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Guideline of guidelines: kidney stones

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Several professional organizations have developed evidence-based guidelines for the initial evaluation, diagnostic imaging selection, symptomatic management, surgical treatment, medical therapy, and prevention of recurrence for both ureteric and renal stones. The purpose of this article is to summarize these guidelines with reference to the strength of evidence. All guidelines endorse an initial evaluation to exclude concomitant infection, imaging with a non-contrast computed tomography scan, and consideration of medical expulsive therapy or surgical intervention depending on stone size and location. Recommends for metabolic evaluation vary by guideline, but all endorse increasing fluid intake to reduce the risk of recurrence.

Keywords

nephrolithiasis, kidney calculi, ureteric calculi, guideline

Introduction

Acute flank pain is a common presenting symptom, with nephrolithiasis being the most frequent aetiology [1]. The overall prevalence of kidney stones in the USA is estimated at 9% [2]. Given the prevalence of this disease, it is frequently encountered in routine clinical practice. Therefore, several professional organisations have developed evidence-based guidelines for the evaluation, surgical management and medical treatment of patients with nephrolithiasis. The purpose of this article is to summarise these guidelines with reference to the strength of evidence.

The AUA grades the strength of evidence from A to C: grade A evidence is obtained from well-conducted randomised controlled trials (RCT) or very strong observational studies; grade B evidence is from less well-conducted RCT or strong observational studies; and grade C evidence is from weak observational studies [3]. From this evidence, the AUA generates statements. These statements are categorised as a 'Standard' (directive statement based on grade A or B evidence), a 'Recommendation' (directive statement based on grade C evidence), an 'Option' (non-directive statement based on grade A, B or C evidence), a 'Clinical Principle' (widely agreed upon by clinicians, with or without evidence) or an 'Expert Opinion' (consensus of the panel without evidence) [3]. Similarly, the European Association of Urology (EAU) makes 'Recommendations' [4]. These Recommendations are graded from A (high) to C (low), based on the underlying evidence [4].

Although the guidelines to be discussed do provide an evidence-based framework for the appropriate care of patients with nephrolithiasis, it should be noted that the guidelines do have shortcomings. New literature is constantly released, but guidelines are not updated in real time and can therefore become outdated. For example, the AUA guidelines on the management of staghorn calculi and ureteric calculi were last updated in 2005 and 2007, respectively [5,6]. Updates are likely forthcoming, but until then newer data may need to be consulted. The EAU guidelines on urolithiasis referenced below were updated recently, in 2014, and thus provide a more contemporary review of the literature [4]. Another limitation of the guidelines is that the recommendations do not cover all clinical scenarios and are not applicable to every patient. Therefore, treatment decisions should still be made for the individual patient by relying on the clinical expertise of the provider to utilise the recommendations appropriately.

Evaluation of Nephrolithiasis

Initial Evaluation

Only the EAU has recommendations on the initial evaluation of acute flank pain, which were recently updated in 2014 [1,4]. The EAU recommends an initial evaluation with a history and a physical examination with special attention to body temperature. All patients should have a urine dipstick test with microscopy, serum chemistry, complete blood count and, if febrile, a urine culture and a C-reactive protein test (grade A). If an intervention is planned, coagulation studies should also be performed (grade A).

Diagnostic Imaging

The AUA, in 2012, outlined imaging protocols for patients with suspected or confirmed ureteric stones [7]. These

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protocols were designed to maximise the effectiveness of imaging and support clinical decision-making [7].

At initial presentation, non-contrast CT (NCCT) is the preferred imaging method, due to its high sensitivity and specificity for the detection of ureteric stones (grade A). For patients with a body mass index (BMI) of <30 kg/m^2, a low-dose protocol (defined as <4 mSv) is recommended, as this limits the dose of ionizing radiation while maintaining diagnostic accuracy. However, this is not recommended for patients with a BMI of >30 kg/m^2, in which a full-dose NCCT is recommended. In patients with a stone not visible on the NCCT scout image, a formal kidneys–ureters–bladder (KUB) X-ray should be obtained. If the stone is visible on the NCCT scout or KUB, then it can be followed with KUB alone.

