# EAU Guidelines on
# Bladder Stones

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European
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of Urology

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# 1. INTRODUCTION

## 1.1 Aims and Scope

The European Association of Urology (EAU) Bladder Stones Guidelines Panel, a sub-panel of the EAU Urolithiasis Guidelines Panel, has prepared these guidelines to help urologists assess evidence-based management of calculi in native urinary bladders and urinary tract reconstructions and to incorporate recommendations into clinical practice. The management of upper urinary tract stone is addressed in a separate document: the EAU Guidelines on Urolithiasis.

It must be emphasised that clinical guidelines present the best evidence available to the experts but following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account. Guidelines are not mandates and do not purport to be a legal standard of care.

## 1.2 Panel Composition

The EAU Bladder Stones Guidelines Panel consists of an international group of clinicians with particular expertise in this area. All experts involved in the production of this document have submitted potential conflict of interest statements which can be viewed on the EAU website Uroweb: http://uroweb.org/guideline/bladder-stones/.

## 1.3 Available Publications

A quick reference document (Pocket Guidelines) is available, both in print and as an app for iOS and Android devices. These are abridged versions, which may require consultation together with the full text versions. The EAU Urolithiasis Panel has also published a number of scientific publications in the EAU journal European Urology [1-3]. All documents can be accessed through the EAU website: http://uroweb.org/guideline/bladder-stones/.

## 1.4 Publication History and Summary of Changes

### *1.4.1 Publication History*

This document is the first manuscript published on bladder stones on behalf of the EAU Bladder Stones Guidelines Panel.

# 2. METHODS

## 2.1 Data Identification

For the Bladder Stones guideline a structured assessment of the literature including lower levels of evidence was performed to assess prevalence, aetiology, risk factors, diagnostic evaluation, other aspects of bladder stone treatment (including medical treatment and concomitant treatment of the underlying causing including bladder outlet obstruction), and follow-up. It included a supplementary search with extended publication date range up to December 2018 to capture imaging studies concerning bladder stones. After deduplication, a total of 394 additional records were identified, retrieved and screened for relevance. Both the primary literature search and supplementary search results were assessed separately for this structured review. Databases covered by the search included Pubmed, Ovid, EMBASE and the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews. A detailed search strategy is available online: http://uroweb.org/guideline/bladder-stones/?type=appendices-publications.

The treatment chapters are based on a systematic review assessing the relative benefits and harms of currently available treatments for bladder stones. This review was conducted using standard Cochrane review methodology: http://www.cochranelibrary.com/about/aboutcochranesystematic-reviews.html.
All methodological information can be accessed online [4].

For each recommendation within the guidelines there is an accompanying online strength rating form, the basis of which is a modified GRADE methodology [5, 6]. 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 [7];
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’ [8]. 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 strength rating forms will be available online.

Additional information can be found in the general Methodology section of this print, and online at the EAU website; http://www.uroweb.org/guideline/. A list of associations endorsing the EAU Guidelines can also be viewed online at the above address.

### 2.2 Review
This document was subjected to peer review prior to publication.

# 3. GUIDELINES

### 3.1 Prevalence, aetiology and risk factors
Bladder stones constitute only approximately 5% of all urinary tract stones [9], yet are responsible for 8% of urolithiasis-related mortalities in developed nations [10]. The incidence is higher in developing countries [11]. The prevalence of bladder stones is higher in males, with a reported male:female ratio between 10:1 and 4:1 [12, 13]. The age distribution is bimodal: incidence peaks at three years in children in developing countries [12, 14], and 60 years in adulthood [13].

The aetiology and pathogenesis of bladder stones is typically multifactorial. Bladder stones can be classified as primary, secondary or migratory [15]. Primary or endemic bladder stones occur in the absence of other urinary tract pathology, typically seen in children in areas with a diet deficient in animal protein, poor hydration and recurrent diarrhoea [16].

