis. 2. A low protein diet should be encouraged to reduce the risk of stone formation.	1. LE:1, GR: A 2. LE:2, GR: B	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
Patients should increase their daily fluid intake to 2.5 to 3 L per day to prevent recurrence of kidney stones.	Evidence rating: A	American Family physician, 2019
Nonsteroidal anti-inflammatory drugs are the first choice for pain relief in patients with kidney stones.	Evidence rating: A	American Family physician, 2019
Alpha blockers are the first choice for medical expulsive therapy in patients with distal ureteric stones.	Evidence rating: A	American Family physician, 2019
Thiazide diuretics, potassium citrate, or allopurinol should be prescribed by a stone specialist after recurrence of calcium stones and a full metabolic workup.	Evidence rating: A	American Family physician, 2019
<u>Diagnosis</u> 1. Medical history is very important to diagnose stone disease. Physicians should ask detailed questions regarding symptoms, including pain, nausea/vomiting, urine color, discomfort on urination and previous stone episodes**.** 2. Obtaining information on habitual behavior regarding diet and physical activity, family history, age of onset,	1. LE:1, GR: A 2. LE:1, GR: A	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019

and previous stone episodes are to predict the risk and recurrence of stones		
Metabolic Evaluation 1. It is advisable to conduct initial assessments, which include serum chemistry and urinary analysis, for all patients who present with stones. 2. Patients who have a high risk of stone recurrence or formation should undergo metabolic evaluations, including a 24-hour urine collection	1. LE:4, GR: B 2. LE:4, GR: B	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
Medical management 1. **Alpha1-blockers** have been recommended for muscle relaxation of the lower ureter and to promote spontaneous ureter stone passage**.** 2. **Tamsulosin** significantly facilitated the passage of distal ureteral stones in patients with well-controlled pain, no infections, abnormal anatomy, renal insufficiency, or high-grade obstruction	1. LE:1, GR: A 2. LE:1	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
Medical treatment is appropriate for pyelonephritis accompanying urinary stone. 1. Active antibiotic treatment and timely drainage of kidney if necessary. 2. Percutaneous nephrostomy and ureteral catheter insertion. 3. Nephrectomy is advocated as the treatment of choice for a kidney that has lost most of its function and the contralateral kidney is normal. 4. Remove and cure of the lithiasis after the treatment of UTI, which is the main etiological factor in this pathology.	1. LE:1, GR: A 2. LE:2, GR: A 3. LE:1, GR: A 4. LE:1, GR: A	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019

<u>Management of urinary stones in specific situations, such as children and pregnant women</u> 1. In pregnant patients with uncomplicated urinary stones, conservative management as a first-line therapy (LE:4, GR: B). 2. In children with uncomplicated ureteral stones ≤10 mm, offer conservative management as a first-line therapy (LE:4, GR: B).	1. LE:4, GR: B 2. LE:4, GR: B	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
Recurrence prevention • Normalization of dietary habits with adequate fluid intake and a balanced diet, adequate physical activity, and maintenance of a normal BMI level are the main strategies for preventing stone disease	LE:1, GR: A	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
• Magnesium as sole therapy is ineffective and is not recommended	LE:4, GR:D	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
• For infectious stones, Fluid intake and diet is generally recommended (LE:2, GR: B). Other treatments, such as short- or long-term antibiotic treatment, methionine or ammonium chloride, restricted intake of urease, or acetohydroxamic acid, might be considered for recurrent or severe infection (LE:1, GR: A). Phytolysi improves general clinical signs and laboratory parameters of blood and urine and reduces the number of relapses of UTI and stone formation (LE:2, GR: B).	(LE:2, GR: B)	THE UAA CLINICAL GUIDELINE FOR URINARY STONE DISEASE, 2019
Surgical management	LE:2, GR: B	THE UAA CLINICAL GUIDELINE FOR

SWL is highly effective in pediatric cases due to its noninvasive nature and higher SFRs compared with adults.		URINARY STONE DISEASE, 2019

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Renal and Ureteric Stones clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Renal and Ureteric Stones report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the May 2020 CHI Renal and Ureteric Stones Report and the corresponding recommendations:

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
Section 1.1 National institute for Health and Care Excellence (**NICE**) guidance for Renal and ureteric stones: assessment and management [**2019**]	N/A*
Section 1.2 Medical management of Kidney stones: American Urological Association (**AUA**) Guideline [Published: 2014, reviewed **2019**]	N/A*
Section 1.3 **British Association of Urological Surgeons** standards for management of acute ureteric colic [**2018**]	N/A*

Section 1.4 **European Association of Urology** Guidelines on Urolithiasis [**2015**]	Section 1.1.1 **European Association of Urology** Guidelines on Urolithiasis [**2023**][5]
Section 1.5 **European Association of Urology** guidelines on Pain Management & Palliative Care [**2014**]	**European Association of Urology** guidelines on Pain Management & Palliative Care [**2015**][6] There is a new download on the website (2015), but it is still an update of March 2013 with no mentioned changes with the same publication history as the 2014 guidelines.
Section 1.6 Prevention of Recurrent Nephrolithiasis: Dietary and Pharmacologic Options Recommended by the **American College of Physicians** (ACP) [**2014**]	N/A*
Section 1.7 **Canadian Urological Association** (CUA) guideline on the evaluation and medical management of the kidney stone patient [**2016**]	Section 1.1.2 **Canadian Urological Association** guideline: Evaluation and medical management of kidney stones {**2022**][7]
Section 1.8 **Canadian Urological Association** Guideline: Management of Ureteral Calculi [**2015**]	Section 1.1.3 **Canadian Urological Association** guideline: Management of ureteral calculi [**2021**][7]

*****: *No updated versions available*

1.1.1 European Association of Urology Guidelines on Urolithiasis [2023]

*Please refer to **Section 1.4** of CHI Renal and Ureteric Stones original clinical guidance.*

The 2023 revised edition of **European Association of Urology Guidelines on Urolithiasis [2023]**[5] introduced a set of recommendations accompanied by a grading scheme, outlined as follows:

Table 2. European Association of Urology Guidelines' grading scheme for recommendations

Grading Scheme for Recommendations	
For each recommendation within the guidelines there is an accompanying online strength rating form which includes an assessment of the benefit to harms ratio and patients' preferences for each recommendation. The strength rating forms draw on the guiding principles of the GRADE methodology but do not purport to be GRADE.	
Each strength-rating form addresses a number of key elements, namely: 1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence; 2. the magnitude of the effect (individual or combined effects); 3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors); 4. the balance between desirable and undesirable outcomes; 5. the impact of patient values and preferences on the intervention; 6. the certainty of those patient values and preferences. These key elements are the basis which panels use to define the strength rating of each recommendation	
Strength of recommendation	The strength of each recommendation is represented by the words '**strong'** or '**weak'**. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and nature and variability of patient values and preferences.

The recommendations listed below are assigned to the grades defined in the preceding table.

The European Association of Urology (EAU) Urolithiasis Guidelines Panel has prepared these guidelines to help urologists assess evidence-based management of stones/calculi in the urinary tract and incorporate recommendations into clinical practice.

Prevalence, etiology, risk of recurrence

Risk groups for stone formation

- High-risk stone formers have been updated to include:
  - Diseases associated with stone formation.
  - Increased levels of vitamin D
  - Environmental factors

- High ambient temperatures
- Chronic lead and cadmium exposure

Risk factors for CKD and ESKD in stone formers

- Female gender
- Overweight
- Frequent urinary tract infection (UTI)
- Struvite stones
- Acquired single kidney.
- Neurogenic bladder
- Previous obstructive nephropathy
- Ileal conduit

Furthermore, some specific kinds of urolithiasis also carry a particular risk of developing CKD/ESKD as shown below.

Risk factors for CKD and renal stones

- Possible risk of CKD: Xanthine stones, Indinavir stones, Distal renal tubular acidosis (incomplete), Primary hyperparathyroidism, eating disorders and laxative abuse, Medullary sponge kidney
- Moderate risk of CKD: Brushite stones, 2,8-Dihydroxyadenine stones, Sarcoidosis, Pyelo-ureteral or ureteral strictures
- High risk of CKD: Cystine stones, Struvite stones, Stones in a single kidney, Distal renal tubular acidosis (complete), Secondary hyperoxaluria (bariatric surgery, inflammatory bowel disease, bowel resection and malabsorptive syndromes), Other forms of nephrocalcinosis (often associated with genetic conditions with hypercalciuria), Anatomical abnormalities of the kidney and urinary tract (for example, horseshoe kidney, ureterocele and vesicoureteral reflux), Neurological bladder.
- Very high risk of CKD: Primary hyperoxaluria „ Autosomal dominant polycystic kidney

Diagnostic evaluation

Diagnostics - metabolism-related

Recommendations for laboratory examinations and stone analysis

- **Urine (Weak Recommendations)**

  Dipstick test of spot urine sample:

- Red cells.
- White cells.
- Nitrite.
- Approximate urine ph.
- Urine microscopy and/or culture.

➢ **Blood (Strong Recommendations)**

Serum blood sample:

- Creatinine
- Uric acid
- Ionized calcium
- sodium;
- potassium;
- blood cell count;
- C-reactive protein. Strong

➢ Perform a coagulation test (partial thromboplastin time and international normalized ratio) if intervention is likely or planned. Strong

➢ Perform stone analysis in first-time 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

<u>Diagnosis in special groups and conditions</u>

Diagnostic imaging during pregnancy

➢ Use ultrasound 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 as a last-line option in pregnant women. Strong

Diagnostic imaging in children

- Complete a metabolic evaluation based on stone analysis in all children. Strong
- Collect stone material for analysis to classify the stone type. Strong
- Perform ultrasound 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 computed tomography) if ultrasound will not provide the required information. Strong

Disease Management

Summary of evidence and recommendations for the management of **renal colic**

- Offer a non-steroidal anti-inflammatory as the first drug of choice, e.g., **metamizole*** (dipyrone); alternatively, paracetamol or, depending on cardiovascular risk factors, **diclofenac****, **indomethacin**, or **ibuprofen*****. Strong
- Offer opioids (**hydromorphine**, **pentazocine** or **tramadol**) as a second choice. Weak
- Offer **renal decompression** or ureteroscopic stone removal in case of analgesic refractory colic pain. Strong

* Maximum single oral dose recommended 1000 mg, total daily dose up to 5000 mg, not recommended in the last three months of pregnancy.

** Affects glomerular filtration rate (GFR) in patients with reduced renal function.

*** Recommended to counteract recurrent pain after ureteral colic

Summary of evidence and recommendations for the management of **sepsis and anuria**

- 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
- 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

3.4.3 Medical expulsive therapy

- Consider α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm. Strong.

3.4.4 Chemolysis

Percutaneous irrigation chemolysis Percutaneous chemolysis is rarely used nowadays, for practical reasons. Percutaneous irrigation chemolysis may be an option for infection-stones and theoretically also for uric acid stones.

Oral chemolysis of uric acid stones:

- Inform the patient how to monitor urine-pH by dipstick and to modify the dosage of **alkalizing 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

3.4.5.1 Summary of evidence and recommendations for SWL

- Ensure correct use of the coupling agent because this is crucial for effective shock wave transportation. 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
- Prescribe antibiotics prior to SWL in the case of infected stones or bacteriuria. Strong

3.4.6.1 Summary of evidence and recommendations for retrograde URS, RIRS and antegrade ureteroscopy

- Use holmium: yttrium-aluminium-garnet (Ho: YAG) laser lithotripsy for (flexible) ureteroscopy (URS). Strong
- Perform stone extraction only under direct endoscopic visualization 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 Ho:YAG laser lithotripsy to facilitate the passage of fragments. Strong
- Use percutaneous antegrade removal of ureteral stones as an alternative when shock wave lithotripsy (SWL) is not indicated or has failed, and when the upper urinary tract is not amenable to retrograde URS. Strong

- Use flexible URS in cases where percutaneous nephrolithotomy or SWL are not an option (even for stones > 2 cm). However, in this case there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed. Strong

3.4.7.1 Summary of evidence and recommendations for endourology techniques for renal stone removal

- Perform pre-procedural imaging, including contrast medium where possible 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 (PNL) procedure, in uncomplicated cases. Strong
- Take a stone culture or urine culture directly from the renal pelvis at time of PNL, if possible. Strong

3.4.8 General recommendations and precautions for stone removal

Antibiotic therapy

As national and regional antibiotic resistance patterns can differ significantly, the choice of antibiotic prophylaxis should be tailored to institutional or regional antimicrobial susceptibility.

- 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

Antithrombotic therapy and stone treatment

Patients who are on anticoagulant treatment should discontinue their anticoagulation medication at the appropriate time before undergoing interventional stone management, as outlined in table 3 below:

Table 3. Suggested Strategy for Antithrombotic Therapy in Stone Removal

Medication/Agent	Bleeding risk of planned procedure	Risk of thromboembolism		
		Low risk	Intermediate risk	High risk
Warfarin Dabigatran Rivaroxaban Apixaban	Low-risk procedure	May be continued	Bridging therapy	Bridging therapy
	High-risk procedure	May be temporarily discontinued at appropriate interval. Bridging therapy is strongly recommended.	Bridging therapy	Bridging therapy
Aspirin	Low-risk procedure	Continue	Continue	Elective surgery: postpone. Non-deferrable surgery: continue.
	High-risk procedure	Discontinue	Elective surgery: postpone. Non-deferrable surgery: continue, if it is possible.	Elective surgery: postpone. Non-deferrable surgery: continue.
Thienopyridine agents (P2Y12 receptor inhibitors)	Low-risk procedure	Discontinue five days before intervention. Resume within 24-72 hours with a loading dose.	Continue	Elective surgery: postpone. Non-deferrable surgery: continue.
	High-risk procedure	Discontinue five days before intervention and resume within 24-72 hours with a loading dose.	Elective surgery: postpone. Non-deferrable surgery: discontinue five days before procedure and resume within 24-72 hours with a loading dose. Bridging therapy -glycoprotein IIb/IIIa inhibitors if aspirin is discontinued.	Elective surgery: postpone. Non-deferrable surgery: discontinue five days before procedure and resume within 24-72 hours, with a loading dose. Bridging therapy -glycoprotein IIb/IIIa inhibitors.

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

- For patients with a bleeding disorder, consulting with an internist is advisable. In cases where a bleeding disorder remains uncorrected, certain high-risk procedures such as SWL, PCNL, percutaneous nephrostomy, laparoscopic surgery, or open surgery can pose an increased risk of hemorrhage or perinephric hematoma.
- After addressing and correcting the underlying coagulopathy, SWL can be considered a feasible and safe option. However, in situations where a bleeding disorder remains uncorrected or antithrombotic therapy continues, URS may

be a preferable alternative to SWL and PCNL due to its lower associated morbidity. It's important to note that while URS is generally safer, a personalized approach for each patient is crucial, and there is still a potential risk of bleeding if antithrombotic therapy is maintained.

