



International Alliance of Urolithiasis (IAU) guidelines on the management of pediatric urolithiasis

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Abstract

The aim of this study was to construct the sixth in a series of guidelines on the treatment of urolithiasis by the International Alliance of Urolithiasis (IAU) that by providing a clinical framework for the management of pediatric patients with urolithiasis based on the best available published literature. All recommendations were summarized following a systematic review and assessment of literature in the PubMed database from January 1952 to December 2023. Each generated recommendation was graded using a modified GRADE methodology. Recommendations are agreed upon by Panel Members following review and discussion of the evidence. Guideline recommendations were developed that addressed the following topics: etiology, risk factors, clinical presentation and symptoms, diagnosis, conservative management, surgical interventions, prevention, and follow-up. Similarities in the treatment of primary stone episodes between children and adults, incorporating conservative management and advancements in technology for less invasive stone removal, are evident. Additionally, preventive strategies aiming to reduce recurrence rates, such as ensuring sufficient fluid intake, establishing well-planned dietary adjustments, and selective use pharmacologic therapies will also result in highly successful outcomes in pediatric stone patients. Depending on the severity of metabolic disorders and also anatomical abnormalities, a careful and close follow-up program should inevitably be planned in each pediatric patient to limit the risk of future recurrence rates.

Keywords Urolithiasis · IAU · Pediatrics · Prevention · Follow-up

Introduction

The prevalence of pediatric stone disease is on the rise globally, highlighting the need for specialized attention in this healthcare domain [1]. Population-based studies conducted in the United States have estimated the incidence of pediatric urolithiasis to be around 65/100,000 person/years during the 2005–2016 period, a sharp increase from the 1999 estimated of 18/100,000 person/years [2, 3]. In contrast, a

Chinese population study involving 14,256 asymptomatic children indicated a stone prevalence of up to 0.53% [4], while a review of pediatric urolithiasis in countries with emerging economies suggested rates as high as 15% in the pediatric population under the age of 15 [5].

Pediatric stone disease demonstrates marked distinctions when compared to its adult counterpart, necessitating a multidisciplinary approach. The key to minimize the need for surgical interventions and preserve renal function lies in a

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two-fold strategy: firstly, a well-planned medical management based on the metabolic evaluation outcomes, and secondly, minimal invasive surgical management based on the anatomical characteristics of the child's kidney as well as body habitus.

Over the past two decades, substantial progress has been made in the field of pediatric stone disease, including an enhanced understanding of the genetic metabolic predispositions, the development of appropriately sized instruments suitable for pediatric patients, and the categorization of minimally invasive endoscopic techniques.

The International Alliance of Urolithiasis (IAU) Pediatric Stone Guideline Panel has prepared these guidelines with the aim of improving the quality of care for children with urolithiasis. It is important to note that these guidelines are based on the most reliable evidence currently accessible to experts and that they do not over-ride the clinical expertise required when making treatment decisions tailored to individual patients. Instead, they serve as a valuable tool to guide decisions-making, taking into consideration not only the unique circumstances of each child but also their personal values, preferences, and the input of their caregivers as well as the surgical expertise and equipment available.

Methods

Data identification

All recommendations in these IAU guidelines on management of pediatric urolithiasis are based on a systematic review and assessment of the literature obtained from the MEDLINE, Embase, The Cochrane Library, and Web of Science, followed by determination of consensus by the IAU Panel. The comprehensive search covers all aspects of management of pediatric urolithiasis. The search terms included (but were not limited to) "urolithiasis", "nephrolithiasis", and "pediatric". The publication dates ranged from January 1952 to December 2023. Searches were not restricted by language. The focus of the searches was identification of all level 1 scientific papers (systematic reviews and meta-analyses of randomized controlled trials). If no sufficient data were found to support the clinical recommendation, the search was expanded to include lower-level literatures. In total, 1198 article titles were reviewed and 532 were identified as potential relevant for inclusion in the literature assessment for this guideline.