Secondary bladder stones occur in the presence of other urinary tract abnormalities, which include bladder outlet obstruction (BOO), neurogenic bladder dysfunction, chronic bacteriuria, foreign bodies including catheters, bladder diverticulae and bladder augmentation or urinary diversion. In adults, BOO is the most common predisposing factor for bladder stone formation and accounts for 45% to 79% of vesical calculi [13, 17, 18]. Migratory bladder stones are those which have passed from the upper urinary tract where they formed and may then serve as a *nidus* for bladder stone growth; patients with bladder calculi are more likely to have a renal stone history and other risk factors for renal stone formation [19].

A wide range of metabolic urinary abnormalities can predispose to calculi anywhere in the urinary tract, a topic which is covered in more detail in the EAU Urolithiasis Guideline [20]. There is a paucity of evidence as to which specific metabolic abnormalities predispose to bladder stones. Hypocitraturia and a low urine volume were found in 89.5% and 49% of 57 children with endemic bladder stones in Pakistan, respectively [21], whilst a low urinary pH and hypomagnesuria were associated with bladder stones in 57 men with chronic urinary retention secondary to benign prostatic hyperplasia (BPH) [19].

### 3.2 Diagnostic evaluation
The symptoms most commonly associated with bladder stones are urinary frequency, haematuria (which is typically terminal) and dysuria or suprapubic pain, which is worst towards the end of micturition. Sudden movement and exercise may exacerbate these symptoms. Detrusor overactivity is found in over two thirds of adult male patients with vesical calculi and is significantly more common in patients with larger stones (> 4 cm). However, recurrent urinary tract infections may be the only symptom [18, 22].

In children, symptoms may also include pulling of the penis, difficulties in micturition, urinary retention, enuresis and rectal prolapse (resulting from straining due to bladder spasms). Bladder stones may also be an incidental finding in 10% of cases [16, 23].

#### 3.2.1 *Diagnostic investigations*
Ultrasound (US) of the bladder has a reported sensitivity and specificity for detecting bladder stones between 20-83% and 98-100%, respectively [24, 25]. Ultrasound has a lower sensitivity than computed tomography (CT) for detecting bladder stones [24]. Computed tomography or cystoscopy are the diagnostic modalities of choice for detecting calculi in urinary tract reconstructions [26].

In adults, CT and/or cystoscopy are the optimum diagnostic investigations for detection of bladder stones [24, 27]. No study compares cystocopy vs. CT. Plain X-ray (XR) kidney ureter bladder (KUB) has a reported overall detection rate for cystoscopically verified bladder stones of 21 to 78% [18, 27]. The size of the bladder stone determines the detection rate by XR KUB while composition of the stone plays only a minor role; stones with a largest diameter measurement ≥ 2.0 cm are detected in over half of cases, as are stones with a total volume ≥ 1.0 $cm^3$ [27].

There is a paucity of evidence for the investigation of bladder stones, particularly in children. See also EAU-Guidelines on Urolithiasis, Section 3.3, for further information on diagnostic imaging for urolithiasis [20]. Of course, the principle of ALARA (As Low As Reasonably Achievable) applies, especially in children.

### 3.3 Disease Management
#### 3.3.1 *Conservative treatment and Indications for active stone removal*
Asymptomatic migratory bladder stones in adults may be left untreated, especially if stones are small. Rates of spontaneous stone passage are unknown, but data on ureteric stones suggest stones < 1 cm are likely to pass in patients without urinary stasis, infection or foreign body [20].

Primary and secondary bladder stones are usually symptomatic, they are unlikely to pass spontaneously; thus, active treatment of such stones is usually indicated.

#### 3.3.2 *Medical management of bladder stones*
There is insufficient evidence to make recommendations on the medical management of bladder stones specifically; therefore, we refer the reader to the general guidance on the medical management of urinary tract stones in Chapter 3.4.9 of the EAU Urolithiasis Guidelines [20].

Stones composed of uric acid or struvite can be dissolved by chemolysis. Uric acid stones can be dissolved by oral urinary alkalinisation when a pH > 6.5 is consistently achieved, typically using an alkaline citrate or sodium bicarbonate. Careful monitoring is required during therapy [20].