- 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 internist. 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

Stone Composition

- Consider the stone composition before deciding on the method of removal, based on patient history, former stone analysis of the patient or Hounsfield unit on unenhanced computed tomography. Strong
- Attempt to dissolve radiolucent stones. Strong

<u>Summary of evidence and guidelines for selection of procedure for active removal of ureteral stones</u>

- Offer α-blockers as MET as one of the treatment options for (distal)ureteral stones ≥ 5 mm. Strong.
- In cases of severe obesity use ureterorenoscopy as first-line therapy for ureteral (and renal) stones. Strong

<u>Summary of evidence and recommendations for the management of renal stones</u>

- Follow-up periodically in cases where renal stones are not treated (initially after six months then yearly evaluating symptoms and stone status either by ultrasound or kidney-ureter bladder radiography. Use computed tomography (CT) when intervention is required. Strong
- 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 CT. Stones with density > 1,000 HU (and with high homogeneity) on non-contrast-enhanced CT are less likely to be disintegrated by shock wave lithotripsy. Strong
- Perform percutaneous nephrolithotomy (PNL) 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 PNL 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 PNL or retrograde intrarenal surgery for the lower pole, even for stones > 1 cm, as the efficacy of SWL is limited (depending on favorable and unfavorable factors for SWL). Strong

Summary of evidence and guidelines for laparoscopy and open surgery

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

Summary of evidence and recommendations for steinstrasse

- 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

- Perform imaging after shock wave lithotripsy, ureteroscopy or percutaneous antegrade ureteroscopy to determine the presence of residual fragments. Strong

Management of specific patient groups

- Treat all uncomplicated cases of urolithiasis in pregnancy conservatively (except when there are clinical indications for intervention). Strong

Summary of evidence and recommendation for the management of stones in patients with 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

Summary of evidence and recommendation for the management of stones in patients with neurogenic bladder

- Take appropriate measures regardless of the treatment provided since in myelomeningocele patients latex allergy is common. Strong

Summary of evidence and guidelines for the management of stones in patients with transplanted kidneys

- Offer patients with transplanted kidneys, any of the contemporary management options, including shock wave lithotripsy, flexible ureteroscopy and percutaneous nephrolithotomy. Weak

Summary of evidence and guidelines for the management of stones in children

- Offer children with ureteral stones **shockwave lithotripsy** as first line option but consider uretero-renoscopy if SWL is not possible and larger distal ureteral stones. Strong
- Offer children with renal pelvic or calyceal stones with a diameter > 20 mm (~300 mm2) percutaneous nephrolithotomy. Strong

Summary of evidence and guidelines for the management of stones in children

- Offer children with single ureteral stones less than 10 mm shock wave lithotripsy (SWL) if localization is possible as a 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 mm2) shock wave lithotripsy. Strong
- Offer children with renal pelvic or calyceal stones with a diameter > 20 mm (~300 mm2) 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 ionizing radiation exposure to patients. Currently, there are no studies estimating the lifetime radiation exposure of stone formers or the subsequent risk of malignancy development. The radiation exposure of endourologists has been extensively studied. Still, there are no studies assessing the risk of radiation induced malignancies in urologists or operating theatre staff members.

Current evidence from atomic bomb patients, retrospective epidemiological data on medical exposure and modelling studies suggest an age and dose dependent risk of secondary malignancy from ionizing radiation.

The International Commission on Radiological Protection (ICRP) recommends a maximum annual occupational exposure of 50mSv. However, the risk of radiation induced malignancy follows a stochastic model having no known safe threshold of

exposure. Taking this into consideration as well as the length of a urologist's career the upper limit of 50mSv is still highly concerning.

Table 4 shows the EAU Urolithiasis guidelines panel recommended protection methods to reduce radiation exposure to patients, surgical, anesthesiologic and nursing staff.

Table 4. 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).

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

METABOLIC EVALUATION AND RECURRENCE PREVENTION

- Advise patients that a generous fluid intake is to be maintained, allowing for a 24-hour urine volume > 2.5 L. Strong
- All stone formers, independent of their individual risk, should follow the preventive measures in table 5 below.

Table 5. General Preventive Measures

Fluid intake (drinking advice)	Fluid amount: 2.5-3.0 L/day
	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 advice to normalise general risk factors	BMI: 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.*

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

The diagnostic algorithms for calcium oxalate stones and uric acid stones were updated as shown in figures 1 and 2.

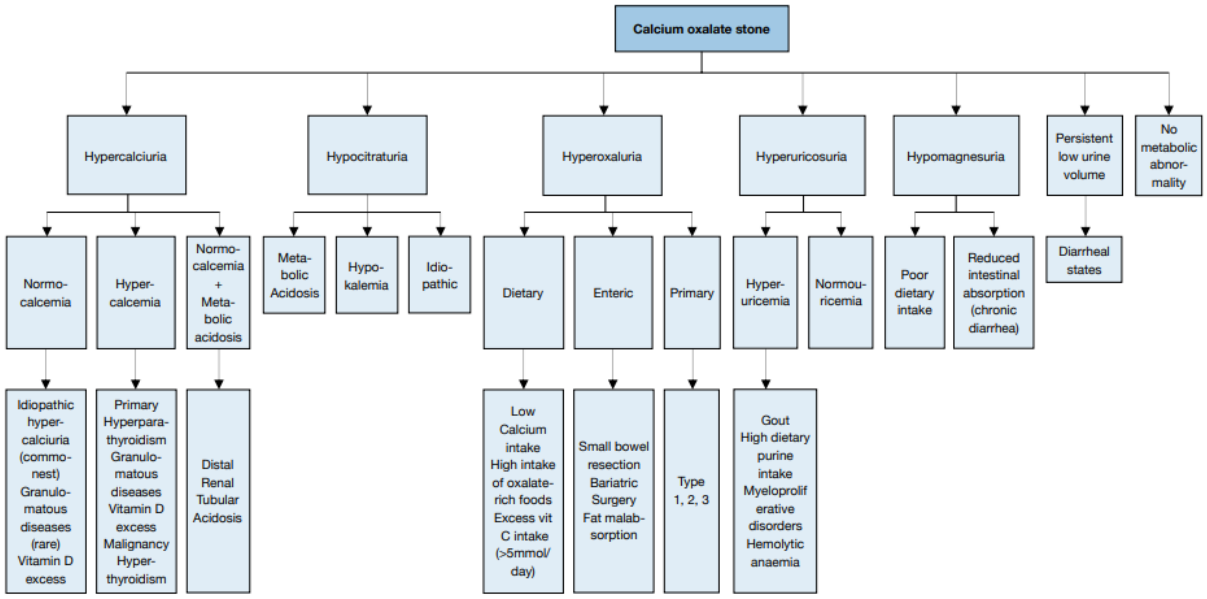

Figure 1. Diagnostic Algorithm for Calcium Oxalate Stones

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

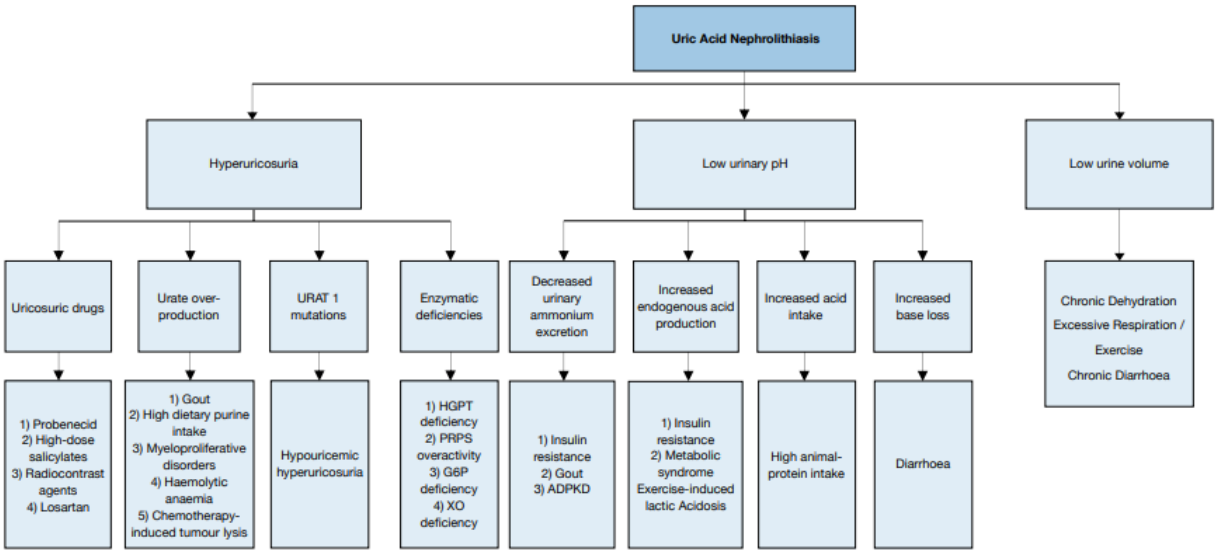

Figure 2. Diagnostic Algorithm for Uric Acid Stones

ADPKD = autosomal dominant polycystic kidney disease; G6P = glucose-6 phosphate dehydrogenase; HGPT = hypoxanthine guanine phosphorybosyl transferase; PRPS = phosphoribosyl-pyrophosphate synthetase superactivity; XO = xanthine oxidase.

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

<u>Summary of evidence and recommendations for pharmacological treatments for patients with specific abnormalities in urine composition (based on 24-hour urine samples)</u>

- Prescribe thiazide or alkaline citrates or both 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 reducing 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

Summary of evidence and recommendation for the management of calcium phosphate stones

- Prescribe thiazide in case of hypercalciuria. Strong

Disorders and diseases related to calcium stones.

A. Patients with primary hyperoxaluria (PH)
   - Prescribe pyridoxine for primary hyperoxaluria type 1. Strong

B. Enteric hyperoxaluria
   - Prescribe alkaline citrates for enteric hyperoxaluria. Weak
   - Advise patients to take calcium supplements with meals. Strong
   - Advise patients to follow a diet with a low fat and oxalate content. Weak

C. Renal tubular acidosis
   - Prescribe alkaline citrates for distal renal tubular acidosis. Strong
   - Prescribe thiazide and alkaline citrates for hypercalciuria. Strong

D. Uric acid- and ammonium urate stones
   - Prescribe alkaline citrates to alkalinize the urine in uric acid stone formers. Strong
   - Prescribe **allopurinol** in hyper uricosuric urate stone formers. Strong

E. Struvite and infection stones
   - 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

F. Cystine stones
   - *Therapeutic measures* Urine dilution Advise patients to increase their **fluid intake** so that 24-hour urine volume exceeds 3 L. Strong
   - *Alkalinization* Prescribe **potassium citrate** 3-10 mmol two or three times daily, to achieve pH > 7.5 for patients with cystine excretion < 3 mmol/day. Strong
   - *Complex formation with cystine* for patients with cystine excretion, > 3 mmol/day, or when other measures are insufficient: prescribe in addition to other measures **tiopronin**, 250-2,000 mg/day. Strong

G. Drug-induced stones

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

- stones formed by crystallized compounds of the drug.
- stones formed due to unfavorable changes in urine composition under drug therapy.

Active compounds crystallizing in urine:

- Allopurinol/oxypurinol
- Amoxicillin/ampicillin
- Ceftriaxone
- Quinolones
- Ephedrine
- Indinavir and other HIV-protease inhibitors
- Magnesium trisilicate
- Sulphonamides
- Triamterene

Substances impairing urine composition:

- Acetazolamide
- Allopurinol
- Aluminium magnesium hydroxide
- Ascorbic acid
- Calcium
- Furosemide
- Laxatives
- Losartan
- Methoxyflurane
- Orlistat
- Vitamin D
- Topiramate
- Zonisamide

H. Matrix Stones

- 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 proposed.

I. Stones of unknown composition

- 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 (ionized calcium or total calcium + albumin), Uric acid. Strong
- Perform a urinalysis: Urine pH profile (measurement after each voiding, minimum four times daily), Dipstick test: leukocytes, erythrocytes, nitrites, protein, urine pH, specific weight, Urine cultures, Microscopy of urinary sediment (morning urine), Cyanide nitroprusside test (cystine exclusion) Further examinations depend on the results of the investigations listed above. Strong

FOLLOW-UP OF URINARY STONES

- Patients with larger residual fragments should be offered further definitive intervention, since intervention rates are high (24-100%). Insufficient data exist for high-risk patients, but current literature dictates that patients who are adherent to targeted medical treatment seem to experience less stone growth or re-growth of residual fragments and may be discharged after 36-48 months of non-progressive disease on imaging.

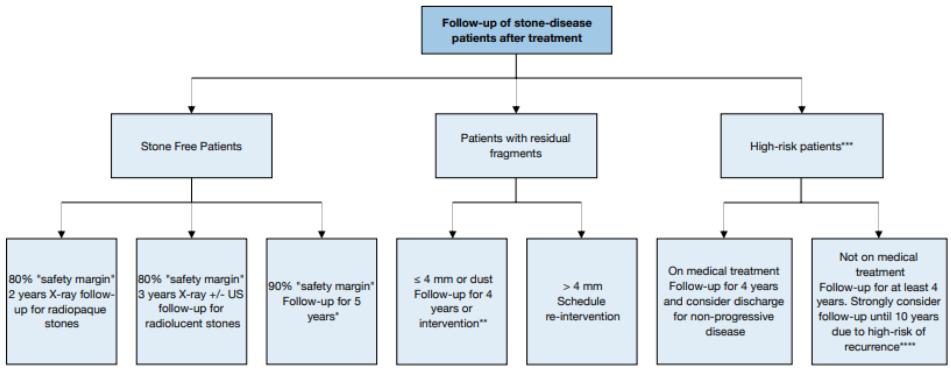

Figure 3. Follow-up Duration of Patients with Urinary Stone After Treatment

* 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

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

- Computed tomography scans should be reserved for symptomatic disease or pre-operative imaging, to avoid extensive radiation exposure.
- Figure 4 shows the Consensus on follow-up frequency and imaging modality to use after treatment.

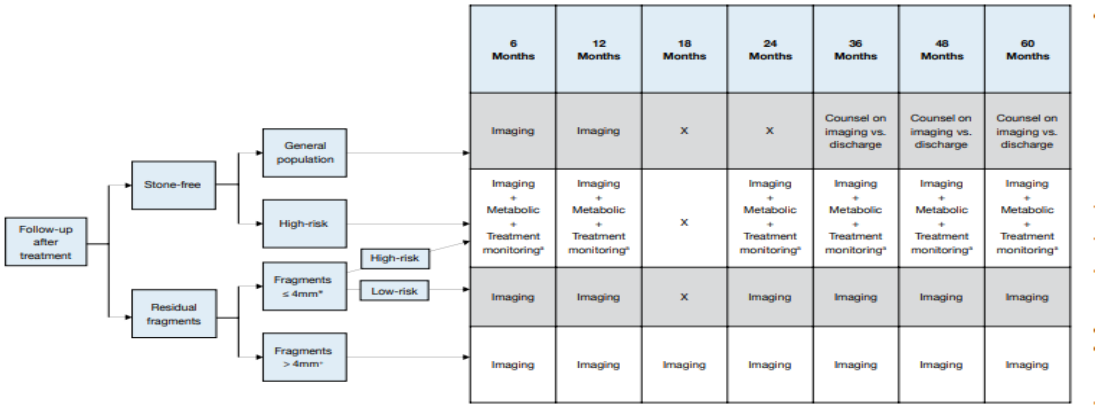

Figure 4. Consensus on Follow-up Frequency and Imaging Modality to Use After Treatment.

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. o Treatment monitoring for side effects, intolerance, and compliance. + Panel recommends reintervention however close follow up may be considered for some patients at high risk for reintervention based on clinicians' preference.

Adapted from Urolithiasis EAU Guidelines; 2023 by A. Skolarikos (Chair), H. Jung, A. Neisius, A. Petřík, B. Somani, T. Tailly, G. Gambaro.

1.1.2 Canadian Urological Association Guideline: Evaluation and Medical Management of Kidney Stones [2022]

*Please refer to **Section 1.7** of CHI Renal and Ureteric Stones original clinical guidance.*

The 2022 revised edition of Canadian Urological Association (CUA)'s guidelines for the evaluation and medical management of kidney stones aims to identify patients at heightened risk of stone recurrence, to outline the required investigations to assess these patients, and to provide contemporary advice on dietary and medical interventions of proven benefit in the Canadian context[8].

This guideline introduced a set of recommendations accompanied by a grading scheme, outlined as follows.

Table 6. CUA Grading Scheme for Recommendations

Grades of recommendations	
A	Consistent level 1 studies
B	Consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies
C	Level 4 studies or extrapolations from level 2 or 3 studies
D	Level 5 evidence or troublingly inconsistent or inconclusive studies of any level
Levels of evidence	
1	Meta-analysis of randomized controlled trials (RCT) or high quality RCTs
2	Lesser quality randomized control trials or prospective comparative studies

3	Case control studies or retrospective studies
4	Case series without the use of comparison or control groups
5	Case report or expert opinion

Importance of stone analysis:

- Stones collected by patients or removed at the time of surgical intervention should be submitted for analysis (LE 3, Grade C recommendation).