Recommendation

A modified GRADE methodology was used to assess the certainty in the evidence and formulate recommendations

Table 1 Interpretation of strong and conditional recommendations

Grade	Implications		
	Patients	Clinicians	Policy
Level 1 'Strong' "We recommend"	Most people in your situation would want the recommended course of action, and only a small proportion would not	Most patients should receive the recommended course of action	The recommendation can be evaluated as a candidate for developing a policy or a performance measure
Level 2 'Conditional' "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined

Table 2 Quality of evidence grades and their definitions

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect is close to the estimate of the effect
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low	The true effect may be substantially different from the estimate of the effect
D	Very low	The estimate of the effect is very uncertain, and often it will be far from the true effect

(GR) [6, 7]. The resulting recommendation were rated as strong ("the guideline panel recommends...") or conditional ("the guideline panel suggests"), based on four potential levels of evidence (high, moderate, low, or very low) (Tables 1 and 2). Recommendations are agreed upon by Panel Members following review and discussion of the evidence. The Panel Members deliberate on the interpretation of the clinical evidence, and vote on how the evidence should be incorporated into the existing guidelines.

Guidelines

Risk factors and etiology

Environmental and metabolic risk factors

- Unbalanced diet, dehydration, and prolonged exposure to high temperatures are risk factors for urinary stone formation in pediatrics. (2B)

Stone formation in children is influenced by various factors, including dietary habits, water intake, environmental conditions, and metabolic abnormalities such as hypercalciuria, hyperoxaluria, and hypocitraturia [8]. Dietary factors, particularly high sodium and protein intake, contribute to increased urinary calcium excretion and the formation of new stone [9]. Infants and toddlers who are not breastfed often experience malnutrition and dehydration, which may lead to urinary stone formation [10]. Environmental factors such as elevated temperatures and low humidity increase water loss through the skin, resulting in reduced urinary volume and increased urinary concentration, which promotes the precipitation of salts like calcium oxalate and contributes to stone formation. Metabolic disorders are prevalent in a significant proportion (33–95%) of children with urolithiasis and can contribute to stone formation [11]. Similar to adults, maintaining a balanced diet, staying hydrated, and avoiding prolonged exposure to high temperatures are critical for preventing urinary stone formation. Breastfeeding is recommended as a preventive measure against urolithiasis in infants and toddlers.

Genetic risk factors

- Genetic factors may contribute to abnormalities in mineral metabolism, increasing the likelihood of pediatric stone development. (2B)

Understanding the genetic predisposition to stone formation is crucial in pediatric cases. Approximately 30% of pediatric kidney stones cases are associated with genetic disorders [12]. Genetic factors may contribute to abnormalities mineral metabolism, increasing the likelihood of stone development [13]. We have summarized the existing genetic risk factors associated with urinary stone formation in Table 3 [14–16]. For pediatric urolithiasis, relatively common causes such as cystinuria, primary hyperoxaluria as well as the rare causes including infant hypercalcemia, familial hypomagnesemia with hypercalciuria and nephrocalcinosis, primary distal renal tubular acidosis, Bartter syndrome should be investigated including the corresponding genetic mutations for each of these types. While the possible impact of genetic mutations on the increased risk of stone formation in children is often emphasized by many authors, both the credible research to elucidate the proportion of cases attributable to genetic mutations and the specific numerical values regarding the increased incidence rates following such mutations are lacking.

Diseases and co-morbid conditions

- Congenital anomalies of the urinary system are risk factors for pediatric stone disease. (2C)

Pediatric stone disease is often associated with anatomical abnormalities including ureteropelvic junction obstruction, vesicoureteral reflux, and duplex collecting systems [17]. The risk of pediatric stone formation is further increased by conditions such as cystic fibrosis [18], renal tubular acidosis [19], and inflammatory bowel disease [20], necessitating a thorough medical history assessment for effective management [21]. It is widely accepted that congenital anomalies of the urinary system are risk factors for pediatric stone disease is already a consensus view. Subsequent urinary tract infection or urinary stasis play a role in the formation of stones [22].

Clinical presentation & symptoms

Signs and symptoms of pediatric urinary stones

- Symptoms of urinary stones are often non-specific, particularly in infants and young children. (1B)

Children with urinary stones can be asymptomatic or present with non-specific symptoms [23, 24]. Among those with symptomatic disease, pain is the most common symptom. Other symptoms include gross hematuria, recurrent urinary tract infections, failure to thrive, metabolic acidosis, and lower urinary tract dysfunction, such as frequent urination, urgency, urinary incontinence, and dysuria [25]. Approximately 15 to 25% of children are asymptomatic, especially young children who are diagnosed incidentally during physical examination or abdominal radiology imaging for other reasons [26].