Specific populations also deserve special mention. In patients with a known history of radio-opaque stone formation, an alternative diagnostic imaging strategy is a combination of formal renal ultrasonography (US) and KUB (grade C). In children, the first-line imaging method is US, with low-dose NCCT reserved if the initial US is negative and the clinical suspicion for stone disease remains high. For the pregnant patient in the first trimester, US is the initial method, with MRI without contrast reserved for second-line use. Similarly, in the second and third trimesters, US is again the preferred imaging strategy but low-dose NCCT may be used (also supported by the American College of Obstetricians and Gynecologists guidelines [8]) if clinically indicated.

Similar to the AUA, the EAU recommends NCCT (low-dose protocol, if BMI <30 kg/m^2) to confirm a stone in a patient presenting with acute flank pain (grade A) [4]. This is further qualified for patients presenting with fever (>38 °C) or a known solitary kidney, in which case imaging should be performed urgently (grade B) [1]. The EAU also identifies special populations and, in accordance with the AUA, recommends US during pregnancy (grade A) and in children, with KUB or NCCT reserved if US does not provide the required information (grade B) [4].

The American College of Radiology developed 'Appropriateness Criteria' to assist referring providers in selecting the correct imaging method [9]. These guidelines were considered in the development of the AUA imaging protocols [7]. Therefore, their recommendations largely parallel those of the AUA, with a low-dose NCCT usually appropriate (highest recommendation) for patients with acute-onset flank pain and, in those with recurrent symptoms, either a low-dose NCCT or US are usually appropriate (highest recommendation) [9].

It should be noted that none of the guidelines address point-of-care US, which is increasingly used in the emergency department setting for suspected renal colic [10]. A recent RCT of patients presenting to the emergency department with suspected renal colic were randomised to point-of-care US, radiology-performed US or CT [11]. This study demonstrated lower radiation dosages for the US groups, but no differences in adverse events, return visits or diagnostic accuracy between the three imaging methods [11]. As the data on point-of-care US in acute renal colic continues to mature, it will likely need to be incorporated into future guidelines. At the present time, it appears to be a safe alternative imaging method to screen for nephrolithiasis in patients presenting to the emergency department with acute flank pain.

Symptomatic Control and Observation/Medical Expulsive Therapy

For symptomatic control, the EAU recommends a trial of a NSAID (grade A), with narcotics reserved as second-line therapy (grade C) [1,4]. It is also recommended to provide supportive care with i.v. hydration and anti-emetics. If symptomatic relief is achieved and the patient does not meet additional criteria for urgent intervention, such as urinary infection with obstruction, urosepsis, renal insufficiency, obstruction of a solitary/transplant kidney, bilateral obstruction or obstruction in pregnancy, then a trial of observation or medical expulsive therapy is appropriate [1].

In 2007, the AUA and EAU released a joint, internationally endorsed guideline on the management of ureteric calculi [6]. An option for the management of newly diagnosed ureteric stones <10 mm, is observation with periodic evaluation (grade A). As an adjunct to observation, patients may also be offered medical expulsive therapy, with daily α-blockers to facilitate stone passage and decrease renal colic episodes (grade A). Patients offered this approach should be counselled about the side-effects of the medication and that this indication is off-label (grade A). According to the EAU, periodic evaluation should be conducted, with interval imaging between 1 and 14 days to monitor stone position and assess for hydronephrosis (grade A) [4]. Although the EAU does not provide recommendations on imaging method, the AUA does have an algorithm based on whether the stone is radio-opaque [7]. Known radio-opaque stones can be monitored with a combination of KUB and US, while non-radio-opaque stones can be monitored with a low-dose NCCT (grade C). Indications for active stone removal during a period of observation include increasing symptoms, persistent obstruction/hydronephrosis, failure of progression/passage, increasing stone size and/or loss of renal function [6,7].

The EAU does provide recommendations on the observation of kidney stones, particularly in the calyces [4]. Asymptomatic calyceal stones can be monitored with active surveillance, consisting of an annual evaluation of symptoms and stone characteristics with imaging (grade C).

Intervention should be considered at the end of a 2–3-year surveillance period (grade C), or earlier if there is demonstrated growth, obstruction, infection and/or acute or chronic pain (grade A).

Surgical Treatment

Emergent Indications

An obstructing stone in the presence of infected urine is a urological emergency. Both the AUA and the EAU recommend urgent decompression of the collecting system with either percutaneous drainage or ureteric stenting, as both are equally effective (grade A) [4,6]. The EAU recommends obtaining urine for culture, starting antibiotics and then re-evaluating the antibiotic regimen based on culture data (grade A) [4]. Both groups endorse delaying definitive treatment of the stone until the sepsis has resolved and the infection has cleared (grade A).