General dietary measures:

- When possible, specific dietary assessments and recommendations should be made with the involvement of a registered dietician (LE 3, Grade C recommendation)

Fluid intake: All stone formers should be counselled to achieve a daily urine output of 2.5 liters (LE 2, Grade B recommendation)

Calcium: The goal for dietary calcium intake should be 1000–1200 mg/day, and if calcium supplementation is required, it should be taken at mealtimes (LE 3, Grade B recommendation).

Vitamin D and bone health:

- In calcium stone formers with vitamin D deficiency, repletion is appropriate; however, monitoring of vitamin D levels and hypercalciuria on repeat testing is necessary (LE 2–3, Grade C recommendation).
- Consider bone mineral density (BMD) testing in calcium stone formers with evidence of hypercalciuria and/or distal renal tubular acidosis (dRTA) (LE 2–3, Grade C recommendation).
- Treatment of calcium stone formers with either a thiazide diuretic, alkali citrate, or ideally both has been shown to reduce stone recurrence risk and increase BMD and should be considered in patients with documented low BMD (LE 2–3, Grade C recommendation).

Animal protein: Patients with recurrent calcium or uric acid stones should moderate their animal protein intake and avoid purine-rich foods (LE 2–3, Grade C recommendation)

Sodium: Patients with recurrent calcium nephrolithiasis should limit their sodium intake to 1500 mg daily and not exceed 2300 mg daily (LE 1–2, Grade B recommendation).

Fruits and vegetables: A diet high in fiber, fruits, and vegetables may offer a small protective effect against stone formation (LE 2–3, Grade C recommendation)

Vitamin C: Vitamin C supplementation of more than 1000 mg daily is not recommended due to the associated risk of hyperoxaluria and nephrolithiasis (LE 2–3, Grade C recommendation).

Metabolic syndrome: Stone disease highly correlates with obesity, diabetes, and metabolic syndrome; patients should be counseled that proper management of these conditions may reduce their future stone risk (LE 2–3, Grade D recommendation).

Oxalate

- Patients with hyperoxaluria should minimize their intake of high-oxalate foods. Vitamin B6 supplementation can be considered to lower urinary oxalate levels when dietary modification has been unsuccessful (LE 2–3, Grade C recommendation).
- In patients with enteric hyperoxaluria, elemental calcium or calcium citrate should be given with meals to bind with dietary oxalate to reduce its intestinal absorption (LE 2–3, Grade C recommendation)

Pediatric stone disease

- Dietary factors, such as sodium and purine intake, low urine volume, and climate are thought to play a role in increased stone risk. Obesity may not have the same effect on stone risk in children as it does in adults. Prematurity, medications (e.g., loop diuretics), and genetic factors also increase the risk of pediatric stone disease.
- All children with stone disease should undergo an in-depth medical evaluation and may benefit from a multidisciplinary approach with urology and nephrology (LE 3, Grade D recommendation).
- Hypercalciuria is the most common metabolic abnormality and is often idiopathic; Management includes increasing fluid intake and reducing sodium intake and thiazide diuretics if refractory.
- Hypocitraturia can be idiopathic or associated with other metabolic conditions (e.g., dRTA, high meat protein diet).
- Hyperoxaluria can be primary (increased endogenous production), dietary, or enteric.
- Hyperuricosuria is relatively uncommon, as are uric acid stones. Most children with urinary stones will benefit from a multidisciplinary approach with urology and nephrology involvement.

Specific prophylaxis based on stone composition:

Calcium oxalate or mixed calcium oxalate/calcium phosphate stones

- **Thiazide diuretics** decrease urinary calcium and stone recurrence in calcium stone forming patients (LE 1–3, Grade A–B recommendation).
- **Alkali citrates** are effective in increasing urinary citrate and reducing stone recurrence in calcium stone formers (LE 1–3, Grade A–B recommendation).
- In calcium stone formers, **allopurinol** is effective in reducing stone recurrence in patients with hyperuricemia but does not provide any benefit in patients with normal serum uric acid levels (LE 1–2, Grade B recommendation).

  Empiric treatment with either thiazide diuretics and/or alkali citrates reduces stone recurrence in calcium stone formers with active stone disease who have normal metabolic evaluations (LE 1–3, Grade B recommendation).

Pure calcium phosphate stones

- Patients with incomplete or complete dRTA (distal renal tubular acidosis) should be treated with **alkali citrate** therapy (LE 2–3, Grade C recommendation).

Uric acid stones

- In patients with uric acid stones, **urinary alkalization** to a pH of 6.5 is first-line therapy. Allopurinol may be used as adjunctive therapy in patients with hyperuricemia or hyperuricosuria (LE 1–3, Grade B recommendation).

Cystine stones

- Cystine stone formers should be counselled to target 3 L of urine output daily, restrict their sodium intake, and moderate their protein intake to reduce stone formation. Urinary alkalization of the urine targeting a urine pH of 7–7.5 is the initial therapy. Thiol-binding agents should be considered second-line therapy (LE 3–4, Grade C recommendation).
- If alkalizing agents fail to adequately control cystine stone formation, thiol-binding agents, such as *penicillamine* 1–2 g or *tiopronin* 800–1200 mg in daily divided doses may be used. Side effects from penicillamine can be significant and include fever, arthralgias, rash, dysgeusia, leukopenia, and proteinuria. Where available, tiopronin, should be prioritized due to its better side effect profile (asthenia, gastrointestinal distress, rash, joint aches, and mental status changes) compared to penicillamine.
- For individuals who are at risk of recurrent kidney stones, it is crucial to undergo a thorough medical evaluation and receive personalized guidance on dietary and medication-based prevention.
- The optimal frequency of follow-up and the necessity for repeated metabolic testing vary from person to person and are not clearly outlined in existing literature. Therefore, these aspects should be tailored to each patient's specific needs. If a patient is on a specific medical regimen for stone prevention, it is

advisable to schedule re-evaluations with metabolic testing every six months initially and then annually to assess the effectiveness of the treatment and any potential side effects.

- Periodic imaging is also recommended for individuals who have small, symptom-free kidney stones. In addition to delivering cutting-edge surgical care, urologists should be proficient in offering contemporary metabolic assessments and the best prevention strategies as part of a comprehensive approach to managing kidney stones.

1.1.3 Canadian Urological Association Guideline: Management of Ureteral Calculi [2021] *Please refer to **Section 1.8** of CHI Renal and Ureteric Stones original clinical guidance.*

The aim of this Canadian Urological Association (CUA) guideline document is to provide evidence-based consensus recommendations on various aspects relevant to the management of ureteral stones; the major topic areas included were conservative management, medical expulsive therapy, shockwave lithotripsy (SWL), ureteroscopy (URS), and special clinical scenarios (e.g., pregnancy, pediatrics)[7]. The grading scheme of the recommendations is like the one detailed in table 6 above concerning levels of evidence but no further explanations for strong, weak, and expert.

1. Conservative management of ureteral stones

- Many patients with ureteral stones can initially be managed non-operatively, as spontaneous passage rates are high, particularly for smaller stones (<5 mm). Close follow up is necessary for those being managed conservatively, to ensure spontaneous stone passage or to decide upon the need for timely intervention (level 2, strong recommendation).
- Obstructive pyelonephritis requires early goal-directed therapy, including timely decompression in an antegrade or retrograde fashion, whichever method is most expedient (level 2, strong recommendation)

Imaging

- Ultrasonography with KUB X-ray should be considered the initial modality of choice for acute ureteral stones. Judicious use of CT scans, preferably low dose, provides valuable information for management decisions (level 1, strong recommendation).
- While often omitted, the utility of a KUB X-ray at the time of presentation is very important for future follow up and decision-making regarding definitive treatment options (level 4, expert opinion).

Discharge planning

- The role of MET in promoting spontaneous passage is controversial, but the current literature suggests if there is any benefit, it is for larger (5–10 mm) ureteral (distal) stones. The advantages and disadvantages of MET should be discussed with the patient in a shared decision-making process (level 1, strong recommendation).
- The use of ***opioid-sparing analgesic regimens*** has been shown to be efficacious and opioids for management of renal colic should be minimized; patient education is paramount (level 1, strong recommendation).
- Forced **IV hydration** for the purposes of stone expulsion is not recommended (level 1, moderate recommendation)
- Renal colic follows up: Resolution of symptoms and patient reported stone passage after a bout of renal colic do not always confirm passage of an obstructing ureteral stone. Follow-up imaging is recommended to confirm stone passage (level 3, strong recommendation). The recommended duration of conservative management is unique to each patient, with multiple factors to be considered. Surgical intervention should likely be considered if a patient has not passed an obstructing ureteral stone after 4–6 weeks (level 5, moderate recommendation)

2. Shockwave lithotripsy

- Alpha-blockers (e.g., tamsulosin) should be prescribed after SWL for ureteral stones to improve treatment success rates (level 1, moderate recommendation).
- Ureteral stents do not improve SFRs after SWL and do not reduce the risk of steinstrasse or infection following SWL for most patients (i.e., stones <2 cm) (level 1, moderate recommendation).

3. Ureteroscopy

- Preoperative alpha-blockers may improve intraoperative and postoperative outcomes for patients undergoing URS. However, the optimal duration of preoperative alpha-blocker therapy is still uncertain (level 1, moderate recommendation)

Stenting:

- Routine pre-URS stenting is not necessary but may facilitate UAS insertion and improve SFRs in patients with larger stones (level 2, weak recommendation).
- Routine stenting after uncomplicated URS is likely unnecessary (level 2, strong recommendation) but stent placement after UAS use is warranted (level 3, weak recommendation).

- Stent-related symptoms following URS may be ameliorated with alpha-blocker and/or anticholinergic medications (level 2, moderate recommendation). If access to the ureteral stone is complicated or impossible, placement of a stent and repeat URS is the safest option (level 5, strong recommendation).

4. Comparing treatment outcomes – SWL vs. URS

- SWL produces a similar SFR to URS for ureteral stones, albeit with a higher retreatment rate and lower complication rate (level 1, strong recommendation).
- While local/regional cost models need to be considered, SWL may be a more cost-effective option for ureteric stones (level 4, weak recommendation)

5. Special clinical considerations

Anticoagulation

- SWL and antegrade URS are contraindicated in patients with uncorrected coagulopathies. When the risk of holding antiplatelet or anticoagulants outweighs the benefits, proceeding with URS while a patient is anticoagulated is an acceptable option (level 2, moderate recommendation).

Ureteral stones in children

Imaging

- Ultrasound is the first-line diagnostic modality used in children with suspected ureteral stones. This may be coupled with a KUB X-ray to increase accuracy. Low-dose NCCT may be used in certain situations (level 3, strong recommendation)

Management

- Unless there is an indication to intervene acutely, a trial of passage of at least two weeks is the first-line management in children with urolithiasis <5 mm. A trial of passage with/without MET is recommended for children with smaller (<5 mm) stones (level 2, strong recommendation).
- If urinary drainage is urgently required, ureteral stent insertion is preferred in children due to decreased complications compared to percutaneous decompression. Evidence suggests MET in children may be effective and safe.
- In children with mid to distal urolithiasis, URS has been consistently shown to be superior to SWL and thus is recommended as first-line management.
- For children with proximal ureteral stones, the overall SFRs between SWL and URS have been shown to be similar so both SWL and URS may be considered first-line options.
- SWL is a safe and effective option for ureteral stones in children (level 2, strong recommendation).

- If ureteral dilation is required, passive dilation is preferred (level 4, moderate recommendation).
- It is recommended that ureteroscopes <8 French be used for URS in children (level 4, moderate recommendation).

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Renal and Ureteric Stones report, along with their recommendations.

Table 7. List of Additional Guidelines

Additional Guidelines
Section 1.2.1 Asian Guidelines: The Urological Association of Asia clinical guideline for urinary stone disease [2019][9]
Section 1.2.2 American Guidelines: American Family Physician, Kidney Stones: Treatment and Prevention [2019][10]
Section 1.2.3 Saudi Guidelines: Current evaluation and management of renal and ureteral stones [2001][11]

1.2.1 The Urological Association of Asia clinical Guideline for Urinary Stone Disease [2019]

The Urological Association of Asia, consisting of 25 member associations and one affiliated member since its foundation in 1990, has planned to develop Asian guidelines for all urological fields. The field of stone diseases is the third of its guideline projects. This guideline covers all fields of stone diseases, from etiology to recurrence prevention. Levels of evidence and grades of recommendation for each management were decided according to the relevant strategy (table 8)[9].

Table 8. The Urological Association of Asia's Grading Scheme for Recommendations

Level of Evidence (LE)	Type of Evidence
1	Evidence obtained from multiple large-scale RCTs
2	Evidence obtained from a single RCT or a low-quality RCT
3	Evidence obtained from non-randomized controlled studies
4	Evidence obtained from observational studies

5	Evidence obtained from case studies or expert opinions

For each clinical question (CQ) below, the conclusions drawn from the relevant papers and evidence levels have been judged using a GR, ranging from a strong recommendation (grade A) to not recommended (grade D) as indicated below

Grade of Recommendation (GR)	Nature of Recommendation
A	Highly recommended
B	Recommended
C	No firm evidence for recommendation
C1	May be considered
C2	Not recommended
D	Recommended not to do

LE=level of evidence; RCT=randomized controlled trial; GR=grade of recommendation

Stones classification:

- Stones can be categorized by etiology, chemical/mineral names, size and location (LE:3, GR: A).
- Stone composition is often associated with metabolic and/ or genetic abnormalities (LE:3, GR: B)
- Calcium phosphate stone composition is more likely to be associated with certain medical conditions or medications, such as renal tubular acidosis type 1, primary hyperparathyroidism, medullary sponge kidney and the use of carbonic anhydrase inhibitors (LE:3)

The role of lifestyle in urinary stone disease

- Metabolic syndrome is associated with stone formation (LE:4, GR: B).
- Fluid intake volume has been shown to be inversely related to urolithiasis (LE:1, GR: A).
- Soft drink consumption should be discouraged to reduce new stone formation (LE:2, GR: B)

The role of metabolic components in urinary stone disease

- Calcium intake should not be restricted, as there is an inverse relationship between dietary calcium and stone formation (LE:4, GR: A)

- High sodium intake is associated with an increased risk of stone formation (LE:4, GR: A)
- Increased dietary ascorbic acid intake is associated with hyperoxaluria (LE:3, GR: A).
- A low animal protein diet should be encouraged to reduce the risk of stone formation (LE:2, GR: B).
- Dietary fiber content should be increased, and oxalate content should be restricted in recurrent calcium oxalate stone-forming cases (LE:4, GR: B).

The role of genetic factors in urinary stone disease

- Genetic factors play a significant role in both the development and clinical results of urinary stone disease. It is important for clinicians to consider a patient's genetic heritage, including their family's medical history (LE:3, GR: A).
- A confirmed family history of urinary stone disease is linked to an earlier onset of the condition and an increased likelihood of it recurring (LE:3, GR: B)
- Gene mutations have been documented as contributors to the development of urinary stone disease, not only in rare inherited disorders such as cystine stones but also in cases of idiopathic calcium stones (LE:3).

Diagnosis

- US is the recommended choice of diagnosis for most renal stones and ureteric stones, particularly in children (LE:4, GR: B).
- NCCT has the best sensitivity and specificity for the detection of renal stones, and would be superior to US, for ureteric stones. However, risks of radiation exposure should be considered (LE:4, GR: B).
- If possible, a low-dose NCCT (Non-contrast computed tomography) protocol should be used for patients with BMI
- Medical history is very important to diagnose stone disease. Physicians should ask detailed questions regarding symptoms, including pain, nausea/vomiting, urine color, discomfort on urination and previous stone episodes (LE:1, GR: A)
- Obtaining information on habitual behavior regarding diet and physical activity, family history, age of onset, and previous stone episodes are also helpful to predict the risk and recurrence of stones (LE:1, GR: A)

Children and pregnant patients

- In pregnant women, use US as a first-line imaging modality and MRI as a second-line approach (LE:2, GR: B).
- In pregnant women, reserve low-dose CT as a last-line option (LE:2, GR: B).