Physical examination findings

- Physical examination should include measurement of blood pressure, growth parameters, as well as abdominal examination for signs of urinary obstruction or abdominal pain. (1C)

Poor weight gain and/or failure to thrive may indicate a congenital or chronic condition that could be associated with urinary stones [24]. An abdominal examination for tenderness or mass can be evidence of urinary obstruction [27].

Table 3 Genetic risk factors

Genetic Urolithiasis	Classification and Subtyping	Corresponding Gene Defects	Enzymatic defects
Primary hyperoxaluria	Type 1	AGXT	Glyoxylate aminotransferase (AGT)
	Type 2	GRHPR	Glyoxylate reductase/hydroxypyruvate reductase
	Type 3	HOGA1	4-hydroxy-2-oxoglutarate aldolase (HOGA)
Cystinuria	Type A	SLC3A1	-
	Type B	SLC7A9	-
	Type AB	SLC3A1 and SLC7A9	-
Calcium abnormalities	Infant Hypercalcemia (Type I)	CYP24A1	24-hydroxylase
	Infant Hypercalcemia (Type II)	SLC34A1	-
	FHHNC	CLDN16, CLDN19	-
	Primary dRTA	ATP6V0A4, ATP6V1B1, SLC4A1	-
	Dent disease (Type I)	CLCN5	-
	Dent disease (Type II)	OCRL	-
	Bartter syndrome (Type I)	SLC12A1	-
	Bartter syndrome (Type II)	KCNJ1	-
	Bartter syndrome (Type III)	CLCNKB	-
	Bartter syndrome (Type IV A)	BSND	-
	Bartter syndrome (Type IV B)	CLCNKB, CLCNKA	-
	Bartter syndrome (Type V)	MAGED2	-
	Purine abnormalities	APRT deficiency	APRT
HGPRT deficiency		HGPRT1	Hypoxanthine-guanine phosphoribosyltransferase (HGPRT)
Hereditary xanthinuria (Type I)		XDH	Xanthine dehydrogenase
Hereditary xanthinuria (Type II)		MOCOS	Molybdenum cofactor sulfuryase

Diagnosis

Laboratory tests

- Pediatric patients diagnosed with urolithiasis should undergo a screening evaluation with a detailed dietary and medical history including serum laboratory tests and urinalysis. (1B)

The medical history of the children and their families should be thoroughly examined to identify predisposing genetic factors and assess the risk factors. Anatomical conditions,

such as congenital urinary tract anomalies, should be given priority, followed by an assessment of dietary habits, supplements, vitamins, medications, history of urinary tract infection, and any previous instances of stone passage.

Laboratory examinations should include blood, and urine analyses. Levels of blood electrolytes (sodium, potassium, calcium, phosphorus, bicarbonate and chloride), blood urea nitrogen, calcium, creatinine, phosphate, alkaline phosphatase, uric acid, total protein, bicarbonate, albumin, and parathyroid hormone (when hypercalcemia is suspected) should be assessed [28]. In well-equipped centers or special cases, blood tests for vitamin A, C, D, thyroid-stimulating

hormone, and oxalate can be conducted simultaneously. Urine culture should be performed for all pediatric patients.

- Metabolic assessment including 24-hour urinary analysis and stone composition analysis should be done in every child being evaluated for stone disease. (1B)

Analysis of stone composition is essential for specifying preventive measures and selecting dissolution methods for stones. A comprehensive 24-hour urine analysis should measure urinary calcium, phosphate, magnesium, oxalate, uric acid, citrate, protein, and creatinine clearance. This analysis should be conducted after the stone has been cleared. It is generally recommended to perform two 24-hour urine collections on non-consecutive days for a thorough metabolic evaluation. Urine pH is recommended to be measured in fresh urine. If cystinuria is suspected, cystine analysis should be performed in the 24-hour urine sample. Table 4 displays normal values for 24-hour urine collection in children. It's important to note that normative values of assessed metabolites differ by age and geographically in childhood, which should be taken into account during the assessment [9].

A spot urine is not suitable to be used interchangeably in place of the 24-hour urine collections in the evaluation of urinary metabolic abnormalities in stone-formers [29].