Irrigation chemolysis is possible for struvite or uric acid stones; a two-way or three-way Foley catheter can be used [28]. See also Chapter 3.4.4. of EAU Urolithiasis Guidelines [20].

#### 3.3.3 *Bladder stone interventions*
Minimally invasive techniques for the removal of bladder stones have been widely adopted to reduce the risk of complications and shorten hospital stay and convalescence. Bladder stones can be treated with open, laparoscopic, robotic assisted laparoscopic, endoscopic (transurethral or percutaneous) surgery or extracorporeal shock wave lithotripsy (SWL). The EAU Urolithiasis Guidelines panel has performed a systematic review on interventions for bladder stones in adults and children [4].

##### 3.3.3.1 *Suprapubic cystolithotomy*
Open suprapubic cystolithotomy is successful, but is associated with a need for catheterisation and longer hospital stay in both adults and children compared to all other stone removal modalities [4]. In children, a non-randomised study found that "tubeless" (i.e. drain-less and catheter-less) cystolithotomy was associated with a significantly shorter length of hospital stay compared with traditional cystolithotomy, while there were non-significant differences between groups regarding late or intra-operative complications provided there was no urinary tract infection, no previous stones, or previous surgery for anorectal malformation [29].

##### 3.3.3.2 *Transurethral cystolithotripsy*
In both adults and children, transurethral cystolithotripsy provides similar, high stone-free rates (SFR) and appears to be safe, with a very low risk of unplanned procedures and major post-operative and late complications [4].

###### 3.3.3.2.1 Transurethral cystolithotripsy in adults:
In adults meta-analysis of three randomised controlled trials (RCT) demonstrates that transurethral cystolithotripsy has a shorter hospital stay and convalescence with less pain, but equivalent SFR and complications to percutaneous cystolithotripsy. One small RCT demonstrated a shorter duration of catheterisation, hospital stay and procedure with transurethral cystolithotripsy than cystolithotomy with similar

SFR [4]. Meta-analysis of four RCTs found a shorter procedure duration for transurethral cystolithotripsy using a nephroscope vs. cystoscope with similar SFRs, hospital stay, convalescence, pain and complications [4, 30-33]. A retrospective study (n= 107) reported that using a resectoscope was associated with a shorter procedure duration ($p < 0.05$) than a cystoscope for transurethral cystolithotripsy [96].

When considering transurethral cystolithotripsy, mechanical lithotripsy does not differ from electrohydraulic (EHL) lithotripsy regarding SFR and risk of unplanned procedures or major post-operative complications, although hospital stay may be shorter with mechanical lithotripsy [4]. A non-randomised study compared EHL, washout and combination of EHL and mechanical devices in 112 spinal injury patients [34]. There were no differences in primary or secondary outcomes except length of hospital stay, which was shorter following mechanical lithotripsy and washout compared with EHL and combination treatment. Cervical spine injury and combination of EHL and mechanical lithotripsy were independent predictors of complications on multivariate analysis [34]. One prospective, controlled study compared treatment with Ho:YAG laser at 30W and 100W, finding no difference in SFR, duration of procedure or unplanned procedures [35]. A non-randomised study on laser lithotripsy vs. pneumatic lithotripsy found no difference in SFR, but a significantly shorter procedure time for pneumatic lithotripsy [36].

3.3.3.2.2 Transurethral cystolithotripsy in children:

In children, non-randomised studies suggest that transurethral cystolithotripsy has a shorter hospital stay and catheterisation time but a longer procedure duration and more urethral strictures than open cystolithotripsy; SFRs were similar. One RCT found a shorter procedure time using laser vs. pneumatic lithotripsy for < 1.5 cm bladder stones with no difference in SFR or other outcomes [4, 37].

*3.3.3.3 Percutaneous cystolithotripsy*

3.3.3.3.1 Percutaneous cystolithotripsy in adults:

One non-randomised study found a shorter duration of catheterisation and duration of procedure and less estimated blood loss for percutaneous, compared with open surgery in patients with urethral strictures; all patients in both groups were rendered stone-free [4].

