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Guidelines

EAU Guidelines on Vesicoureteral Reflux in Children

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Abstract

Context: Primary vesicoureteral reflux (VUR) is a common congenital urinary tract abnormality in children. There is considerable controversy regarding its management. Preservation of kidney function is the main goal of treatment, which necessitates identification of patients requiring early intervention.
Objective: To present a management approach for VUR based on early risk assessment.
Evidence acquisition: A literature search was performed and the data reviewed. From selected papers, data were extracted and analyzed with a focus on risk stratification. The authors recognize that there are limited high-level data on which to base unequivocal recommendations, necessitating a revisiting of this topic in the years to come.
Evidence synthesis: There is no consensus on the optimal management of VUR or on its diagnostic procedures, treatment options, or most effective timing of treatment. By defining risk factors (family history, gender, laterality, age at presentation, presenting symptoms, VUR grade, duplication, and other voiding dysfunctions), early stratification should allow identification of patients at high potential risk of renal scarring and urinary tract infections (UTIs). Imaging is the basis for diagnosis and further management. Standard imaging tests comprise renal and bladder ultrasonography, voiding cystourethrography, and nuclear renal scanning. There is a well-documented link with lower urinary tract dysfunction (LUTD); patients with LUTD and febrile UTI are likely to present with VUR. Diagnosis can be confirmed through a video urodynamic study combined with a urodynamic investigation. Early screening of the siblings and offspring of reflux patients seems indicated.

Conservative therapy includes watchful waiting, intermittent or continuous antibiotic prophylaxis, and bladder rehabilitation in patients with LUTD. The goal of the conservative approach is prevention of febrile UTI, since VUR will not damage the kidney when it is free of infection. Interventional therapies include injection of bulking agents and ureteral reimplantation. Reimplantation can be performed using a number of different surgical approaches, with a recent focus on minimally invasive techniques.
Conclusions: While it is important to avoid overtreatment, finding a balance between cases with clinically insignificant VUR and cases that require immediate intervention should be the guiding principle in the management of children presenting with VUR.

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1. Methodology

The scientific literature on reflux disease is limited, and the level of evidence is generally low. Most of the studies are retrospective, include different patient groups, and have poor stratification of quality. Also, there is a high risk of presenting misleading results by combining different types of studies when systematically extracting data. Therefore, producing recommendations for managing reflux disease based on high-quality studies is unfortunately not possible. The authors have assessed the current literature but, in the absence of conclusive findings, have provided recommendations based on panel consensus. These guidelines aim to provide a practical approach to the treatment of vesicoureteral reflux (VUR) based on risk analysis.

2. Background

VUR, or the retrograde flow of urine from the bladder into the ureter, is an anatomic and/or functional disorder with potentially serious consequences such as renal scarring, hypertension, and renal failure. Patients with VUR demonstrate a wide range of severity, and a majority of reflux patients will not develop renal scars and probably will not need any intervention [1].

The main goal in the management of patients with VUR is the preservation of kidney function by minimizing the risk of pyelonephritis. By defining and analyzing the risk factors for each patient (age, sex, reflux grade, lower urinary tract dysfunction [LUTD], anatomic abnormalities, and kidney status), it is possible to identify those patients with a potential risk of upper urinary tract infection (UTI) and renal scarring. Controversy persists over the optimal management of VUR, particularly the choice of diagnostic procedures, the treatment (medical, endoscopic, or open surgical), and the timing of treatment.

Many children with VUR have no symptoms of UTI, and invasive diagnostic procedures are performed only when clinically indicated; therefore, the exact prevalence of VUR is unknown. However, the prevalence of VUR in normal children has been estimated at 0.4–1.8% [2]. Among infants prenatally identified by ultrasonography to have hydronephrosis and who were screened for VUR, the prevalence was 16.2% (range: 7–35%) [3]. Siblings of children with VUR had a 27.4% (range: 3–51%) risk of also having VUR, whereas the offspring of parents with VUR had a higher incidence, 35.7% (range: 21.2–61.4%) [3].