Imaging methods

- Ultrasonography is the preferred imaging modality for pediatric urolithiasis. Non-contrast-enhanced computed tomography (NCCT) can be used when ultrasound cannot provide a clear diagnosis. (1B)

Table 4 Normal solute excretion values for 24-Hour urine samples in children

Parameter	Group	Normal Value per 24 h (mmol)	Normal Value per 24 h (mg)
Calcium	All ages	<0.10 mmol/kg	<4 mg/kg
Oxalate	All ages	<0.50 mmol/1.73 m ²	<45 mg/1.73 m ²
Citrate	Male	>1.90 mmol/1.73 m ²	>365 mg/1.73 m ²
	Female	>1.60 mmol/1.73 m ²	>310 mg/1.73 m ²
Uric Acid	All ages	<0.033 mmol/dl per GFR	<0.56 mg/dl per GFR
Magnesium	All ages	>0.04 mmol/kg	>0.8 mg/kg
Phosphate	<3 months	<3.30 mmol/L	<313.40 mg/L
	<6 months	<2.60mmol/L	<247.00 mg/L
	2–15 years	<2.44 mmol/L	<231.70 mg/L
Cystine	<10 years	<0.055 mmol/1.73 m ²	<13 mg/1.73 m ²
	>10 years	<0.200 mmol/1.73 m ²	<48 mg/1.73 m ²

Ultrasonography is the recommended primary imaging modality for suspected nephrolithiasis, as it is effective in detection of renal and ureteral stones while avoiding radiation exposure. Ultrasonography can identify radiolucent stones, such as uric acid stones, and urinary tract obstruction. However, it has limitations in detecting small stones, papillary or calyceal stones, or ureteral stones [30].

Kidney-ureter-bladder radiography (KUB) will detect radiopaque stones (calcium, struvite, and cystine stones), but it will miss radiolucent stones (uric acid stones), and might miss small stones or those that are overlay by bony structures. Additionally, KUB cannot detect urinary obstruction. In settings where renal ultrasonography and CT are unavailable for children, plain abdominal radiography remains a reasonable alternative, recognizing its reported sensitivity of this imaging modality is only 57% [31].

NCCT is the most sensitive modality to detect renal or ureteral stones in children [32]. CT is particularly useful when there is a strong clinical suspicion for a stone, but none is seen on ultrasound [33]. Radiation doses can be significantly reduced by adjusting exposure parameters for pediatric CT based on Child size/weight, the region scanned, and the targeted organ systems being scanned [34]. To ensure effective and safe radiation doses, CT should be implemented as outlined by guidelines from the National Cancer Institute [35].

Magnetic resonance urography (MRU) MRU provides less clear images of urolithiasis compared to NCCT. However, MRU can provide detailed anatomical information about the collecting system, such as the location and extent of obstruction, and the condition of renal parenchyma [36]. Another limiting factor for the utilization of MRU is its high cost, as well as the need for sedation in the pediatric population.

Conservative management of upper urinary tract stones

- Conservative management can be attempted for small stones (<5 mm) in a well child with no signs of infection, obstruction or intractable pain. (2C)

It is commonly believed that spontaneous stone passage is more likely in children than in adults due to the ureter's greater compliance. However, no study has ever demonstrated this and pediatric studies are lacking. There is a lack of evidence regarding the size of stones eligible for clearance at different ages and the duration of conservative follow-up. A conservative strategy can be the initial management in children with asymptomatic small size stones (<5 mm) with a possibility of spontaneous clearance [37, 38]. Robinson

and colleagues [39] observed that 83% of stones 5 mm or smaller passed spontaneously in their cohort, with decreasing chance of spontaneous passage with larger stones (69% in stones 5–10 mm, 33% for stones > 10 mm). Good supportive management with hydration and analgesia should be provided. Adequate hydration and increased fluid intake are mandatory for all children with stone disease. A minimum fluid intake of 1.5 to 2 L/m²/day is recommended [25].

- Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended as the first-line analgesic option in children presenting with acute renal colic. (2C)

Most patients with acute renal colic can be managed without hospital admission, with an emphasis on the importance of adequate analgesia upon presentation. While literature specific to children is lacking, NSAIDs are recommended as the first-line analgesic options in acute renal colic in children in several clinical guideline and expert options [40]. Opioids should be considered if severe pain is still inadequately controlled. The use of antispasmodics such as hyoscine butylbromide in children with renal colic is not recommended.