- In children, US is a first-line imaging modality, and low-dose CT is an alternative option if US cannot exclude urinary calculi (LE:2, GR: B)

Metabolic Evaluation

- Basic evaluation with serum chemistry and urinary analysis is recommended for all patients presenting with stones (LE:4, GR: B).
- Metabolic evaluation including 24-h urine collection is recommended for patients at high risk of stone recurrence or formation (LE:4, GR: B)
- Stone analysis should be carried out for all first-time stone formers (LE:4, GR:C).
- Stone analysis should be repeated at every attack or intervention for patients with early stone recurrence after intervention, or late recurrence after a stone-free period (LE:3, GR:C).

Medical management

Recommended treatment for ureter stone pain management

- Use **NSAIDs** to control the colic pain (LE:2, GR: A).
- Use **alpha1-blockers** (e.g., tamsulosin) as a treatment option for distal ureteral stones of >5 mm in size (LE:1, GR: A).
- Small stones (ureteral stones of <10 mm in size) are highly likely to pass spontaneously (LE:2, GR: A).
- **Anti-inflammatory drugs**. Inflammatory changes in the ureter provoke a reduction in the rate of spontaneous passage of urinary stones; therefore, anti-inflammatory drugs, such as **NSAIDs** and **steroids**, are generally considered to increase spontaneous passage of urinary stone rates (LE:4, GR: B).
- **Alpha1-blockers** have been recommended for muscle relaxation of the lower ureter and to promote spontaneous ureter stone passage (LE:1, GR: A).
- Use of external physical vibration lithecbole is a treatment option (LE:1, GR: B).
- Tamsulosin significantly facilitated the passage of distal ureteral stones in patients with well-controlled pain, no infections, abnormal anatomy, renal insufficiency, or high-grade obstruction (LE:1)

The role of medical chemolysis in uric acid stone

- Uric acid stones can be dissolved by medical chemolysis using oral alkaline citrate or sodium bicarbonate through alkalinization of urine (LE:2, GR: A).

Medical treatment is appropriate for pyelonephritis accompanying urinary stone

- Active antibiotic treatment and timely drainage of kidney if necessary (LE:1, GR: A).
- Percutaneous nephrostomy and ureteral catheter insertion (LE:2, GR: A).
- Nephrectomy is advocated as the treatment of choice for a kidney that has lost most of its function and the contralateral kidney is normal (LE:1, GR: A).
- Remove and cure of the lithiasis after the treatment of UTI, which is the main etiological factor in this pathology (LE:1, GR: A)

Surgical management

SWL as the first option for patients with renal stones

- While SWL is an option for most renal stones, it should not be applied to patients who are contraindicated for SWL or have abnormal renal anatomy, such as caliceal diverticulum and so on (LE:5, GR: A).
- For renal stones <20 mm, SWL is a recommended first-line treatment for patients (LE:3, GR: A)
- For renal stones > 20 mm or for renal stones presenting less favorable factors, such as high mean stone density or located in calices with poor anatomy, the treatment outcome will be less favorable. Therefore, the pros and cons of each treatment modality should be discussed in detail with the patient before a joint decision on treatment plan can then be taken (LE:5, GR: B).
- SWL is highly effective in pediatric cases due to its noninvasive nature and higher SFRs compared with adults (LE:2, GR: B)

Complications of SWL: In general, the incidence of complications of SWL is low, and the majority are clinically not severe (LE:4, GR: B). The most severe complication, symptomatic hematoma, is detected in <1% of cases (LE:4, GR: B). There is no evidence suggesting SWL has long-term side-effects for patients (LE:4, GR: B)

Complications of lithotripsy by URS

- The overall complication rate after URS is 9–25%. Most complications are minor and do not require intervention (LE:1, GR: A).
- The following complications are the most relevant: sepsis; ureteral stricture; ureteral injury; and UTI. Serious complications, including death and loss of kidney, were sufficiently rare that data were not available to estimate their rates of occurrence (LE:1, GR: A)

Complications of PCNL

- The most common postoperative complications associated with PCNL are fever and bleeding, and urinary leakage (LE:1, GR: B).

Situation(s) that require(s) open/laparoscopic/ robotic-assisted stone surgery.

- Although endoscopic management is a standard approach for most stone removal surgery, open/laparoscopic/ robotic-assisted surgery might be alternatives in selected situations, such as stones requiring complete removal within a single session (infection stones) or stones with urinary tract anatomical abnormalities requiring simultaneous reconstruction (LE:5, GR:C1)

Urinary stones that are eligible for ECIRS: Possible indications requiring combined approaches to the kidney or ureter (LE:2, GR:B): large and complex stones; large renal and concomitant ureteral stones or strictures; ipsilateral medium-to-large renal stones and contralateral small renal stones; diverticular stones with a difficult angle to the infundibulum or a narrow infundibulum; difficulty of angle to approach from the calyx of the percutaneous puncture to other calyces to avoid multiple tracts; impacted UPJ stones with complete obstruction; and ureteral strictures that require an antegrade incisional procedure

Urinary stones are eligible for miniaturized PCNL (Percutaneous Nephrolithotripsy: Miniaturized PCNL can be recommended to treat medium-sized renal stones with promising good surgical outcomes with comparable SFRs and reduced risk of morbidity (LE:1, GR: B)

The algorithm for treatment of adult patients with symptomatic renal stones

- Considering its low stone-free rate for stones >15 mm, RIRS could be carried out for stones up to 20 mm in size (LE:2, GR: B).
- Although there is limited evidence about the choice of appropriate surgical approach for symptomatic renal stones, mini-PCNL with 14–20-Fr tracts are accumulating more evidence regarding the reliability and safety considerations (LE:1, GR: B).
- However, ultramini-, micro-PCNL, or the ancillary use of miniaturized nephoscopes and flexible ureteroreno- or nephoscopes has shown limited evidence based on observational or retrospective studies (LE:4, GR:C1).

The algorithm for treatment of adult patients with ureteral stones

- Expectant management or MET might be considered for non-obstructing ureteral stones without complications (LE:1, GR: B).
- Once the surgery is indicated, URS or SWL are acceptable (LE:2, GR: B).

Management of urinary stones in specific situations, such as children and pregnant women

- In pregnant patients with uncomplicated urinary stones, conservative management as a first-line therapy (LE:4, GR: B).
- URS has emerged as a preferred treatment for pregnant patients who failed conservative management (LE:2, GR: B).
- Placement of a ureteral stent or a percutaneous nephrostomy tube is an alternative option, with frequent stent or tube changes usually being necessary (LE:2, GR:C).
- In children with uncomplicated ureteral stones ≤10 mm, offer conservative management as a first-line therapy (LE:4, GR: B).
- Both SWL and URS are the treatments of choice for children with ureteral stones who are unlikely to pass the stones or who have failed conservative management (LE:2, GR: B). • All three surgical modalities (SWL, URS, PCNL) are acceptable treatment options for children with renal stones (LE:2, GR: B).

Asymptomatic small renal stone management

- Clinicians can offer active surveillance for patients with asymptomatic renal stones due to their low probability for developing symptomatic events requiring interventions (LE:2, GR:C).
- Asymptomatic renal stones should be treated in situations of rapid growth and development of symptoms (LE:2, GR: A).

Recurrence prevention

Hydration

- Hydration is clinically useful for secondary stone prevention by a urine dilutional effect. Urinary stone patients should be advised to achieve a goal of 2–2.5 L of urine daily (LE:2, GR: A)

The components that affect the risk of recurrence are effective for prevention of stone disease.

- Stone type and disease severity determine recurrent risk, including general factors, diseases associated with stone formation, genetically determined stone formation, drug-induced stone formation, anatomical abnormalities associated with stone formation and environmental factors (LE:2, GR: B).
- Normalization of dietary habits with adequate fluid intake and a balanced diet, adequate physical activity, and maintenance of a normal BMI level are the main strategies for preventing stone disease (LE:1, GR: A).

Foods that are effective for preventing the recurrence of calcium stones

- A common-sense approach to diet should be taken; that is, a mixed balanced diet with contributions from all food groups, without any excesses. Fruit and vegetable intake are encouraged; oxalate-rich products, vitamin C and animal protein should be restricted; and excessive intake of calcium should be limited (LE:2, GR: B)

Salt intake and the risk of urinary stones.

- Clinicians should provide patients with calcium stones suitable information about restriction of sodium intake and the necessity of appropriate intake of dietary calcium of 1000–1200 mg per day (LE:2, GR:C1).

Animal protein intake and the risk of urinary stones

- Animal protein lowers urinary pH and increases uric acid in urine. Intake of excessive animal protein is one of the risk factors for excessive uric acid excretion and calcium stone formation (LE:1, GR: B).

Thiazide and urinary stones

- Clinicians might recommend **thiazide medication** with or without potassium citrate to patients with high or relatively high urinary calcium, as well as recurrent calcium stone formers without definite evidence of metabolic abnormalities (LE:1, GR: B)

Citric acid and urinary stones

- Various citrus juices can be utilized to induce citraturia. However, whether this approach can reduce calcium stone recurrence is still under investigation (LE:4, GR:C1).

Magnesium and urinary stones

- Magnesium inhibits calcium oxalate stone formation either in vitro or in vivo, and several studies have shown its protective effects based on urinary parameters. Most clinical trials utilizing magnesium in combination with other stone inhibitors showed promising results. However, magnesium as sole therapy is ineffective and is not recommended (LE:4, GR:D)

Prevention of uric acid stone formation

- Hydration and urine alkalinization are the mainstays of uric acid stone prevention. The latter can be achieved either by diet manipulation or by pharmacotherapy using citrate supplementation (LE:4, GR: B).

Prevention of cystine stones

- In cystine stone formers, prevention with **proper hydration and urine alkalinization** is generally utilized as first-line prevention. If stone recurrence still

occurs, second-line prevention with a cystine-binding agent is offered (LE:4, GR: B).

Prevention of infectious stones

- **Fluid** intake and **diet** is generally recommended (LE:2, GR: B).
- Other treatments, such as short- or long-term **antibiotic** treatment, **methionine** or **ammonium chloride**, restricted intake of urease, or **acetohydroxamic acid**, might be considered for recurrent or severe infection (LE:1, GR: A).
- **Phytolysin** improves general clinical signs and laboratory parameters of blood and urine and reduces the number of relapses of UTI and stone formation (LE:2, GR: B).

Useful imaging test for follow up of urinary stone recurrence.

- Plain radiography, nephrotomography, US, IVU and CT have all been used to evaluate residual fragments (LE:1, GR: A).
- The routine use of CT scan for follow-up studies should be carried out cautiously and only when necessary (LE:1, GR: A).
- Imaging plays a critical role in the initial diagnosis, follow up and urological management of urinary tract stone disease (LE:1, GR: A).

1.2.2 American Academy of Family Physicians (AAFP) Guidance for the Treatment and Prevention of Kidney Stones (2019)

The American Academy of Family Physicians (AAFP) published in 2019 a clinical guidance for the treatment and prevention of kidney stones. The definitions for the evidence rating are outline in table 9[10]:

Table 9. AAFP Evidence Rating

Evidecne Rating	Explanation
A	Consistent, good-quality patient-oriented evidence
B	Inconsistent or limited-quality patient-oriented evidence
C	Consensus, disease-oriented evidence, usual practice, expert opinion, or case series

The main recommendations are detailed below:

Diagnosis:

The initial workup of a patient with suspected kidney stones in the primary care setting should include point-of-care urinalysis to detect blood, because hematuria helps confirm the diagnosis as shown in the figure below:

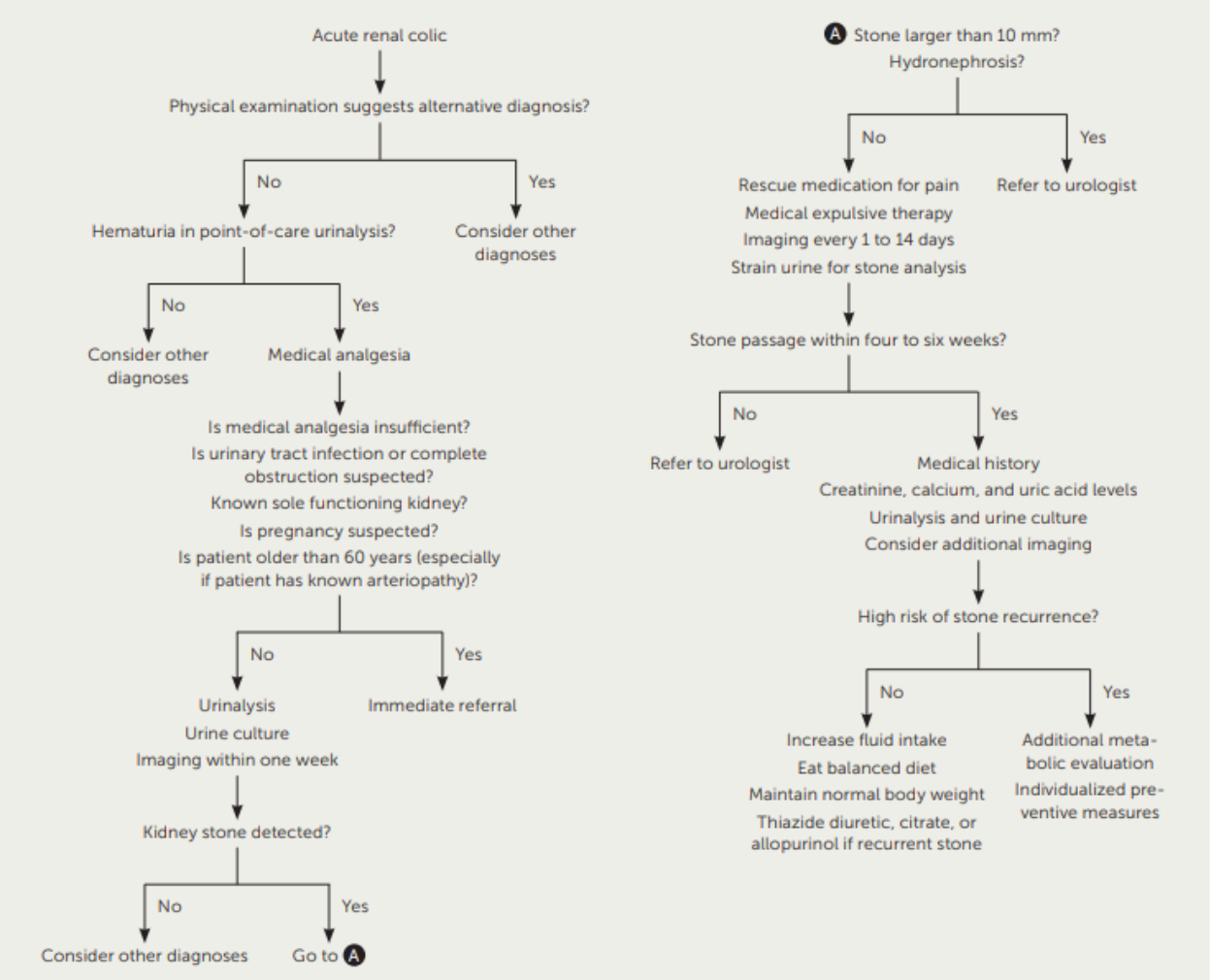

Figure 5. Algorithm for the Diagnosis and Management of Acute Kidney Stones

Adapted from New- American Family Physician by Leonardo Ferreira Fontenelle, MD, MPH, PhD and Thiago Dias Sarti, MD, MPH, PhD - Kidney Stones - Treatment and Prevention 2019

As a best practice according to American College of Emergency Physicians, it is recommended to avoid ordering computed tomography of the abdomen and pelvis in young (younger than 50 years), otherwise healthy emergency department patients with histories of kidney stones or ureterolithiasis who present with symptoms consistent with uncomplicated renal colic.

Acute management

- Nonsteroidal anti-inflammatory drugs (e.g., ***ketorolac***, 30 to 60 mg intramuscularly) are more effective and have fewer adverse effects than opioids.
- If an **opioid** is used, meperidine (Demerol) should be avoided because of the significant risk of nausea and vomiting. Neither scopolamine nor increased fluid intake alleviates renal colic.