Meta-analysis of three RCTs demonstrated a shorter hospital stay for transurethral cystolithotripsy over percutaneous surgery. There were no significant differences in SFR, major post-operative complications or urethral stricture formation [4]. The duration of procedure did not differ significantly between approaches; however, the quality of evidence was low due to an inconsistent magnitude of effect, which could be ascribed to one study in which a laparoscopic entrapment bag was used in the percutaneous approach before fragmentation of the stone, which is likely to have shortened the duration of the procedure [4].

3.3.3.3.2 Percutaneous cystolithotripsy in children:

In children, non-randomised studies suggest that percutaneous cystolithotripsy has a shorter hospital stay and catheterisation time but a longer procedure duration and more peri-operative complications than open cystolithotripsy; SFRs were similar [4].

One small non-randomised study found a non-significant increased risk of unplanned procedures (within 30 days of primary procedure) and major post-operative complications for percutaneous operations compared with transurethral procedures; however, age and stone size determined which intervention children underwent and all patients were rendered stone free [4].

*3.3.3.4 Extracorporeal shock wave lithotripsy*

Extracorporeal SWL was found to be an attractive, safe and least invasive therapeutic option in all ages [38].

3.3.3.4.1 Shock wave lithotripsy in adults

In adults, non-randomised studies found a lower SFR and higher rate of unplanned procedures for SWL vs. transurethral cystolithotripsy, despite continuous irrigation in all patients and fragment evacuation in 16% of cases [4, 39].

3.3.3.4.2 Shock wave lithotripsy in children

One large non-randomised study found lower SFR for SWL than both transurethral cystolithotripsy and cystolithotomy, despite treating smaller stones with SWL. However, the length of hospital stay favoured SWL over cystolithotomy, although this appeared to be comparable between SWL and transurethral cystolithotripsy [97].

#### 3.3.4 *Treatment for bladder stones secondary to bladder outlet obstruction in adult men*

Bladder stones in men aged over 40 years are typically related to BPH, the management of which should also be considered. Bladder stones were traditionally an indication for surgical BPH treatment, a doctrine which has been questioned by recent studies. One non-randomised study compared 64 men undergoing transurethral cystolithotripsy with either transurethral resection of prostate (TURP) or medical management for BPH ($\alpha$-blocker with or without 5-alpha reductase inhibitor). After 28 months follow-up, no men on medication had had a recurrence, but 34% underwent a TURP: a high post-void residual urine volume predicted the need for subsequent TURP [40]. An observational study of 23 men undergoing cystolithotripsy and commencing medical management for BPH found 22% developed a BPH related complication, including 17% who had recurrent stones [41].

Large studies support the safety of performing BPH and bladder stone procedures during the same operation with no difference in major complications [42, 43]. An observational study on 2,271 patients undergoing TURP found no difference in complications except urinary tract infections, which occurred slightly more frequently in patients with simultaneously treated bladder stones: 0% vs. 0.6%, $p=0.044$ [42]. An observational study of 321 men undergoing Holmium laser enucleation of the prostate (HoLEP) found a higher rate of early post-operative incontinence (26.8% vs. 12.5%, $p = 0.03$) [43] but no difference in long-term continence rates.

#### 3.3.5 *Urinary tract reconstructions and special situations*

##### 3.3.5.1 *Neurogenic bladder*

Patients with neurogenic bladder secondary to spinal cord injury or myelomeningocele are at increased risk of forming bladder stones. Within eight to ten years, 15-36% of patients with spinal cord injury will develop a bladder stone [44, 45]. The absolute annual risk of stone formation in patients with a catheter is 4% compared with 0.2% for those voiding with clean intermittent self-catheterisation (CISC) [46]. Patients with an indwelling urethral catheter are approximately six times more likely to develop bladder stones than patients with normal micturition [45]. The risk of stone recurrence in patients who have previously formed a stone is 16% per year [46]. Bladder stones occur twice as frequently in patients managed with suprapubic catheters as in those performing CISC [47]. However, bladder stones are no more likely to form in patients with suprapubic catheters compared to those with indwelling urethral catheters [46].