- Alpha-blockers can aid spontaneous passage of ureteral stones (< 10 mm) in children. (1B)

Several small randomized-controlled trials have been performed to outline the role of medical expulsive therapy in children applied for ureteral stones [41]. Although far from being conclusive, results from meta-analysis have shown a significant increase in probability in spontaneous stone passage in children when using alpha-blockers (tamsulosin 0.2–0.4 mg/day, silodosin 4 mg/day, and doxazosin 0.03 mg/kg/day) [42]. A multi-institutional retrospective cohort study demonstrated that use of alpha-blockers was associated with 55% spontaneous passage rate which was significantly higher compared to 44% success rate obtained with analgesics alone, with over 3-fold increased odds of spontaneous passage [43]. Health care professionals should be aware that the use of alpha-blockers is off-label and beneficial only for ureteral calculi. Stone passage may take 4 to 6 weeks and confirmation of passage by either repeated imaging or visualization of the passed calculus is mandatory.

Surgical interventions of upper urinary tract stones

Extracorporeal shockwave lithotripsy (SWL)

- SWL is recommended as the first treatment option for single small stones < 20 mm. (1B)

General anesthesia is advisable in children of 10 and younger undergoing SWL, while intravenous sedation or analgesia is an alternative for older children [44]. Anesthesia helps limit pain-induced movements, preventing the stone from moving out of the shock wave focus [45]. Fluoroscopy or ultrasound is commonly used to monitor stone localization [46, 47].

The number of SWL's needs to be limited to 2000 with a mean power setting varying between 14 and 21 kV. The optimal shock wave frequency is 1.0 to 1.5 Hz [48, 49]. The total energy required to fragment a stone depends largely on its size, location, hardness and composition of the stone and other risk factors. Starting with a low-energy level and ramping up slowly is recommended to activate a protective effect in the kidney. Stone localization should be reconfirmed at every 100–200 shockwaves to ensure an effective disintegration [48, 50].

Stone-free rates are significantly influenced by various factors, such as stone location, size and hardness. As the stone size increases, the stone-free rate decreases and the need for additional sessions increases. The overall success rate of SWL after 1 session is 44–82% and 90% can be achieved with multiple sessions [33]. However, technical challenges with localization and focusing for distal ureteral stones in children have resulted in low success rates [51–53]. Cystine, brushite, and whewellite stones generally respond poorly to SWL [53].

Complications arising from SWL in children are typically self-limiting and transient [54, 55]. The most common complications include renal colic, hematoma, transient hydronephrosis and steinstrasse. Steinstrasse and urinary obstruction have a high risk for complication in larger stones and solitary kidneys. Post-SWL stent placement or ureteroscopy may be necessary in cases with prolonged obstruction [52, 53, 56]. Antibiotic prophylaxis is recommended in cases with internal stent placement, infected stones, or bacteriuria.

Rigid/semi-rigid ureteroscopy

- Rigid/semi-rigid ureteroscopy is recommended as the treatment option for middle and distal ureteral stones. (1B)

The increasingly smaller ureteroscopes (such as 4.5/6.5 F size) have led to the growing use of ureteroscopic lithotripsy in children, which has also proven to be safe and effective. Generally, ureteral dilation is not necessary before ureteral lithotripsy except in some difficult cases. Routine pre-stenting is not recommended as it requires an additional session under anesthesia [57]. At present, pneumatic ballistic lithotripsy and laser lithotripsy are the most commonly

used methods of fragmentation, both of which have been proven to be safe and effective [57, 58]. Laser lithotripsy, in particular, is more suitable for small ureteroscopes and easier to use for pediatric cases due to the smaller size of the laser probe. While rigid/semi-rigid ureteroscopy is recommended for middle and distal ureteral stones, the failure rate is higher for children with proximal ureteral stones due to the difficulty in accessing the upper ureter and the tendency for stones to be easily washed into the kidney.

Retrograde Intra-renal surgery (RIRS)

- Flexible ureteroscopy is a valuable alternative for stones sizing <20 mm particularly for in older children. (1B)

Numerous articles have demonstrated the safety and effectiveness of flexible ureteroscopy in the treatment of kidney and ureteral stones in children. It is recommended to use ureteral access sheath (UAS), which can decrease intrapelvic pressure, facilitate the scope access and increase the durability of the instrument [59, 60]. However, UAS placement may sometimes be unsuccessful due to the narrow calibre of the ureter, especially in younger children [61]. The failure rate in kids would be between 21% and 61% [62–64]. In such cases, the solution is to insert a ureteral stent for 2–4 weeks before undergoing a second session for stone removal [65]. Pre-stenting is not recommended as it requires general anesthesia [66, 67].