Follow-up

- *Conservative management* is indicated if referral is not necessary. Patients should receive pain medication as needed, and follow-up imaging (ultrasonography and possibly plain radiography) should be obtained once within 14 days to monitor evolving stone position and assess for hydronephrosis.
- *Medical expulsive therapy* with **alpha blockers** (e.g., tamsulosin [Flomax], 0.4 mg per day; **doxazosin** [Cardura], 4 mg per day) hastens and increases the likelihood of stone passage, reduces pain, and prevents surgical interventions and hospital admissions.
    - These medications should be offered to patients with distal ureteral stones 5 to 10 mm in diameter. **Tamsulosin** is the most studied medication, but other alpha blockers seem equally effective. Calcium channel blockers (e.g., **nifedipine**) are less effective and may be no more effective than placebo. Coadministration of **oral corticosteroids** or increasing fluid intake does not hasten stone passage or alleviate renal colic.

<u>Further Evaluation in the Subacute Setting</u>

- Patients who have recently been diagnosed with kidney stones should undergo an initial assessment that involves a comprehensive review of their medical history, analysis of serum chemistry, and urinalysis/urine culture.
- For individuals with a heightened risk of stone recurrence, it is advisable to recommend further metabolic testing, such as a 24-hour urine collection to assess parameters like total volume, pH, calcium oxalate, uric acid, citrate, sodium, potassium, and creatinine levels. Additionally, personalized preventive strategies should be discussed. The medical history should encompass a thorough exploration of their stone history (including any family history of kidney stones), dietary habits, current medications, and any medical conditions associated with an increased susceptibility to kidney stones.

Special Considerations

ASYMPTOMATIC KIDNEY STONES

- Conservative management can be considered for adults who are in good health, not suitable candidates for surgery, or pregnant, provided they have access to healthcare and can commit to active surveillance, which includes periodic imaging (initially after six months, followed by annual assessments).
- If symptoms, obstruction, recurrent infections occur, or if the stone increases in size, referral for stone removal should be pursued.

CHILDREN

- Children with kidney stones are more prone to having underlying metabolic, neurological, or congenital abnormalities in their urinary system. They are also at a higher risk of concurrent urinary infections and recurrent stone formation.

PREGNANT WOMEN

- During pregnancy, diagnostic and treatment options are limited due to potential risks to the fetus. Kidney stones may elevate the risk of preterm labor and other complications for both the mother and the baby.

Prevention

- To prevent the recurrence of kidney stones, various measures can be adopted, including lifestyle adjustments, citrate supplementation, and medications.
- For patients with a low risk of stone recurrence after their first episode, lifestyle modifications serve as the primary preventive approach. Citrate supplementation and medications are typically reserved for patients who experience recurrent stones.
- Patients at a high risk of stone recurrence should receive tailored preventive measures based on the results of their metabolic assessment.

CITRATE SUPPLEMENTATION AND MEDICATIONS

- Thiazide diuretics, potassium citrate, or allopurinol should be prescribed after recurrence of calcium stones, even in the absence of metabolic abnormalities. Evidence rating: A
- Thiazide diuretics, allopurinol, and citrate supplementation are effective in preventing calcium stones that recur despite lifestyle modification, even in the absence of hyperuricemia, urinary acidosis, hypocitraturia, or hyperuricosuria.

➢ The effectiveness of thiazide diuretics has been documented only with high dosages (e.g., **hydrochlorothiazide**, 50 mg per day; **chlorthalidone**, 25 to 50 mg

per day; **indapamide**, 2.5 mg per day); lower dosages have fewer adverse effects, but their effectiveness is unknown.

- **Allopurinol** should be started at 100 mg once per day and increased gradually to 100 mg three times per day.

  There is no evidence that combination therapy with thiazide diuretics or alkaline citrates is more effective than monotherapy.

  Allopurinol is one of the mainstays of therapy for patients with calcium stones, but most patients with uric acid stones have acidic urine that requires treatment with alkaline citrates.

- Citrate supplementation is used not only for calcium stones, but also for uric acid (urine pH target 6.0 to 7.5 or greater) and cystine stones (urine pH target of 7.0 to 7.5 or greater).

  The preferred salt for supplementation is ***potassium citrate*** at a target dosage of 5 to 12 g per day. The initial dosage should be 9 g per day, divided into three doses and taken within 30 minutes of meals or a bedtime snack.

- ***Sodium citrate*** is an alternative for citrate supplementation, but the resulting excretion of sodium and calcium may partially counteract the intended effect.

- Unsweetened lemonade is a more palatable and less expensive alternative for citrate supplementation.

- If medication or citrate supplementation is prescribed, serum potassium levels (for patients taking thiazide diuretics or potassium citrate) and liver enzymes (allopurinol) should be monitored to detect potentially serious adverse effects. Potassium levels should be monitored before prescription, within two weeks of prescription, and then every 12 months (earlier if illness occurs or another medication is added).

- There are no recommendations on the frequency of monitoring for hepatotoxicity.

1.2.3 Saudi Medical Journal: Saudi Guidelines: Current Evaluation and Management of Renal and Ureteral Stones [2001]

The Saudi article published by Saudi Medical Journal in 2001 about the current evaluation and management of renal and ureteral stones focuses mainly on clinical presentation, evaluation, and surgical management. These clinical guidelines being over 20 years old, they will not be detailed as part of this report as recommendations may be outdated[11].

Section 2.0 Drug Therapy in Renal and Ureteric Stones

This section comprises four subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, the third one outlines the drugs that have been withdrawn from the market, and the fourth details drugs that have recently received FDA and/or EMA approval but are not currently SFDA-registered.

2.1 Additions

Since May 2020, no additional drugs for the management of renal and ureteric stones have been registered by the SFDA.

2.2 Modifications

Added MD as a prescribing edit for potassium sodium hydrogen citrate; MD: Potassium citrate use should be reviewed and approved by the specialist.

2.3 Delisting

The medications below are no longer SFDA registered[12], therefore, it is advisable to delist the following drugs from CHI formulary. *Please refer to* ***Drugs in the disease - section 2*** *of CHI Renal and Ureteric Stones original clinical guidance*

- Acemetacin
- Tiaprofenic acid
- Metoclopramide hydrochloride, suppository 10 mg
- Penicillamine

2.4 Other Drugs

Two drugs have recently been approved by the FDA for the management of renal and ureteric stones. However, they are not registered by the SFDA as of yet.

2.4.1 Nedosiran (Rivfloza)

The FDA has approved nedosiran (Rivfloza; Novo Nordisk Inc) injection in 80 mg, 120 mg, and 160 mg strengths to lower urinary oxalate levels in children aged 9 years and older and adults with primary hyperoxaluria type 1 (PH1) with relatively preserved kidney function, according to a statement from Novo Nordisk on Monday October 2, 2023[13].

The approval was based on results from the phase 2 PHYOX2 clinical trial (NCT03847909) and data from the ongoing phase 3 PHYOX3 extension study (NCT04042402). In the PHYOX2 study, the data met the primary endpoint, demonstrating that those treated with nedosiran had a marked reduction from baseline in 24-hour urinary oxalate (Uox) excretion from day 90 to day 180. Investigators used the area under the curve (AUC) analysis to measure the percentage change from baseline in 24-hour Uox[13].

2.4.2 Thiola EC (tiopronin)

June 28. 2019, The US Food and Drug Administration (FDA) has approved an enteric-coated delayed-release formulation of tiopronin (*Thiola EC,* Retrophin) for treatment of cystinuria, a rare inherited disorder that causes an increase in cystine levels in the urine, leading to recurring cystine kidney stones[14].

The FDA approved Thiola EC tablets through the 505(b)(2) regulatory pathway, which allows the agency to reference previous findings of safety and efficacy for an already-approved product, as well as review findings from further studies of the product[14].

Section 3.0 Key Recommendations Synthesis

Role of lifestyle, metabolic components in urinary stone disease

- Fluid intake volume has been shown to be inversely related to urolithiasis (LE:1, GR: A). [9]
- A low animal protein diet should be encouraged to reduce the risk of stone formation (LE:2, GR: B).[9]
- Dietary fiber content should be increased, and oxalate content should be restricted in recurrent calcium oxalate stone-forming cases (LE:4, GR: B). [9]
- Increasing fluid intake does not relieve pain or accelerate passage of kidney stones. Evidence rating: B[10]

Diagnosis

- Medical history is very important to diagnose stone disease. Physicians should ask detailed questions regarding symptoms, including pain, nausea/vomiting, urine color, discomfort on urination and previous stone episodes (LE:1, GR: A). [9]
- Obtaining information on habitual behavior regarding diet and physical activity, family history, age of onset, and previous stone episodes are also helpful to predict the risk and recurrence of stones (LE:1, GR: A).[9]

Metabolic Evaluation

- It is advisable to conduct initial assessments, which include serum chemistry and urinary analysis, for all patients who present with stones (LE:4, GR: B).[9]
- Patients who have a high risk of stone recurrence or formation should undergo metabolic evaluations, including a 24-hour urine collection (LE:4, GR: B).[9]
- For individuals experiencing their first occurrence of stones, stone analysis should be performed as a standard procedure (LE:4, GR: C).[9]
- In cases where patients encounter early stone recurrence following an intervention or experience late recurrence after a stone-free period, it is recommended to repeat the stone analysis at each episode or intervention (LE:3, GR: C).[9]
- Patients at low risk of stone recurrence should not routinely undergo extensive metabolic evaluation. Evidence rating: C. [10]

Medical management

Recommended treatment for ureter stone pain management

- Use **NSAIDs** to control the *colic pain* (LE:2, GR: A). [9]
- Use **alpha1-blockers** (e.g., tamsulosin) as a treatment option for *distal ureteral stones of >5 mm in size* (LE:1, GR: A). [9]
- Small stones (ureteral stones of <10 mm in size) are highly likely to pass spontaneously (LE:2, GR: A).[9]
- **Anti-inflammatory drugs**. Inflammatory changes in the ureter provoke a reduction in the rate of spontaneous passage of urinary stones; therefore, anti-inflammatory drugs, such as **NSAIDs** and **steroids**, are generally considered to increase spontaneous passage of urinary stone rates (LE:4, GR: B). [9]
- **Alpha1-blockers** have been recommended for muscle relaxation of the lower ureter and to promote spontaneous ureter stone passage (LE:1, GR: A). [9]
- Use of external physical vibration lithecbole is a treatment option (LE:1, GR: B).[9]
- **Tamsulosin** significantly facilitated the passage of distal ureteral stones in patients with well-controlled pain, no infections, abnormal anatomy, renal insufficiency, or high-grade obstruction (LE:1).[9]

The role of medical chemolysis in uric acid stone

- Uric acid stones can be dissolved by medical chemolysis using **oral alkaline citrate** or **sodium bicarbonate** through alkalinization of urine (LE:2, GR: A).[9]

Medical treatment is appropriate for pyelonephritis accompanying urinary stone.

- **Active antibiotic treatment** and timely drainage of kidney if necessary (LE:1, GR: A). [9]
- Percutaneous nephrostomy and ureteral catheter insertion (LE:2, GR: A). [9]
- Nephrectomy is advocated as the treatment of choice for a kidney that has lost most of its function and the contralateral kidney is normal (LE:1, GR: A).[9]
- Remove and cure of the lithiasis after the treatment of UTI, which is the main etiological factor in this pathology (LE:1, GR: A).[9]

Surgical management

SWL as the first option for patients with renal stones

- While SWL is an option for most renal stones, it should not be applied to patients who are contraindicated for SWL or have abnormal renal anatomy, such as caliceal diverticulum and so on (LE:5, GR: A).[9]

- For renal stones <20 mm, SWL is a recommended first-line treatment for patients (LE:3, GR: A).[9]
- SWL is highly effective in pediatric cases due to its noninvasive nature and higher SFRs compared with adults (LE:2, GR: B).[9]

Complications

- Most complications of lithotripsy by URS are minor and do not require intervention. (LE:1, GR: A).[9]
- The incidence of complications of SWL is low, and the majority are clinically not severe (LE:4, GR: B). [9]
- The most common postoperative complications associated with PCNL are fever and bleeding, and urinary leakage (LE:1, GR: B).[9]

Urinary stones are eligible for miniaturized PCNL (Percutaneous Nephrolithotripsy: Miniaturized PCNL can be recommended to treat medium-sized renal stones with promising good surgical outcomes with comparable SFRs and reduced risk of morbidity (LE:1, GR: B)[9]

For the treatment of adult patients with symptomatic renal stones: Although there is limited evidence about the choice of appropriate surgical approach for symptomatic renal stones, mini-PCNL with 14–20-Fr tracts are accumulating more evidence regarding the reliability and safety considerations (LE:1, GR: B).[9]

For the treatment of adult patients with ureteral stones: Expectant management or MET might be considered for non-obstructing ureteral stones without complications (LE:1, GR: B).[9]

Management of urinary stones in specific situations, such as children and pregnant women

- In pregnant patients with uncomplicated urinary stones, conservative management as a first-line therapy (LE:4, GR: B)[9]
- URS has emerged as a preferred treatment for pregnant patients who failed conservative management (LE:2, GR: B).[9]
- In children with uncomplicated ureteral stones ≤10 mm, offer conservative management as a first-line therapy (LE:4, GR: B).[9]
- Both SWL and URS are the treatments of choice for children with ureteral stones who are unlikely to pass the stones or who have failed conservative management (LE:2, GR: B). • All three surgical modalities (SWL, URS, PCNL) are acceptable treatment options for children with renal stones (LE:2, GR: B)[9]

Recurrence prevention

- Hydration is clinically useful for secondary stone prevention by a urine dilutional effect. Urinary stone patients should be advised to achieve a goal of 2–2.5 L of urine daily (LE:2, GR: A).[9]
- Normalization of dietary habits with adequate fluid intake and a balanced diet, adequate physical activity, and maintenance of a normal BMI level are the main strategies for preventing stone disease (LE:1, GR: A).[9]
- *Fruit and vegetable* intake are encouraged; oxalate-rich products, vitamin C and animal protein should be restricted; and excessive intake of calcium should be limited (LE:2, GR: B).[9]
- Animal protein lowers urinary pH and increases uric acid in urine. Intake of excessive animal protein is one of the risk factors for excessive uric acid excretion and calcium stone formation (LE:1, GR: B).[9]
- Clinicians should provide patients with *calcium stones* suitable information about restriction of sodium intake and the necessity of appropriate intake of dietary calcium of 1000–1200 mg per day (LE:2, GR:C1). [9]
- Clinicians might recommend **thiazide medication** with or without potassium citrate to patients with high or relatively high urinary calcium, as well as recurrent calcium stone formers without definite evidence of metabolic abnormalities (LE:1, GR: B).[9]
- Various citrus juices can be utilized to induce citraturia. However, whether this approach can reduce calcium stone recurrence is still under investigation (LE:4, GR:C1).[9]
- Magnesium as sole therapy is ineffective and is not recommended (LE:4, GR:D).[9]

<u>Prevention based on the stone types</u>:

- Hydration and urine alkalinization are the mainstays of uric acid stone prevention. The latter can be achieved either by diet manipulation or by pharmacotherapy using citrate supplementation (LE:4, GR: B).[9]
- In cystine stone formers, prevention with **proper hydration and urine alkalinization** is generally utilized as first-line prevention. If stone recurrence still occurs, second-line prevention with a cystine-binding agent is offered (LE:4, GR: B).[9]
- For infectious stones, **Fluid** intake and **diet** is generally recommended (LE:2, GR: B). Other treatments, such as short- or long-term **antibiotic** treatment, **methionine** or **ammonium chloride**, restricted intake of urease, or **acetohydroxamic acid**, might be considered for recurrent or severe infection (LE:1, GR: A). **Phytolysin** improves general clinical signs and laboratory

parameters of blood and urine and reduces the number of relapses of UTI and stone formation (LE:2, GR: B).[9]

Useful imaging test for follow up of urinary stone recurrence.