Ureteric Stones

The two primary methods for active ureteric stone treatment include extracorporeal shockwave lithotripsy (SWL) and ureteroscopy (URS). According to the joint AUA and EAU guidelines on the management of ureteric calculi, both are accepted first-line therapies (Recommendation) [4,6]. Patients should be counselled on both treatment options, including the inherent risks and benefits of each (Standard). Differences do exist between the two, based on stone location and size. For proximal ureteric stones of <10 mm, SWL had a higher stone-free rate (SFR), while URS had a higher SFR for proximal ureteric stones of >10 mm. For mid-ureteric stones, URS appears to have a superior SFR but, given the small number of patients, when stratified by stone size there was a lack of significance [6]. URS is superior to SWL for distal ureteric stones, independent of stone size. Routine placement of a ureteric stent before SWL is not indicated (Recommendation) and after uncomplicated URS it is optional (Option). Alternative procedures, such as percutaneous antegrade URS and laparoscopic or open surgery, may be considered in selected cases.

Specific populations have unique considerations for the management of ureteric stones. In children, both SWL and URS are effective but patient size and anatomy should be considered, with preference given to SWL, due to its non-invasive nature (Option) [6]. In pregnancy, conservative management should be the first-line therapy (grade A) [4]. When intervention is necessary placement of a ureteric stent or percutaneous nephrostomy tube are options, with URS as a reasonable alternative.

After active ureteric stone removal, the AUA imaging protocols recommend obtaining interval imaging to document clearance/fragmentation of the stone, resolution of hydronephrosis and detection of unanticipated obstruction [7]. For patients who undergo SWL, US with KUB (radio-opaque stones) or without KUB (radiolucent stones) should be performed. Further management will be determined by the degree of hydronephrosis and presence/absence of stone fragments. For patients who undergo URS, imaging depends on whether there was intact stone removal or fragmentation. For intact stone removal, patients without symptoms should have US, while patients with persistent symptoms should have CT with i.v. contrast. For stone removal with fragmentation, patients without symptoms should have US with KUB (radio-opaque stones) or without KUB (radiolucent stones), while patients with symptoms should have US with KUB (radio-opaque stones) or low-dose NCCT (radiolucent stones). Again, further management will be dictated by the imaging results.

Renal Stones

Staghorn calculi are branched stones that fill more than one portion of the collecting system and can be partial or complete. The initial guidelines on the management of staghorn calculi were released in 1994, with the most recent complete update in 2005 [5]. The guideline outlines that all patients with a newly diagnosed staghorn calculi should be actively treated (Standard), with a therapeutic goal of complete stone removal, especially with struvite/calcium carbonate/apatite stones. The methods to achieve this goal include percutaneous nephrolithotomy (PCNL), SWL monotherapy, combined PCNL and SWL, and open surgery. It is interesting to note that URS was not included as a treatment method, because at the time of guideline development there was insufficient evidence to warrant its inclusion [5].

According to the guideline, PCNL is the first-line treatment method for most patients (Recommendation). This is based on the higher SFR with PCNL compared with SWL (78% vs 54%, respectively) [5]. An acceptable alternative is combined therapy with SWL and PCNL. However, PCNL should always be the last procedure in the sequence to ensure complete stone removal (Recommendation). SWL monotherapy and open surgery should not be used for most patients (Recommendation), except in specific circumstances, such as low-volume stone burden with normal collecting system anatomy and pretreatment renal drainage in SWL (Option), or in open surgery where a reasonable number of endoscopic procedures would not be expected to remove the stone (Option).

Special considerations for select populations include those with cystine stones or negligible kidney function, and in children. For those with known large or staghorn cystine stones, SWL should be avoided, given the poor SFR (Recommendation). In patients with negligible function in the

affected kidney, nephrectomy should be considered, given the risk of persistent or recurrent infection (Recommendation). Finally, in children, both SWL and PCNL may be used (Option).

Unlike the AUA guidelines, which are specific for staghorn calculi, the EAU guidelines offer a treatment algorithm for renal stones based on size and location [4]. For stones in the upper or middle pole or renal pelvis, SWL is the first-line method for stones of <20 mm (grade B). URS is not recommended as first-line treatment for stones of >15 mm, due to decreasing SFR with increasing stone size (grade B). For stones of >20 mm, PCNL is the optimal treatment strategy (grade B). Stones located in the lower pole can be treated by SWL, which has satisfactory results for stone sizes of <15 mm, but for larger stones URS or PCNL are the methods of choice (grade B).