During RIRS procedure, surgeons should pay attention to the level of renal pelvic pressure and control the balance of the perfusion in conjunction with outflow. Stone size and lower pole location were the two important factors affecting the stone-free rates to a certain extent. For stones smaller than 20 mm, it is necessary to inform the parents about the advantages and disadvantages of SWL and flexible ureteroscopy and have them involved in decision making. SWL has the shorter hospital stay but higher retreatment and auxiliary procedure rates while the failure of inserting the UAS may require an additional general anesthesia for stenting and a second session for laser lithotripsy.

Percutaneous nephrolithotomy (PCNL)

- Miniaturized PCNL is a well-established procedure for the management of large burden stones in pediatrics. (1B)

PCNL is always the first line treatment choice for large burden stones in both adults and pediatrics. PCNL has shown to have no adverse effect on kidney development and function

children [68, 69]. The indications for PCNL in pediatrics are similar to those in adults; it is considered the optimal modality for upper urinary tract stones larger than 2 cm, lower pole stones larger than 1.5 cm or other symptomatic stones fail treatment with RIRS or SWL, either as a monotherapy or in combination with RIRS and/or SWL [70, 71]. No differences in term of safety, stone-free rate and complication in prone or supine position PCNL have been demonstrated [72].

PCNL continues to provide the highest SFR in large burden stones, despite a potential increased in complications compared to RIRS and SWL mono-therapy. With the development of miniaturized PCNL techniques, such as mini-PCNL (14-18Fr), ultra-mini PCNL (11-13Fr), super-mini PCNL (14-18Fr) and micro-perc (4.85Fr), standard PCNL with adult instruments and large size sheath is no longer preferred in children [73, 74], making miniaturized PCNL more suitable for children [75, 76]. Additionally, the miniaturization of the tract also made tubeless PCNL better tolerated in carefully selected pediatric patients, and is associated with a shorter hospital stay, less time required to return to normal activity, lower postoperative pain and reduced urinary leakage [77, 78]. Thus, miniaturized PCNLs are a well-established procedure for the management of large burden stones in pediatrics.

Endoscopic Combined Intra-renal Surgery (ECIRS) involves retrograde and antegrade endoscopic surgery for complex upper urinary tract stones using both rigid and flexible endoscopes [79, 80]. The ECIRS technique integrates the advantages of PCNL and RIRS, taking into account the high lithotripsy efficiency of PCNL and the capability of RIRS to handle residual stones in parallel renal calices, thereby reducing tract related injuries and improves SFR [81]. However, it is rarely reported in pediatrics, the success rate of RIRS in pediatrics is lower than in adults and is largely influenced by the ureteral conditions [67]. Pre-stenting has been found to increase the success rate of RIRS in pediatrics. However, it requires extra anesthesia and incurs additional costs, and the necessity of pre-stenting is not yet definitively established [82]. As a result, while an initial attempt can be made during the first session, success is not guaranteed. Thus, ECIRS is preferred in selected pediatric cases with proper ureteral conditions.

Open and laparoscopy

- Open surgery and (robot assisted) laparoscopy are preferably indicated for pediatrics with complex urinary calculi presenting with anatomic abnormalities, or cases which have failed endourological procedures (2B).

With the development of endourological minimally invasive procedures, including rigid/semirigid ureteroscopy, RIRS and PCNL, the incidence of open surgery, which is associated with higher complications and significant injuries, has reduced tremendously [28, 83]. However, open surgery in pediatric urolithiasis patients is still prevalent in certain developing and/or developing nations as well as other cases [84]. Open surgery is preferably indicated for pediatrics with staghorn calculi, complex stones presenting with anatomical anomalies, or cases fail in minimally invasive procedures [85, 86]. Furthermore, laparoscopic surgery in pediatric urolithiasis involves less intra-operative bleeding and requires less postoperative analgesia than the open operation, and it is an alternative in experienced hands [87, 88]. Robot assisted laparoscopy is a feasible, safe and effective treatment option for pediatric urolithiasis in selected cases such as large bladder stones, bilateral kidney stones, staghorn stones or concomitant anomalies such as obstruction of the pelvi-ureteric junction requiring simultaneous pyeloplasty [89, 90].

Management of bladder stones

- Endoscopic surgery is equally effective as open surgery in managing bladder stones in children, while endourological management offers a shorter hospital stay (1A).
- Open surgery is preferable and has a shorter operative time for large stones (2B).