- Plain radiography, nephrotomography, US, IVU and CT have all been used to evaluate residual fragments (LE:1, GR: A).[9]
- The routine use of CT scan for follow-up studies should be carried out cautiously and only when necessary (LE:1, GR: A).[9]
- Imaging plays a critical role in the initial diagnosis, follow up and urological management of urinary tract stone disease (LE:1, GR: A).[9]

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Renal and Ureteric Stones report** and aims to provide recommendations to aid in the management of Renal and Ureteric Stones. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Renal and Ureteric Stones. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses, and sequence of therapy

Appendix B. Renal and Ureteric Stones Scope

Renal and Ureteric Stones Scope

Section	Rationale/Updates
1.1 National institute for Health and Care Excellence (NICE) guidance for Renal and ureteric stones: assessment and management [2019]	N/A
1.2 Medical management of Kidney stones: American Urological Association (AUA) Guideline [Published: 2014, reviewed 2019]	N/A
1.3 British Association of Urological Surgeons standards for management of acute ureteric Colic [2018]	N/A
1.4 European	**European Association of Urology Guidelines on Urolithiasis [2023]**[5]

Association of Urology Guidelines on Urolithiasis [2015]	For each recommendation within the guidelines there is an accompanying online strength rating form which includes an assessment of the benefit to harms ratio and patients' preferences for each recommendation. The strength rating forms draw on the guiding principles of the GRADE methodology but do not purport to be GRADE. Each strength-rating form addresses a number of key elements, namely: 1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence; 2. the magnitude of the effect (individual or combined effects); 3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors); 4. the balance between desirable and undesirable outcomes; 5. the impact of patient values and preferences on the intervention; 6. the certainty of those patient values and preferences. These key elements are the basis which panels use to define the strength rating of each recommendation. The strength of each recommendation is represented by the words 'strong' or 'weak'. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and nature and variability of patient values and preferences. 3.3.2.3 Guidelines for laboratory examinations and stone analysis Recommendations **Urine** Dipstick test of spot urine sample: • red cells; • white cells; • nitrite; • 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

3.4.1.1 Summary of evidence and guidelines for the management of renal colic

- Summary of evidence: Non-steroidal anti-inflammatory drugs are very effective in treating renal colic and are superior to opioids 1b
- Recommendations: Non-steroidal anti-inflammatory drugs are very effective in treating renal colic and are superior to opioids Strong

3.4.1.1 Summary of evidence and guidelines for the management of renal colic

- Offer opiates (hydromorphine, pentazocine or tramadol) as a second choice. Weak

3.4.4.1 Summary of evidence and guidelines for chemolysis

Summary of evidence

- Irrigation chemolysis has been in limited clinical use to dissolve struvite stones. 3
- Uric acid stones can be dissolved based on oral alkalinization of the urine above 7.0. 3
- For obstructing uric acid stones, a combination of oral chemolysis with Tamsulosin is more effective than each substance alone, in particular in stones > 8 mm. 1b

Recommendations (oral chemolysis of uric acid stones)

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

3.4.5.1 Summary of evidence and guidelines for shock wave lithotripsy

Summary of evidence

- Proper acoustic coupling between the cushion of the treatment head and the patient's skin is important. 2
- Careful imaging control of localization of stone contributes to outcome of treatment. 2a
- Careful control of pain during treatment is necessary to limit pain-induced movements and excessive respiratory excursions. 1a
- Antibiotic prophylaxis is recommended in the case of internal stent placement, infected stones or bacteriuria. 1a

3.4.6.1 Summary of evidence and guidelines for retrograde URS, RIRS and antegrade ureteroscopy

Summary of evidence

	• Medical expulsion therapy following Ho:YAG laser lithotripsy accelerates the spontaneous passage of fragments and reduces episodes of colic. 1b • The most effective lithotripsy system for flexible ureteroscopy is the Ho:YAG laser. 2a • Pneumatic and US systems can be used with high disintegration efficacy in rigid URS.2a • Medical expulsion therapy following Ho:YAG laser lithotripsy increases SFRs and reduces colic episodes. 1b • Percutaneous antegrade removal of proximal ureter stones or laparoscopic ureterolithotomy are feasable alternatives to retrograde ureteroscopy in selected cases. 1a Recommendations • Offer MET for patients suffering from stent-related symptoms and after Ho:YAG laser lithotripsy for the passage of fragments. Strong 3.4.8.4 Stone composition Recommendation Consider the stone composition before deciding on the method of removal, based on patient history, former stone analysis of the patient or Hounsfield unit (HU) on unenhanced computed tomography (CT). Strong 3.4.9.4.1 Summary of evidence and guidelines for selection of procedure for active removal of ureteral stones Summary of evidence • Observation is feasible in informed patients who develop no complications (infection, refractory pain, deterioration of renal function). 1a • Compared with SWL, URS was associated with a significantly greater SFR up to four weeks, but the difference was not significant at three months in the included studies. 1a • Ureterorenoscopy was associated with fewer re-treatments and need for secondary procedures, but with a higher need for adjunctive procedures, greater complication rates and longer hospital stay. 1a Recommendations • Offer α-blockers as MET as one of the treatment options for (distal)ureteral stones ≥ 5 mm. Strong • In cases of severe obesity use ureterorenoscopy as first-line therapy for ureteral (and renal) stones. Strong

3.4.10.5 Summary of evidence and guidelines for the management of renal stones

- Consider the stone composition before deciding on the method of removal, based on patient history, former stone analysis of the patient or Hounsfield unit (HU) on unenhanced computed tomography (CT). Stones with density > 1,000 HU (and with high homogeneity) on non-contrast-enhanced CT are less likely to be disintegrated by shock wave lithotripsy. Strong

3.4.11.1 Summary of evidence and guidelines for laparoscopy and open surgery

Recommendation

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

3.4.13.1 Summary of evidence and guideline for management of patients with residual stones

Summary of evidence

- To detect residual fragments after SWL, URS or PNL deferred imaging is more appropriate than immediate imaging post intervention. 3

Recommendation

- Perform imaging after SWL, URS or PNL to determine presence of residual fragments. Strong

3.4.14.4.1 Summary of evidence and guidelines for the management of stones in patients with transplanted kidneys

Summary of evidence

- Shock wave lithotripsy for small calyceal stones is an option with minimal risk of complication, but localization of the stone can be challenging and SFRs are poor.4

3.4.15.6 Summary of evidence and guidelines for the management of stones in children

Summary of evidence

- Ureterenoscopy has become the treatment of choice for larger distal ureteral stones in children. 1a

Recommendation

- Offer children with ureteral stones shockwave lithotripsy as first line option

	but consider uretero-renoscopy if SWL is not possible and larger distal ureteral stones. Strong • Offer children with renal pelvic or calyceal stones with a diameter > 20 mm (~300 mm2) percutaneous nephrolithotomy. Strong 3.4.15.8 Summary of evidence and guidelines for the management of stones in children Summary of evidence • In children, the indications for SWL, URS and PNL are similar to those in adults. 1b Recommendations • Offer children with single ureteral stones less than 10 mm shock wave lithotripsy (SWL) if localization 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 mm2) shock wave lithotripsy. Strong • Offer children with renal pelvic or calyceal stones with a diameter > 20 mm (~300 mm2) percutaneous nephrolithotomy. Strong • Retrograde renal surgery is a feasible alternative for renal stones smaller than 20 mm in all locations. Weak 3.4.3 **NEW ADDED SECTION** Summary of evidence • Medical expulsive therapy seems to be efficacious for treating patients with ureteral stones who are amenable to conservative management. The greatest benefit might be among those with > 5 mm (distal) ureteral stones. 1a • Insufficient data exists to support the use of PDEI-5 or corticosteroids in combination with α-blockers as an accelerating adjunct. 2a • Alpha-blockers increase stone expulsion rates in distal ureteral stones > 5 mm. 1a • A class effect of α-blockers has been demonstrated. 1a Recommendation • Consider α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm. Strong. 3.5 **NEW ADDED SECTION** Radiation exposure and protection during

endourology. The diagnosis and treatment of nephrolithiasis is associated with high levels of ionizing radiation exposure to patients. Currently, there are no studies estimating the lifetime radiation exposure of stone formers or the subsequent risk of malignancy development. The radiation exposure of endourologists has been extensively studied. Still, there are no studies assessing the risk of radiation induced malignancies in urologists or operating theatre staff members.

Current evidence from atomic bomb patients, retrospective epidemiological data on medical exposure and modelling studies suggest an age and dose dependent risk of secondary malignancy from ionizing radiation.

The International Commission on Radiological Protection (ICRP) recommends a maximum annual occupational exposure of 50mSv. However, the risk of radiation induced malignancy follows a stochastic model having no known safe threshold of exposure. Taking this into consideration as well as the length of a urologist's career, the upper limit of 50mSv is still highly concerning.

Table 3.12 shows the EAU Urolithiasis guidelines panel recommended protection methods to reduce radiation exposure to patients, surgical, anaesthesiologic and nursing staff.

Table 3.12 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).

4.6.5.1 Guidelines for the management of tubular acidosis

Prescribe alkaline citrates for distal renal tubular acidosis. Strong

4.7.4 Summary of evidence and guideline for the management of uric acid- and ammonium urate stones

Summary of evidence

- Potassium citrate can be beneficial to alkalinize the urine in urate stone formers.
- Allopurinol can be beneficial in hyperuricosuric urate stone formers.1b

Recommendations

- Prescribe potassium citrate to alkalinize the urine in urate stone formers. Strong
- Prescribe allopurinol in hyperuricosuric urate stone formers. Strong

NEW ADDED SECTION

Follow-up of urinary stones

- Patients with larger residual fragments should be offered further definitive intervention, since intervention rates are high (24-100%). Insufficient data exist for high-risk patients, but current literature dictates that patients who are adherent to targeted medical treatment seem to experience less stone growth or re-growth of residual fragments and may be discharged after 36-48 months of non-progressive disease on imaging (Figure 5.1)

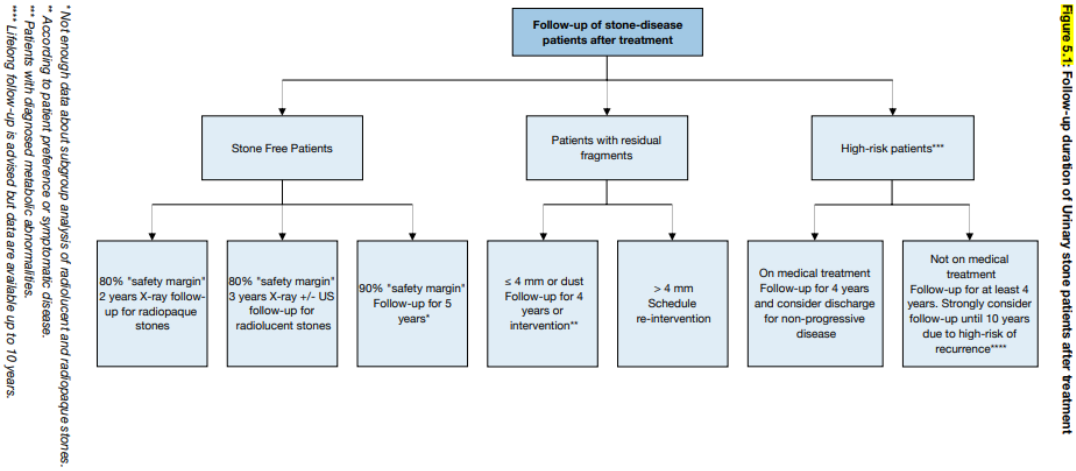

Figure 5.1: Follow-up duration of Urinary stone patients after treatment

- Computed tomography scan should be reserved for symptomatic disease

or pre-operative imaging, to avoid extensive radiation exposure (Figure 5.2)

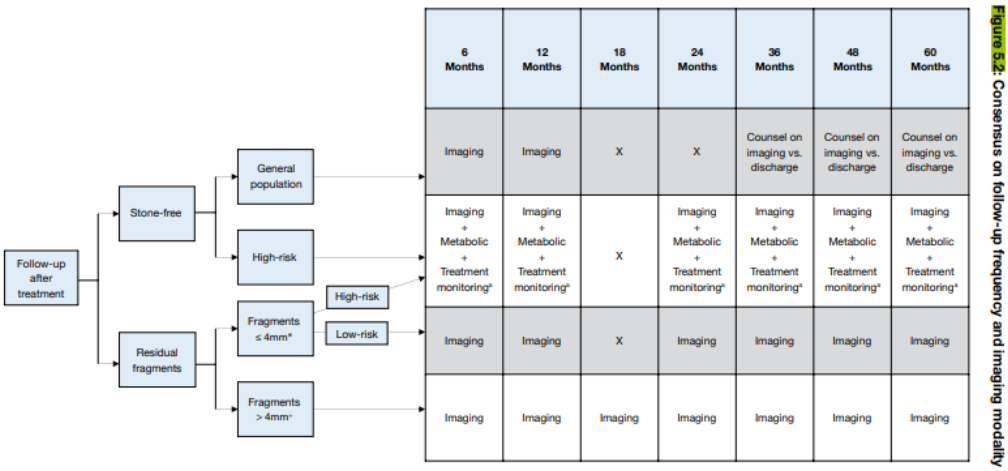

Figure 5.2: Consensus on follow-up frequency and imaging modality to use after treatment

Table 3.3: High-risk stone formers has been updated to include:
Diseases associated with stone formation
Increased levels of vitamin D
Environmental factors
High ambient temperatures
Chronic lead and cadmium exposure

Additional information have been added to the following tables:
Table 3.4 Risk factors for CKD and ESKD in stone formers

Risk factors for CKD/ESKD in stone formers
Female gender
Overweight
Frequent urinary tract infection (UTI)
Struvite stones
Acquired single kidney
Neurogenic bladder
Previous obstructive nephropathy
Ileal conduit

Furthermore, some specific kinds of urolithiasis also carry a particular risk of

	developing CKD/ESKD as shown below. Table 3.5 Risk factors for CKD and renal stones **Risk of chronic kidney disease and renal stones** • Possible risk of CKD ■ Xanthine stones ■ Indinavir stones ■ Distal renal tubular acidosis (incomplete) ■ Primary hyperparathyroidism ■ Eating disorders and laxative abuse ■ Medullary sponge kidney • Moderate risk of CKD ■ Brushite stones ■ 2,8-Dihydroxyadenine stones ■ Sarcoidosis ■ Pyelo-ureteral or ureteral strictures • High risk of CKD ■ Cystine stones ■ Struvite stones ■ Stones in a single kidney ■ Distal renal tubular acidosis (complete) ■ Secondary hyperoxaluria (bariatric surgery, inflammatory bowel disease, bowel resection and malabsorptive syndromes) ■ Other forms of nephrocalcinosis (often associated with genetic conditions with hypercalciuria) ■ Anatomical abnormalities of the kidney and urinary tract (for example, horseshoe kidney, ureterocele and vesicoureteral reflux) ■ Neurological bladder • Very high risk of CKD ■ Primary hyperoxaluria ■ Autosomal dominant polycystic kidney ➢ The Bladder Stones guidelines, previously a separate document, have been integrated into this version. ➢ Four new algorithms have also been added: **Updated figures** Figure 4.2: Diagnostic algorithm for calcium oxalate stones Figure 4.6: Diagnostic algorithm for uric acid stones Figure 5.1: Follow-up duration of urinary stone patients after treatments Figure 5.2: Consensus on follow-up frequency and imaging modality to use after treatment
1.5 European Association of Urology guidelines on Pain Management & Palliative Care [2014]	**European Association of Urology guidelines on Pain Management & Palliative Care [2015]**[6] There is a new download on the website (2015) but it is still an update of March 2013 with no mentioned changes with the same publication history as the 2014 guidelines.