##### 3.3.5.2 *Bladder augmentation*

The incidence of vesical calculus formation after bladder augmentation is 2-44% in adults [48-56], and 4-53% in paediatric patients, [57-69]. In adults, stones form *de novo* a mean 24 to 31 months following cystoplasty [49, 51, 56], and in children, a mean (or median) 25 to 68 months [61, 63, 65, 69-72]. The reported cumulative incidence of bladder stone formation after ten years is 36% [73].

Drainage by vesicoenterocystostomy (Mitrofanoff or Monti) is associated with an increased risk of bladder stone formation [49, 54, 55, 60, 61, 63, 73, 74]. The risk of bladder stone formation is elevated in patients voiding by CISC compared with those voiding spontaneously [53], as it is in patients with augmentations constructed using segments from ileum or colon compared with those constructed with gastric segments [57, 60, 61, 63].

In previous stone formers, the rate of recurrence is 15-44% in adults [49-51, 53, 56], and 19-56% in children [57, 60, 61, 63, 65-67, 72, 74]. The risk of recurrence is greatest during the first two years, at about 12% per patient per year, with the risk decreasing with time [72].

Daily bladder irrigation with 250 mL of saline solution significantly reduces the incidence of recurrent stone formation and bacterial colonisation compared to lower volume bladder irrigations [52]. A paediatric study reported that patients placed on an irrigation protocol using 240 mL saline solution twice a week and gentamicin sulphate solution once a week (240–480 mg gentamicin/L saline, at 120–240 mL per irrigation, depending on patient age and reservoir size), was associated with a significantly lower risk of vesical calculus formation [74]. Stones may be removed via open cystolithotomy or endoscopically [67]. The risk of recurrence is unrelated to the modality used for stone removal [56, 60, 61, 63, 66, 72].

##### 3.3.5.3 *Urinary diversions*

The incidence of stone formation after urinary diversion with an ileal or colon conduit is 0-3% [75, 76]. The incidence of stone formation in orthotopic ileal neobladders (Hautmann, hemi-Kock, Studer, T-pouch or w-neobladder) is 0-34% in adults [53, 75, 77-85], and in orthotopic sigmoid neobladders (Reddy) 4-6% [81, 86]. The risk of pouch stone formation in patients with an ileocaecal continent cutaneous urinary diversion (Indiana, modified Indiana, Kock or Mainz I) is 4-43% in adults [53, 75, 76, 84, 87, 88]. The mean (or median) interval from construction of the urinary diversion to stone detection is about 71 to 99 months [80, 89]. In paediatric patients, the incidence of neobladder stone formation after Mainz II diversion (rectosigmoid reservoir) has been reported to be about 30% [58], and 27% after creation of a Kock ileal reservoir [68].

For stone removal, a percutaneous approach or open procedure may be required if the caliber of the nipple is too small to allow the safe insertion of an appropriately sized endoscopic instrument without risking damage to the continence apparatus. Two studies indicate that percutaneous lithotomy can be safely performed via a 30 Fr sheath placed with guidance of US, or CT in patients with various types of lower urinary tract reconstructions (e.g. enterocystoplasties, ileocaecal continent cutaneous urinary diversions, ileal neobladders and colon reservoirs) [90, 91]. Stone recurrence after successful removal has been reported to be 10-42% [90, 91].

# 4. FOLLOW-UP

Bladder outlet obstruction is the most common predisposing factor for bladder stone formation [13, 17, 18, 22, 92] and evaluation for BOO should therefore be performed. Since the risk of complications in patients treated concomitantly for both bladder stones and BOO is not elevated [42], it is preferable to perform the BOO assessment prior to bladder stone removal to allow simultaneous treatment of the stone and BOO, if present.

There are contradictory reports on a possible association between bladder calculi and urothelial cancer [93] [94, 95]; this might be taken into consideration.