Medical Evaluation and Prevention of Recurrence

In 2014, the AUA released the first version of the guideline on the medical management of kidney stones [3]. The purpose of the guideline is to provide recommendations on the evaluation, treatment and prevention of stone formation in adults [3]. Although this section will focus on the AUA guideline [3], the American College of Physicians (ACP) recently released a clinical guideline [12] and the EAU guideline [4] will also be referenced when applicable.

Evaluation

The initial evaluation of a newly diagnosed patient should consist of a detailed medical and dietary history, serum chemistry, and urine analysis (Clinical Principle). Additional testing, such as an intact parathyroid hormone, if primary hyperparathyroidism is suspected, a stone analysis when available and imaging to quantify stone burden, can all be considered (Clinical Principle). Further metabolic testing should be performed in interested patients or those at high risk, such as patients with recurrent stones, large stone burden at initial presentation, a solitary kidney, medical conditions known to predispose to stone formation, obesity, recurrent infections, a family history of stone disease or intestinal malabsorption (Standard). Metabolic testing should be conducted on a random diet, with one or preferably two 24-h urine collections, with the minimum components of total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium and creatinine analysed (Expert Opinion). Tests to distinguish between the different types of hypercalciuria should not be performed (Recommendation).

Similarly, the EAU also recommends specific metabolic testing only in high-risk patients with two consecutive 24-h urine collections [4]. However, the ACP found that insufficient evidence was available to recommend an initial evaluation with blood chemistry, 24-h urine collection or stone analysis before dietary or pharmacological intervention, as these tests were not shown to reduce stone recurrence [12].

Dietary Therapy

Dietary therapy for all patients with stone disease should include a recommendation to increase fluid intake sufficient to achieve a urine volume of at least 2.5 L/day (Standard). For patients with calcium stones, sodium intake should be restricted (ideally to <2 300 mg/day) and dietary calcium should be maintained within the recommended daily dose of 1 000–1 200 mg (Standard). In patients who develop calcium oxalate stones, they should be counselled to limit oxalate rich foods and to maintain normal dietary calcium intake (Expert Opinion). For patients with calcium stones and low urinary citrate, they should be encouraged to increase their intake of fruits and vegetables but limit non-dairy animal protein (Expert Opinion). Similarly, in the setting of uric acid stones or calcium stones with elevated urinary uric acid, non-dairy animal protein intake should be reduced (Expert Opinion). Finally, patients with cystine stones are recommended to limit sodium and protein intake (Expert Opinion).

The EAU makes similar recommendations to those of the AUA for dietary therapy (depending on the underlying metabolic defect), consisting of increasing fluid intake to achieve a urine output of >2.5 L/day (grade A), limiting sodium and animal protein intake (grade A) and maintaining normal calcium consumption [4]. Unlike the AUA and EAU, the ACP concluded that only a single dietary intervention had sufficient evidence to deserve a recommendation. In this case, the ACP recommends management with increased fluid intake to achieve at least 2 L/day urine [12].

Pharmacological Therapy

Similar to the recommendations for dietary therapy, the pharmacological interventions are based on the underlying stone type or metabolic defect. In patients with high or relatively high urinary calcium and recurrent calcium stones (or high-risk, first-time stone formers), a thiazide diuretic should be offered (Standard). Dietary sodium should also be restricted in this population, to maximise the hypocalciuric effects of the thiazide. For patients with low or relatively low urinary citrate and recurrent calcium stones, potassium citrate therapy should be recommended (Standard). Either thiazides or potassium citrate therapy can be considered in patients with recurrent calcium stones who do not demonstrate metabolic abnormalities on a 24-h urine evaluation (Standard). In the setting of high urinary uric acid, normal urinary calcium and recurrent calcium oxalate stones, allopurinol should be offered (Standard). However,

allopurinol should not be offered as first-line therapy for recurrent uric acid stones, as the underlying metabolic defect is typically a low urinary pH (Standard). Therefore, potassium citrate therapy is recommended for uric acid stone formers to achieve a pH >6.0, and also for cystine stone formers to achieve a pH >7.0 (Expert Opinion). For cystine stone formers who are unresponsive to increased fluid intake, dietary modifications and potassium citrate therapy, a cystine-binding thiol, such as α-mercaptopropionylglycine (tiopronin) should be considered (Expert Opinion). Finally, patients with recurrent or residual struvite stones, in whom surgical stone removal is not feasible or has been exhausted, may be offered acetohydroxamic acid (AHA), with close attention to monitoring for side-effects (Option).