Reflux detected by sibling screening is associated with lower grades [3] and significantly earlier resolution [4]. VUR that is discovered in a sibling after a UTI is usually high-grade and associated with a high incidence of reflux nephropathy (RN), particularly if the sibling is male and the grade of reflux is high in the index patient. Even when asymptomatic, siblings and offspring of individuals with VUR may be diagnosed with high-grade reflux and scarring [5,6].

The incidence of VUR is much higher among children with UTI (30–50%, depending on age). UTIs are more common in girls than boys because of anatomic differences. However, among all children with UTIs, boys are more likely than girls to have VUR (29% compared with 14%). Boys also tend to have higher grades of VUR diagnosed at younger ages, although their VUR is more likely to resolve [7–10].

There is a clear coprevalence between LUTD and VUR [11]. The term *LUTD* refers to the presence of lower urinary tract symptoms (LUTS)—including urge, urge incontinence, weak stream, hesitancy, frequency, and UTIs—that reflect the filling and/or emptying dysfunction, which may be accompanied by bowel problems. Some studies have described a prevalence of 40–60% for VUR in children with LUTD [12]. It is possible that VUR is secondary to LUTD and that treatment of LUTD therefore will result in correction of VUR. In contrast, high-grade VUR may affect bladder dynamics, which subsequently leads to LUTD. Recently published results of a Swedish reflux trial demonstrated LUTD in 34% of patients, and subdivision into group characteristics of children revealed that 9% had isolated overactive bladder and 24% had voiding phase dysfunction. There was a significant negative correlation between dysfunction at 2 yr and improved dilating reflux. Renal damage at study entry and follow-up was associated with LUTD at 2 yr. Recurrent UTIs were seen in 33% of children with LUTD and in 20% of children without LUTD [13].

The spontaneous resolution of VUR is dependent on age at presentation, sex, grade, laterality, mode of clinical presentation, and anatomy [4]. Faster resolution of VUR is more likely in children who are aged $<$1 yr at presentation, have a lower grade of reflux (grade I–III), and have an asymptomatic presentation with prenatal hydronephrosis or sibling reflux. The resolution rate is high in congenital high-grade VUR during the first years of life.

In several Scandinavian studies, the complete resolution rate for high-grade VUR was reported to be $>$25%, which was higher than the resolution rates of high-grade VUR detected after the infant years [14,15].

The presence of renal cortical abnormality, bladder dysfunction, and breakthrough febrile UTIs are negative predictive factors for reflux resolution [16–18].

Dilating VUR increases the risk of developing acute pyelonephritis and renal scarring. Untreated recurrent febrile UTIs may have a negative impact on the somatic growth and medical status of the child. Approximately 10–40% of children with symptomatic VUR have evidence of renal scarring resulting from congenital dysplasia, acquired postinfectious damage, or both [19–21].

Patients with higher grades of VUR present with higher rates of renal scarring. Scarring rates vary in different patient groups. Renal scarring occurs in approximately 10% of patients in the prenatal hydronephrosis group [22–27], whereas in patients with LUTD, this figure may rise to 30% [28–30]. Scarring in the kidney may adversely affect renal growth and function, with bilateral scarring increasing the risk of renal insufficiency. RN may be the most common cause of childhood hypertension. Follow-up studies show that 10–20% of children with RN develop hypertension or end-stage renal disease [31].

3. Diagnostic work-up

The diagnostic work-up should aim to evaluate the health and development of the child, presence of UTI, renal status, presence of VUR, and lower urinary tract function. A basic diagnostic work-up comprises a detailed medical history (including family history and screening for LUTD), a physical examination including blood pressure measurement, urinalysis (assessing for proteinuria), urine culture as indicated, and measurement of serum creatinine level in patients with bilateral renal parenchymal abnormalities.