1.6 Prevention of Recurrent Nephrolithiasis: Dietary and Pharmacologic Options Recommended by the American college of physicians (ACP) [2014]	N/A
1.7 Canadian Urological Association (CUA) guideline on the evaluation and medical management of the kidney stone patient [2016]	**Canadian Urological Association guideline: Evaluation and medical management of kidney stones {2022]**[8] • Management recommendations were modified if needed based on the most current literature since the last guideline was published in 2016. Added the general dietary measures that should be followed: • When possible, specific dietary assessments and recommendations should be made with the involvement of a registered dietician (LE 3, Grade C recommendation) • Animal protein: Patients with recurrent calcium or uric acid stones should moderate their animal protein intake and avoid purine-rich foods (LE 2–3, Grade C recommendation) • Fruits and vegetables: A diet high in fiber, fruits, and vegetables may offer a small protective effect against stone formation (LE 2–3, Grade C recommendation) • Vitamin C: Vitamin C supplementation of more than 1000 mg daily is not recommended due to the associated risk of hyperoxaluria and nephrolithiasis (LE 2–3, Grade C recommendation). • Vitamin D and bone health monitoring and the goal of calcium levels. ➢ Added the part related to pediatric stone disease. ➢ Updates to the Specific prophylaxis based on stone composition: • Calcium oxalate or mixed calcium oxalate/calcium phosphate stones: In calcium stone formers, **allopurinol** is effective in reducing stone recurrence in patients with hyperuricemia but does not provide any benefit in patients with normal serum uric acid levels (LE 1–2, Grade B recommendation). - Empiric treatment with either thiazide diuretics and/or alkali citrates reduces stone recurrence in calcium stone formers with active stone

	disease who have normal metabolic evaluations (LE 1–3, Grade B recommendation). • <u>Pure calcium phosphate stones</u> Patients with incomplete or complete dRTA (distal renal tubular acidosis) should be treated with **alkali citrate** therapy (LE 2–3, Grade C recommendation). ➢ Added the part related to follow-up. • The optimal frequency of follow-up and the necessity for repeated metabolic testing vary from person to person and are not clearly outlined in existing literature. Therefore, these aspects should be tailored to each patient's specific needs. If a patient is on a specific medical regimen for stone prevention, it is advisable to schedule re-evaluations with metabolic testing <u>every six months</u> initially and then annually to assess the effectiveness of the treatment and any potential side effects. • Periodic imaging is also recommended for individuals who have small, symptom-free kidney stones. In addition to delivering cutting-edge surgical care, urologists should be proficient in offering contemporary metabolic assessments and the best prevention strategies as part of a comprehensive approach to managing kidney stones. Figures for Specific dietary and medical treatments for patients with different type of stones
1.8 Canadian Urological Association Guideline: Management of Ureteral Calculi [2015]	**Canadian Urological Association guideline: Management of ureteral calculi [2021]**[7] Updated recommendation on conservative management of ureteral stones and the role MET • Many patients with ureteral stones can initially be managed non-operatively, as spontaneous passage rates are high, particularly for smaller stones (<5 mm). Close follow up is necessary for those being managed conservatively, to ensure spontaneous stone passage or to decide upon the need for timely intervention (level 2, strong recommendation). • The role of MET in promoting spontaneous passage is controversial, but the current literature suggests if there is any benefit, it is for larger (5–10 mm) ureteral (distal) stones. The advantages and disadvantages of MET should be discussed with the patient in a shared decision-making process (level 1, strong recommendation). Addition of the recommendation about the use of opioid-sparing analgesic regimens when planning discharge Updated recommendations on the use of alpha-blockers • **Alpha-blockers** (e.g., tamsulosin) should be prescribed after SWL for

	ureteral stones to improve treatment success rates (level 1, moderate recommendation). • Preoperative alpha-blockers may improve intraoperative and postoperative outcomes for patients undergoing URS. However, the optimal duration of preoperative alpha-blocker therapy is still uncertain (level 1, moderate recommendation) Updated recommendations related to stenting: • Routine pre-URS stenting is not necessary but may facilitate UAS insertion and improve SFRs in patients with larger stones (level 2, weak recommendation). • Routine stenting after uncomplicated URS is likely unnecessary (level 2, strong recommendation) but stent placement after UAS use is warranted (level 3, weak recommendation). • Stent-related symptoms following URS may be ameliorated with alpha-blocker and/or anticholinergic medications (level 2, moderate recommendation). If access to the ureteral stone is complicated or impossible, placement of a stent and repeat URS is the safest option (level 5, strong recommendation). Addition of a part comparing treatment outcomes (SWL vs URS) • SWL produces a similar SFR to URS for ureteral stones, albeit with a higher retreatment rate and lower complication rate (level 1, strong recommendation). • While local/regional cost models need to be considered, SWL may be a more cost-effective option for ureteric stones (level 4, weak recommendation) Addition of recommendations related to special clinical considerations (Ureteral stones in children and updated recommendations related to pregnancy) • First-line diagnostic testing for stones in pregnancy is in the US, but low-dose NCCT or MRI (without gadolinium in the first trimester) can also be used (level 3, strong recommendation). • Obstructing ureteral stones in pregnancy can be managed conservatively in the absence of suspected or confirmed urinary infection (level 3, moderate recommendation). • In pregnant patients presenting with signs of sepsis, antibiotics and urinary decompression via a NT or ureteral stent are of primary importance; consultation with the obstetrics team is recommended. URS with laser lithotripsy is safe in pregnancy; however, SWL is contraindicated (level 2, strong recommendation).

N/A	**The Urological Association of Asia clinical guideline for urinary stone disease [2019]** **Etiology** <u>Stones Classifications</u> • Stones can be categorized by etiology, chemical/mineral names, size and location (LE:3, GR:A). • The most common stone type is calcium oxalate, and some Asian countries have a higher percentage of this chemical composition compared to other parts of the world (LE:3, GR:A). • Stone composition is often associated with metabolic and/ or genetic abnormalities (LE:3, GR:B) • Calcium phosphate stone composition is more likely to be associated with certain medical conditions or medications, such as renal tubular acidosis type 1, primary hyperparathyroidism, medullary sponge kidney and the use of carbonic anhydrase inhibitors (LE:3) <u>The role of lifestyle in urinary stone disease</u> • Metabolic syndrome is associated with stone formation (LE:4, GR: B). • Fluid intake volume has been shown to be inversely related to urolithiasis (LE:1, GR: A). • Soft drink consumption should be discouraged to reduce new stone formation (LE:2, GR: B) <u>The role of metabolic components in urinary stone disease</u> • Calcium intake should not be restricted, as there is an inverse relationship between dietary calcium and stone formation (LE:4, GR: A) • High sodium intake is associated with an increased risk of stone formation (LE:4, GR: A) • Increased dietary ascorbic acid intake is associated with hyperoxaluria (LE:3, GR: A). • A low animal protein diet should be encouraged to reduce the risk of stone formation (LE:2, GR: B). • Dietary fiber content should be increased, and oxalate content should be restricted in recurrent calcium oxalate stone-forming cases (LE:4, GR: B). <u>The role of genetic factors in urinary stone disease</u> • Genetic factors are highly associated with both the pathogenesis and clinical outcomes of urinary stone disease. Clinicians should consider patients' genetic background, including family history (LE:3, GR: A). • Positive family history of urinary stone disease is associated with earlier disease onset and a higher risk of recurrence (LE:3, GR: B).

	• The association of gene mutations with disease development has been reported for both rare inherited disorders causing urolithiasis, as represented by cystine stones, and idiopathic calcium stones (LE:3). **Diagnosis** <u>Imaging</u> • Plain radiography is not sensitive and specific enough for the diagnosis of stone (LE:4, GR: B). • US is the recommended choice of diagnosis for most renal stones and ureteric stones, particularly in children (LE:4, GR: B). • NCCT has the best sensitivity and specificity for the detection of renal stones, and would be superior to US, for ureteric stones. However, risks of radiation exposure should be considered (LE:4, GR: B). • If possible, a low-dose NCCT (Non-contrast computed tomography) protocol should be used for patients with BMI • Medical history is very important to diagnose stone disease. Physicians should ask detailed questions regarding symptoms, including pain, nausea/vomiting, urine color, discomfort on urination and previous stone episodes (LE:1, GR: A) • Obtaining information on habitual behavior regarding diet and physical activity, family history, age of onset, and previous stone episodes are also helpful to predict the risk and recurrence of stones (LE:1, GR: A) <u>Children and pregnant patients</u> • In pregnant women, use US as a first-line imaging modality and MRI as a second-line approach (LE:2, GR: B). • In pregnant women, reserve low-dose CT as a last-line option (LE:2, GR: B). • In children, US is a first-line imaging modality, and low-dose CT is an alternative option if US cannot exclude urinary calculi (LE:2, GR: B) **Metabolic Evaluation** • Basic evaluation with serum chemistry and urinary analysis is recommended for all patients presenting with stones (LE:4, GR: B). • Metabolic evaluation including 24-h urine collection is recommended for patients at high risk of stone recurrence or formation (LE:4, GR: B) • Stone analysis should be carried out for all first-time stone formers (LE:4, GR:C). • Stone analysis should be repeated at every attack or intervention for patients with early stone recurrence after intervention, or late recurrence after a stone-free period (LE:3, GR:C). **Medical management**

	Recommended treatment for ureter stone pain management? • Use **NSAIDs** to control the colic pain (LE:2, GR: A). • Use **alpha1-blockers** (e.g., tamsulosin) as a treatment option for distal ureteral stones of >5 mm in size (LE:1, GR: A). • Small stones (ureteral stones of <10 mm in size) are highly likely to pass spontaneously (LE:2, GR: A). • Stone location at the lower ureter with no obstruction (LE:4, GR: B). • **Anti-inflammatory drugs**. Inflammatory changes in the ureter provoke a reduction in the rate of spontaneous passage of urinary stones; therefore, anti-inflammatory drugs, such as **NSAIDs** and **steroids**, are generally considered to increase spontaneous passage of urinary stone rates (LE:4, GR: B). • **Alpha1-blockers** have been recommended for muscle relaxation of the lower ureter and to promote spontaneous ureter stone passage (LE:1, GR: A). • Use of external physical vibration lithecbole is a treatment option (LE:1, GR: B • Tamsulosin significantly facilitated the passage of distal ureteral stones in patients with well-controlled pain, no infections, abnormal anatomy, renal insufficiency, or high-grade obstruction (LE:1) The role of medical chemolysis in uric acid stone • Uric acid stones can be dissolved by medical chemolysis using oral alkaline citrate or sodium bicarbonate through alkalinization of urine (LE:2, GR: A). Medical treatment is appropriate for pyelonephritis accompanying urinary stone. • Active antibiotic treatment and timely drainage of kidney if necessary (LE:1, GR: A). • Percutaneous nephrostomy and ureteral catheter insertion (LE:2, GR: A). • Nephrectomy is advocated as the treatment of choice for a kidney that has lost most of its function and the contralateral kidney is normal (LE:1, GR: A). • Remove and cure of the lithiasis after the treatment of UTI, which is the main etiological factor in this pathology (LE:1, GR: A) **Surgical management** SWL as the first option for patients with renal stones • While SWL is an option for most renal stones, it should not be applied to patients who are contraindicated for SWL or have abnormal renal anatomy, such as caliceal diverticulum and so on (LE:5, GR: A). • For renal stones <20 mm, SWL is a recommended firstline treatment for

	patients (LE:3, GR:A) • For renal stones > 20 mm or for renal stones presenting less favorable factors, such as high mean stone density or located in calices with poor anatomy, the treatment outcome will be less favorable. Therefore, the pros and cons of each treatment modality should be discussed in detail with the patient before a joint decision on treatment plan can then be taken (LE:5, GR: B). • SWL is highly effective in pediatric cases due to its noninvasive nature and higher SFRs compared with adults (LE:2, GR: B) <u>Complications of SWL</u> • In general, the incidence of complications of SWL is low, and the majority are clinically not severe (LE:4, GR: B). • The most severe complication, symptomatic hematoma, is detected in <1% of cases (LE:4, GR: B). • There is no evidence suggesting SWL has long-term side-effects for patients (LE:4, GR: B) <u>Complications of lithotripsy by URS</u> • The overall complication rate after URS is 9–25%. Most complications are minor and do not require intervention (LE:1, GR: A). • The following complications are the most relevant (Table 5): sepsis; ureteral stricture; ureteral injury; and UTI. • Serious complications, including death and loss of kidney, were sufficiently rare that data were not available to estimate their rates of occurrence (LE:1, GR: A) <u>The complications of PCNL</u> • The complication rate of PCNL was reported to range from 10% to 20%, and most of the complications were not severe (LE:1, GR: A). • The most common postoperative complications associated with PCNL are fever and bleeding, and urinary leakage (LE:1, GR: B). • The complication rates of standard PCNL and minimally invasive PCNL were reported to be 15.9% and 12.8%, respectively. Minimally invasive PCNL is at least as efficacious and safe as standard PCNL (LE:1, GR: A) <u>Situation(s) that require(s) open/laparoscopic/ robotic-assisted stone surgery.</u> • Although endoscopic management is a standard approach for most stone removal surgery, open/laparoscopic/ robotic-assisted surgery might be alternatives in selected situations, such as stones requiring complete removal within a single session (infection stones) or stones with urinary tract anatomical abnormalities requiring simultaneous reconstruction (LE:5, GR:C1) <u>Urinary stones that are eligible for ECIRS</u>

	• Possible indications requiring combined approaches to the kidney or ureter (LE:2, GR:B): large and complex stones; large renal and concomitant ureteral stones or strictures; ipsilateral medium-to-large renal stones and contralateral small renal stones; diverticular stones with a difficult angle to the infundibulum or a narrow infundibulum; difficulty of angle to approach from the calyx of the percutaneous puncture to other calyces to avoid multiple tracts; impacted UPJ stones with complete obstruction; and ureteral strictures that require an antegrade incisional procedure. <u>Urinary stones are eligible for miniaturized PCNL (Percutaneous Nephrolithotripsy</u> • Miniaturized PCNL can be recommended to treat medium-sized renal stones with promising good surgical outcomes with comparable SFRs and reduced risk of morbidity (LE:1, GR: B) <u>The algorithm for treatment of adult patients with symptomatic renal stones</u> • Considering its low stone-free rate for stones >15 mm, RIRS could be carried out for stones up to 20 mm in size (LE:2, GR: B). • Although there is limited evidence about the choice of appropriate surgical approach for symptomatic renal stones, mini-PCNL with 14–20-Fr tracts are accumulating more evidence regarding the reliability and safety considerations (LE:1, GR: B). • However, ultramini-, micro-PCNL, or the ancillary use of miniaturized nephoscopes and flexible ureteroreno- or nephoscopes has shown limited evidence based on observational or retrospective studies (LE:4, GR:C1). <u>The algorithm for treatment of adult patients with ureteral stones</u> • Expectant management or MET might be considered for non-obstructing ureteral stones without complications (LE:1, GR: B). • Once the surgery is indicated, URS or SWL are acceptable (LE:2, GR: B). <u>Management of urinary stones in specific situations, such as children and pregnant women</u> • In pregnant patients with uncomplicated urinary stones, conservative management as a first-line therapy (LE:4, GR: B). • URS has emerged as a preferred treatment for pregnant patients who failed conservative management (LE:2, GR: B). • Placement of a ureteral stent or a percutaneous nephrostomy tube is an alternative option, with frequent stent or tube changes usually being necessary (LE:2, GR:C). • In children with uncomplicated ureteral stones ≤10 mm, offer conservative management as a first-line therapy (LE:4, GR: B). • Both SWL and URS are the treatments of choice for children with ureteral

	stones who are unlikely to pass the stones or who have failed conservative management (LE:2, GR: B). • All three surgical modalities (SWL, URS, PCNL) are acceptable treatment options for children with renal stones (LE:2, GR: B). Asymptomatic small renal stone management • Clinicians can offer active surveillance for patients with asymptomatic renal stones due to their low probability for developing symptomatic events requiring interventions (LE:2, GR:C). • Asymptomatic renal stones should be treated in situations of rapid growth and development of symptoms (LE:2, GR: A). **Recurrence prevention** Hydration • Hydration is clinically useful for secondary stone prevention by a urine dilutional effect. Urinary stone patients should be advised to achieve a goal of 2–2.5 L of urine daily (LE:2, GR: A) The components that affect the risk of recurrence are effective for prevention of stone disease. • Stone type and disease severity determine recurrent risk, including general factors, diseases associated with stone formation, genetically determined stone formation, drug-induced stone formation, anatomical abnormalities associated with stone formation and environmental factors (LE:2, GR: B). • Normalization of dietary habits with adequate fluid intake and a balanced diet, adequate physical activity, and maintenance of a normal BMI level are the main strategies for preventing stone disease (LE:1, GR: A). Foods that are effective for preventing the recurrence of calcium stones • A common-sense approach to diet should be taken; that is, a mixed balanced diet with contributions from all food groups, without any excesses. Fruit and vegetable intake are encouraged; oxalate-rich products, vitamin C and animal protein should be restricted; and excessive intake of calcium should be limited (LE:2, GR: B) Salt intake and the risk of urinary stones. • Clinicians should provide patients with calcium stones suitable information about restriction of sodium intake and the necessity of appropriate intake of dietary calcium of 1000–1200 mg per day (LE:2, GR:C1). Animal protein intake and the risk of urinary stones • Animal protein lowers urinary pH and increases uric acid in urine. Intake of excessive animal protein is one of the risk factors for excessive uric acid excretion and calcium stone formation (LE:1, GR: B). Thiazide and urinary stones