There are no studies examining the merits of differing follow-up modalities or frequencies following conservative, medical or operative treatment of bladder stones in both, adults and children.

| **Summary of evidence** | **LE** |
|---|---|
| The incidence of bladder stones peaks at three years in children (endemic/primary stones in developing countries) and 60 years in adults. | 2c |
| In adults, bladder outlet obstruction (BOO) is the most common predisposing factor for bladder stone formation. | 2a |
| The absolute annual risk of stone formation in patients with an indwelling catheter is significantly higher compared to those voiding with clean intermittent self-catheterisation (CISC). | 2b |
| Suprapubic catheters compared to urethral catheters show no difference in bladder stone formation. | 2b |
| The incidence of vesical calculus formation after bladder augmentation or any kind of vesicoenterocystostomy varies a lot but is up to 50% in adults and children. | 2a |
| Stone formation after urinary diversion in orthotopic ileal neobladders, ileocaecal continent cutaneous urinary diversion and rectosigmoid reservoirs vary between 2% and 40%. | 2a |
| Bladder stone removal with concomitant treatment for BOO is associated with no significant difference in major operative complications when compared to BOO treatment alone. However, concomitant bladder stone treatment does increase the rates of short-term post-operative incontinence and urinary infection. | 2a |
| Endoscopic (transurethral and percutaneous) bladder stone treatments are associated with comparable stone free rates (SFRs) but a shorter length of hospital stay, duration of procedure and duration of catheterisation compared to open cystolithotomy in adults. | 1a |
| Stone-free rate is lower in patients treated with SWL than those treated with open or endoscopic procedures. | 2a |
| Transurethral cystolithotripsy is associated with a shorter length of hospital stay, less pain and a shorter convalescence period than percutaneous cystolithotripsy in adults. | 1b |
| Transurethral cystolithotripsy with a nephroscope is quicker than when using a cystoscope with no differences in SFR in adults. | 1a |
| Transurethral cystolithotripsy with a resectoscope is quicker than when using a cystoscope with no differences in SFR in adults. | 2a |
| Mechanical, pneumatic and laser appear equivalent lithotripsy modalities for use in endoscopic bladder stone treatments in adults and children, although laser may have a shorter length of hospital stay and be quicker for < 1.5 cm stones in children. | 3 |
| Open cystolithotomy without a retropubic drain and urethral catheter can be safely performed in children with primary stones and no prior bladder surgery or infections. | 2a |

| Recommendations | Strength rating |
|---|---|
| Offer adults and children transurethral cystolithotripsy where feasible. | Strong |
| In adult men with bladder outlet obstruction (BOO) and bladder stones, preferably treat the underlying BOO simultaneously with stone removal. | Strong |
| Offer adults and children percutaneous cystolithotripsy where transurethral is not possible or is associated with a high risk of urethral stricture (e.g. young children, previous urethral reconstruction and spinal cord injury). | Strong |
| Discuss open cystolithotomy for very large bladder stones (there is no evidence to suggest a size cut-off). | Weak |
| Open, laparoscopic, robotic and extracorporeal shock wave lithotripsy are alternative treatments where endoscopic treatment is not feasible. | Strong |
| Perform transurethral cystolithotripsy with a continuous flow instrument (e.g. nephroscope or resectoscope) where possible in adults. | Strong |
| In children with primary stones perform open cystolithotomy preferably without placing a catheter or drain in uncomplicated cases (with no prior infection, surgery or bladder dysfunction). | Weak |
| Recommend regular irrigation therapy with saline solution to patients with a bladder augmentation or continent cutaneous urinary reservoirs. | Weak |

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# 6. CONFLICT OF INTEREST

All members of the Bladder Stones Guidelines working group have provided disclosure statements of all relationships that they have that might be perceived as a potential source of a conflict of interest. This information is publically accessible through the European Association of Urology website: http://www.uroweb.org/guidelines. This guidelines document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.

# 7. CITATION INFORMATION

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