Bladder stone is not just a stone but a symptom that need to be very carefully diagnosed. Endoscopic management of pediatric bladder stones includes transurethral cystolithotripsy or percutaneous cystolithotripsy. Compared to open surgery, endourological techniques results in a shorter hospital. However, this advantage is mitigated by a greater number of complications, especially for multiple and complex bladder stones [91, 92]. These procedures carry a higher rate of complications, including intraperitoneal bladder rupture following percutaneous cystolithotripsy and urethral rupture and extravasation after transurethral lithotripsy for larger calculi [93].

Open surgery may also be employed for large bladder stones (> 2 cm) or bladder stones caused by any anatomical issue. Good candidates for open stone surgery include very young children with large stones and/or a congenitally obstructed system requiring surgical correction. Open surgery may be necessary in children with severe orthopedic deformities that limit their positioning for endoscopic procedures [91, 94, 95].

Prevention

- Increasing fluid intake is often the first step for the prevention of stone recurrence in pediatric patients. (2B)

A recommended fluid intake of 1500 to 2000 mL/m² per day is beneficial. In times of fluid losses or illnesses, earlier rehydration, such as intravenous infusions, may be necessary. For infants and toddlers with severe stone disease, such as cystinuria or hyperoxaluria, gastrostomy placements may be required [13, 25].

- Children should not be subjected to protein restrictions while they are growing, but an excessive of protein intake should also be avoided. (2C)

An excessive intake of animal protein can result in urinary acidification, resulting in hypercalciuria and hypocitraturia, whereas their restriction can affect growth. Therefore, both excessive protein intake and protein restriction should be avoided. It is recommended to integrate fruits and vegetables well into the diet, as they provide potassium and citrate, which act as stone inhibitors. For children with calcium oxalate stones, protein intake should be 0.8 to 1.0 g/kg normal body weight/day [25, 96–98].

For detailed information on pharmacological prevention, please refer to our previous IAU guidelines on the metabolic evaluation and medical management of urolithiasis [99].

Follow-up

- Ultrasonography every 6 months should be recommended to evaluate the stone growth in pediatric stone patients (2B).
- Twenty-four hours urinalysis every 6 months should be recommended to assess the risk of stone recurrence in pediatric stone patients (2C).

It is important to remember that in the presence of metabolic disorders (extremely common in children) there is a greater risk of rapid growth of these fragments (as well as recurrence) and follow-up must be stricter. Ultrasonography is suitable for evaluating stone activity in pediatric patients due to its lower radiation exposure and cost-effectiveness, and it can also detect hydronephrosis [100]. In general, follow-up intervals are every 6 months. In more problematic patients, different time schedules for clinical evaluations are necessary. For example, in primary hyperoxaluria Type 1, patients should be seen quarterly. Children with a greater number of stones or a family history of stones tend to

experience a more rapid increase in total stone burden and larger stone size [101]. Patients with abnormal anatomy also have a higher recurrence rate compare to those with normal anatomy [102]. Moreover, patients with lower pole stones face a higher risk of recurrence than those with upper-middle pole stones [103].

Twenty-four-hour urinalysis is valuable for evaluating the risk of stone recurrence and providing the dietary counseling in pediatric stone patients [104]. The most common urinary metabolic risk factors in pediatric stone patients are hyperoxaluria and hypocitraturia [103, 105]. In general the follow-up interval is every 6 months. Completion of a 24-hour urinalysis and adherence to metabolic prophylaxis have been associated with a decreased risk of stone recurrence in pediatric patients [104, 106].

Conclusion

As the incidence of pediatric nephrolithiasis is increasing, the pressure on healthcare systems is becoming more important than ever. Unfortunately, the existing body of research on pediatric patients with nephrolithiasis is limited regarding quality and quantity of these studies. Current clinical practices largely rely on extrapolations from adult literature due to the above-mentioned lack of reliable evidence-based data.

This guideline provides information that is clinically important, albeit slightly less informative than previous ones in the series, probably because of less literature data. This has resulted in a rather vague set of instructions. Notably, similarities in the treatment of primary stone episodes between children and adults, incorporating conservative management and advancements in technology for less invasive stone removal, are evident. Additionally, preventive strategies aiming to reduce recurrence rates, such as ensuring sufficient fluid intake, establishing well planned dietary adjustments, and selective use pharmacologic therapies will also result in highly successful outcomes in pediatric stone patients. Depending on the severity of metabolic disorders and also anatomical abnormalities, a careful and close follow-up program should inevitably be planned in each pediatric patient to limit the risk of future recurrence rates.

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Declarations

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