Both the EAU and ACP have recommendations on specific pharmacological interventions, which largely parallel those of the AUA. The EAU recommends: thiazide and potassium citrate therapy for hypercalciuria (grade A); potassium citrate therapy for hypocitraturia (grade A); allopurinol for hyperuricosuria (grade A); surgical stone removal if possible (grade A); and, if not possible, then urease inhibitors for struvite stones (grade A); and increased fluid intake, urinary alkalinisation and thiol therapy for cystine stones (grade B) [4]. The ACP does not make recommendations for pharmacological therapy based on specific stone composition or metabolic defect, again due to insufficient evidence [12]. However, they do recommend pharmacological monotherapy with thiazide, citrate or allopurinol, based on an overall reduction in recurrence of calcium stones with each of these therapies [12].

Monitoring of Therapy

After initiation of dietary or pharmacological therapy, a single 24-h urine collection should be obtained within 6 months to assess response and adherence (Expert Opinion). Subsequent testing should be done annually (or with greater frequency, depending on stone activity), with a 24-h urine collection to continue to monitor progress (Expert Opinion). A repeat stone analysis, when available, can also be considered (Expert Opinion). In addition, periodic blood testing (tailored to the specific therapy) should also be performed to identify adverse effects of pharmacological therapy (Standard). Specific monitoring for patients with struvite stones should include surveillance for re-infection with urease-producing organisms and strategies to prevent infection (Expert Opinion). Finally, it is recommended that interval imaging be obtained for all patients at least annually to assess stone burden (Expert Opinion).

The EAU recommends a follow-up 24-h urine study after initiation of therapy within 8–12 weeks [4]. It is also recommended to perform a repeat 24-h urine evaluation every 12 months, once therapy is stabilised [4]. Similar to their position on the initial evaluation, the ACP found insufficient evidence to conclude that monitoring blood chemistry, a 24-h urine collection or stone analysis, once therapy is initiated, reduces stone recurrence [12].

Conclusion

Collectively, the AUA and EAU guidelines provide a framework for the appropriate, evidence-based initial evaluation, diagnostic imaging selection, symptomatic management, surgical treatment, medical therapy and prevention of recurrence for both ureteric and renal stones. Information applicable to all stones include an initial evaluation to exclude concomitant infection, imaging to identify the stone location and quantify the stone burden, consideration of medical expulsive therapy or surgical intervention, identification of metabolic risk factors with a 24-h urine evaluation, and prevention of recurrence by increasing fluid intake.

Key points

- NCCT (preferably with low-dose protocol) is the initial imaging method of choice, due to its high sensitivity and specificity for the detection of stones.
- Newly diagnosed ureteric stones of <10 mm may be managed by observation with medical expulsive therapy to facilitate stone passage and decrease renal colic episodes.
- Both SWL and URS are acceptable first-line treatment options for ureteric stones, with URS thought to have a superior SFR for mid- and distal stones.
- PCNL is generally accepted as the treatment of choice for renal stones of >20 mm, including partial or complete staghorn calculi.
- For high-risk stone formers, specific metabolic testing with one, or preferably two, 24-h urine collections should be obtained.
- Dietary therapy for all patients with stone disease should include a recommendation to increase fluid intake sufficiently to achieve a urine volume of at least 2.5 L/day, with further dietary and pharmacological interventions based on metabolic abnormalities or stone composition.

Conflicts of Interest

The authors did not receive payment from a third party for this work. B.R.M. declares that he is a consultant for Boston Scientific, but that this relationship is not directly related to this work. J.B.Z. has no commercial or financial relationships to report. The authors have no patents related to this work. There are no other conflicts of interest to report.

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Abbreviations: ACP American College of Physicians; BMI body mass index; EAU European Association of Urology; KUB kidneys–ureters–bladder X-ray; NCCT non-contrast computed tomography; PCNL percutaneous nephrolithotomy; RCT randomized clinical trial; SFR stone-free rate; SWL shock-wave lithotripsy; URS ureteroscopy; US ultrasonography.