	• Clinicians might recommend **thiazide medication** with or without potassium citrate to patients with high or relatively high urinary calcium, as well as recurrent calcium stone formers without definite evidence of metabolic abnormalities (LE:1, GR: B) Citric acid and urinary stones • Various citrus juices can be utilized to induce citraturia. However, whether this approach can reduce calcium stone recurrence is still under investigation (LE:4, GR:C1). Magnesium and urinary stones • Magnesium inhibits calcium oxalate stone formation either in vitro or in vivo, and several studies have shown its protective effects based on urinary parameters. Most clinical trials utilizing magnesium in combination with other stone inhibitors showed promising results. However, magnesium as sole therapy is ineffective and is not recommended (LE:4, GR:D) Prevention of uric acid stone formation • Hydration and urine alkalinization are the mainstays of uric acid stone prevention. The latter can be achieved either by diet manipulation or by pharmacotherapy using citrate supplementation (LE:4, GR: B). Prevention of cystine stones • In cystine stone formers, prevention with **proper hydration and urine alkalinization** is generally utilized as first-line prevention. If stone recurrence still occurs, second-line prevention with a cystine-binding agent is offered (LE:4, GR: B). Prevention of infectious stones • **Fluid** intake and **diet** is generally recommended (LE:2, GR: B). • Other treatments, such as short- or long-term **antibiotic** treatment, **methionine** or **ammonium chloride**, restricted intake of urease, or **acetohydroxamic acid**, might be considered for recurrent or severe infection (LE:1, GR: A). • **Phytolysin** improves general clinical signs and laboratory parameters of blood and urine and reduces the number of relapses of UTI and stone formation (LE:2, GR: B). Useful imaging test for follow up of urinary stone recurrence. • Plain radiography, nephrotomography, US, IVU and CT have all been used to evaluate residual fragments (LE:1, GR: A). • The routine use of CT scan for follow-up studies should be carried out cautiously and only when necessary (LE:1, GR: A). • Imaging plays a critical role in the initial diagnosis, follow up and urological management of urinary tract stone disease (LE:1, GR: A).

N/A	**American Family Physician, Kidney Stones: Treatment and Prevention 2019** **Diagnosis**: (figure 1) As a best practice according to American College of Emergency Physicians, it is recommended to avoid ordering computed tomography of the abdomen and pelvis in young (younger than 50 years), otherwise healthy emergency department patients with histories of kidney stones or ureterolithiasis who present with symptoms consistent with uncomplicated renal colic. **Acute management** • Nonsteroidal anti-inflammatory drugs (e.g., ***ketorolac***, 30 to 60 mg intramuscularly) are more effective and have fewer adverse effects than opioids. • If an **opioid** is used, meperidine (Demerol) should be avoided because of the significant risk of nausea and vomiting. Neither scopolamine nor increased fluid intake alleviates renal colic. **Follow-up** • *Conservative management* is indicated if referral is not necessary. Patients should receive pain medication as needed, and follow-up imaging (ultrasonography and possibly plain radiography) should be obtained once within 14 days to monitor evolving stone position and assess for hydronephrosis. • *Medical expulsive therapy* with **alpha blockers** (e.g., tamsulosin [Flomax], 0.4 mg per day; **doxazosin** [Cardura], 4 mg per day) hastens and increases the likelihood of stone passage, reduces pain, and prevents surgical interventions and hospital admissions. ➢ These medications should be offered to patients with distal ureteral stones 5 to 10 mm in diameter. **Tamsulosin** is the most studied medication, but other alpha blockers seem equally effective. Calcium channel blockers (e.g., **nifedipine**) are less effective and may be no more effective than placebo. Coadministration of **oral corticosteroids** or increasing fluid intake does not hasten stone passage or alleviate renal colic. Further Evaluation in the Subacute Setting ➢ Patients with newly diagnosed kidney stones should receive a basic evaluation consisting of a detailed medical history, serum chemistry, and urinalysis/urine culture. ➢ Patients at risk of stone recurrence should be referred for additional metabolic testing (e.g., 24-hour urine collection for total volume, pH, and calcium oxalate, uric acid, citrate, sodium, potassium, and creatinine levels) and individualized preventive measures. The medical history should review the stone history (including family

history of kidney stones), diet, current medications, and conditions associated with an increased risk of kidney stones.

Special Considerations

- **ASYMPTOMATIC KIDNEY STONES**
  - Conservative management is an option for adults who are healthy, unfit for surgery, or pregnant, and who have access to health care and can adhere to active surveillance (imaging after six months, then annually)
  - The patient should be referred for stone removal if symptoms, obstruction, or recurrent infection develops, or if the stone grows larger.
- **CHILDREN**
  - Children with kidney stones are more likely to have a metabolic, neurologic, or congenital urinary system structural abnormality; to have concomitant urinary infection; and to have recurrent stones.
- **PREGNANT WOMEN**
  - Diagnostic and treatment options are limited during pregnancy because of risk to the fetus.5 Kidney stones may increase the risk of preterm labor and other maternal and fetal complications.

Prevention

- Measures to prevent recurrence of kidney stones include lifestyle modifications, citrate supplementation, and medications.
- Lifestyle modifications are the cornerstone of prevention after a first kidney stone in patients with *low risk of recurrence*, whereas citrate supplementation and medications are reserved for patients with *recurrent stones.*
- Patients at high risk of stone recurrence should receive preventive measures tailored to the results of the metabolic assessment.

CITRATE SUPPLEMENTATION AND MEDICATIONS

- Thiazide diuretics, potassium citrate, or allopurinol should be prescribed after recurrence of calcium stones, even in the absence of metabolic abnormalities. Evidence rating: A
- Thiazide diuretics, allopurinol, and citrate supplementation are effective in preventing calcium stones that recur despite lifestyle modification, even in the absence of hyperuricemia, urinary acidosis, hypocitraturia, or hyperuricosuria.
- The effectiveness of thiazide diuretics has been documented only with high dosages (e.g., **hydrochlorothiazide**, 50 mg per day; **chlorthalidone**, 25 to 50 mg per day; **indapamide**, 2.5 mg per day); lower dosages have fewer

	adverse effects, but their effectiveness is unknown. ➢ **Allopurinol** should be started at 100 mg once per day and increased gradually to 100 mg three times per day. There is no evidence that combination therapy with thiazide diuretics or alkaline citrates is more effective than monotherapy. Allopurinol is one of the mainstays of therapy for patients with calcium stones, but most patients with uric acid stones have acidic urine that requires treatment with alkaline citrates. ➢ Citrate supplementation is used not only for calcium stones, but also for uric acid (urine pH target 6.0 to 7.5 or greater) and cystine stones (urine pH target of 7.0 to 7.5 or greater). The preferred salt for supplementation is ***potassium citrate*** at a target dosage of 5 to 12 g per day. The initial dosage should be 9 g per day, divided into three doses and taken within 30 minutes of meals or a bedtime snack. ➢ ***Sodium citrate*** is an alternative for citrate supplementation, but the resulting excretion of sodium and calcium may partially counteract the intended effect. ➢ Unsweetened lemonade is a more palatable and less expensive alternative for citrate supplementation. ➢ If medication or citrate supplementation is prescribed, serum potassium levels (for patients taking thiazide diuretics or potassium citrate) and liver enzymes (allopurinol) should be monitored to detect potentially serious adverse effects. Potassium levels should be monitored before prescription, within two weeks of prescription, and then every 12 months (earlier if illness occurs or another medication is added). ➢ There are no recommendations on the frequency of monitoring for hepatotoxicity.
N/A	**Saudi Medical Journal: Saudi Guidelines: Current evaluation and management of renal and ureteral stones [2001]**[11] Saudi guidelines: There are no updated Saudi guidelines for the management of renal and ureteric stones. The last published guidelines by Saudi Medical Journal were in 2001 about the Current evaluation and management of renal and ureteral stones with a focus mainly on clinical presentation, evaluation, and surgical management so it will not be detailed in this report.

Appendix C. MeSH Terms PubMed

C.1 PubMed Search for Renal and Ureteric Stones:

Query	Filters	Search Details	Results
((((((((((Renal stones[MeSH Terms]) OR (Renal stones[Title/Abstract])) OR (Calculi, Kidney[Title/Abstract])) OR (Calculus, Kidney[Title/Abstract])) OR (Kidney Calculus[Title/Abstract])) OR (Nephrolith[Title/Abstract])) OR (Renal Calculus[Title/Abstract])) OR (Kidney Stones[Title/Abstract])) OR (Kidney Stone[Title/Abstract])) OR (Stone, Kidney[Title/Abstract])) OR (Stones, Kidney[Title/Abstract])) OR (Renal Calculi[Title/Abstract])) OR (Calculi, Renal[Title/Abstract])) OR (Calculus, Renal[Title/Abstract])	Guideline, in the last 5 years	("kidney calculi"[MeSH Terms] OR "renal stones"[Title/Abstract] OR "calculi kidney"[Title/Abstract] OR "calculus kidney"[Title/Abstract] OR "kidney calculus"[Title/Abstract] OR "Nephrolith"[Title/Abstract] OR "renal calculus"[Title/Abstract] OR "kidney stones"[Title/Abstract] OR "kidney stone"[Title/Abstract] OR "stone kidney"[Title/Abstract] OR "stones kidney"[Title/Abstract] OR "renal calculi"[Title/Abstract] OR "calculi renal"[Title/Abstract] OR "calculus renal"[Title/Abstract])	3

Appendix D. Treatment Algorithms

1. Calcium Oxalate or Combined Calcium Oxalate/Calcium phosphate stone

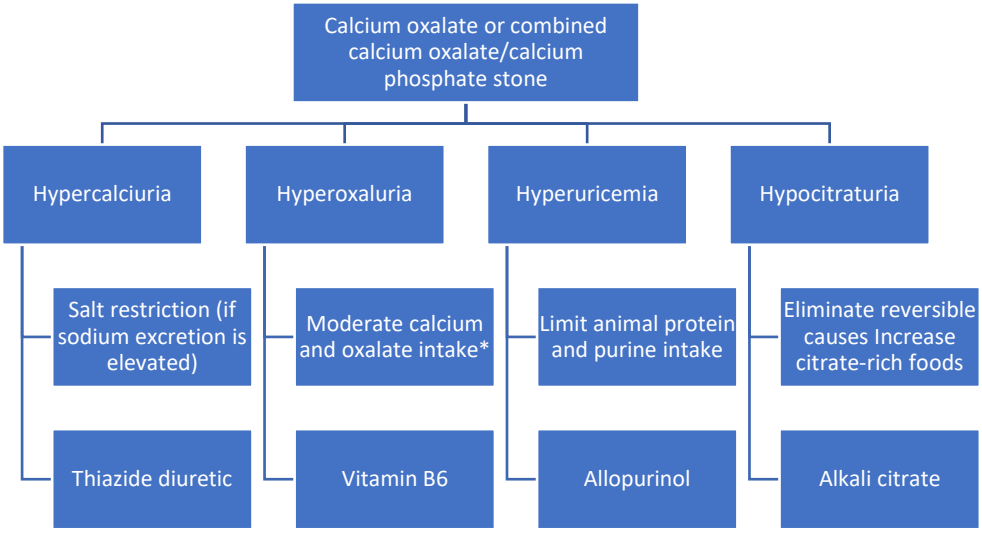

Figure 6. Specific dietary and medical treatments for patients with calcium oxalate or mixed calcium oxalate/calcium phosphate stones. *Calcium intake 1200 mg daily (with meals), moderation of foods high in oxalate, pair oxalate and calcium-containing foods.

2. Uric Acid stones

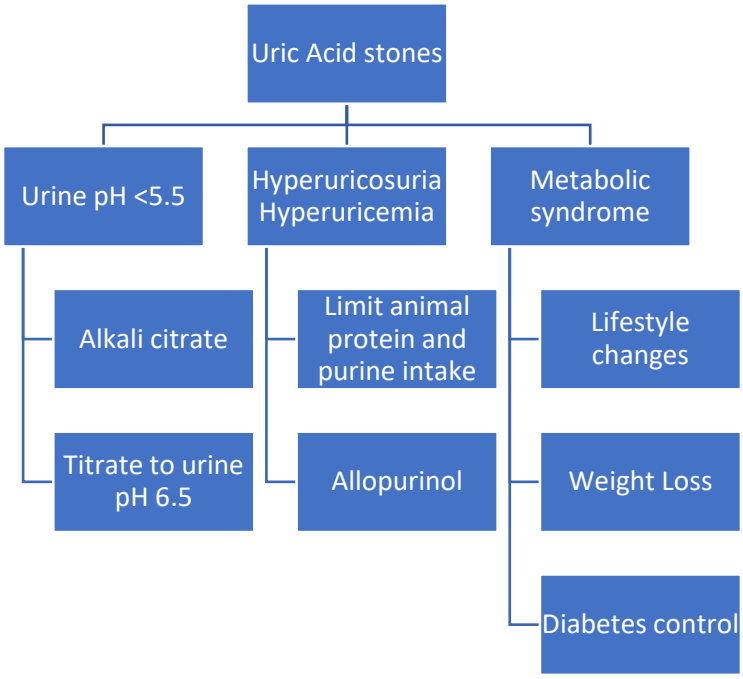

Figure 7. Specific dietary and medical treatments for patients with uric acid stones.

3. Cystine Stone

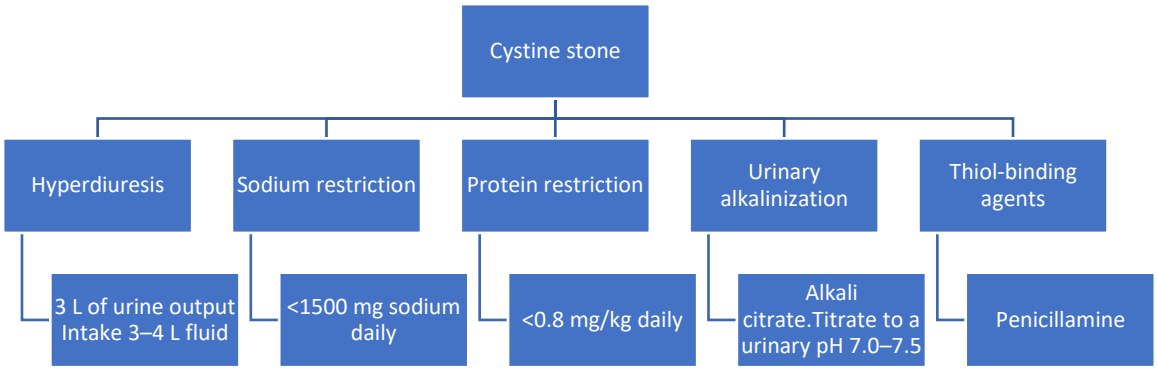

Figure 8. Specific dietary and medical treatments for patients with cystine stones.