The findings from imaging studies are useful for diagnosis and decisions about therapeutic options. The standard imaging tests include renal and bladder ultrasonography, voiding cystourethrography (VCUG), and nuclear renal scanning. The standard criterion for the diagnosis of VUR is detection on VCUG, especially at the initial work-up. VCUG provides precise anatomic detail and allows grading of VUR [32–34]. Clinicians should use the well-established grading system developed by the International Reflux Study Committee (Table 1) to minimize probable interobserver deviations [34].

Radionuclide studies for the detection of reflux have lower radiation exposure than VCUG, but the anatomic detail depicted is inferior [35]. Recent studies on alternative imaging modalities for the detection of VUR have yielded good results with voiding urosonography and magnetic resonance VCUG [36–38]. However, despite the concerns about ionizing radiation and its invasive nature, conventional VCUG remains the gold standard because the test allows better determination of the grade of VUR (in a single or duplicated kidney) and better assessment of bladder and urethral configuration.

Dimercaptosuccinic acid (DMSA) is the best nuclear agent for visualizing the cortical tissue and differential function between both kidneys. DMSA scanning is used to detect and monitor renal scarring. A baseline DMSA scan at the time of diagnosis can be used for comparison with successive scans during follow-up [33,39]. DMSA can also be used as a diagnostic tool during suspected episodes of acute pyelonephritis [40,41].

Video urodynamic studies are important only in patients in whom secondary reflux is suspected, such as patients with spina bifida, and in boys with a diagnosis of posterior urethral valves, for whom bladder dynamics necessitate regular follow-up. In patients with LUTS, diagnosis and follow-up can be limited to noninvasive tests (voiding charts, ultrasonography, or uroflowmetry) [11].

Cystoscopy has a limited role in evaluating reflux except in patients with infravesical obstruction or ureteral anomalies that might influence therapy.

The choice of imaging modalities varies depending on the mode of presentation.

Table 1 – Grading system for VUR on VCUG, according to the International Reflux Study Committee [34]

Grade I	Reflux does not reach the renal pelvis; varying degrees of ureteral dilatation
Grade II	Reflux reaches the renal pelvis; no dilatation of the collecting system; normal fornices
Grade III	Mild or moderate dilatation of the ureter, with or without kinking; moderate dilatation of the collecting system; normal or minimally deformed fornices
Grade IV	Moderate dilatation of the ureter with or without kinking; moderate dilatation of the collecting system; blunt fornices, but impressions of the papillae still visible
Grade V	Gross dilatation and kinking of the ureter, marked dilatation of the collecting system; papillary impressions no longer visible; intraparenchymal reflux

VUR = vesicoureteral reflux; VCUG = voiding cystourethrography.

3.1. *Infants presenting because of prenatally diagnosed hydronephrosis*

Ultrasonography of the kidney and bladder is the first standard evaluation tool for children with prenatally diagnosed hydronephrosis. The procedure is noninvasive and provides reliable information regarding kidney structure, size, parenchymal thickness, and collecting system dilatation [42,43].

Ultrasonography should be delayed until after the first week after birth because of early oliguria in the neonate. It is essential to evaluate the bladder as well as the kidneys. The degree of dilatation in the collecting system detected during ultrasonography when the bladder is both full and empty may provide significant information about the presence of VUR. Characteristics of bladder wall thickness and configuration may be indirect signs of LUTD and reflux. The absence of hydronephrosis on postnatal ultrasonography excludes the presence of significant obstruction; however, it does not exclude VUR.

Careful monitoring avoids unnecessary invasive and irradiating examinations. The first two ultrasonography scans within the first 1–2 mo of life are highly accurate for defining the presence or absence of renal pathology. VUR is rare in infants with two normal successive postnatal ultrasonography examinations and, if present, is likely to be low-grade [23,44].

The degree of hydronephrosis is not a reliable indicator of the presence of VUR, even though cortical abnormalities are more common in high-grade hydronephrosis [3]. The presence of cortical abnormalities on ultrasonography (defined as cortical thinning and irregularity, as well as increased echogenicity) warrants the use of VCUG for detecting VUR [3].

The use of VCUG is recommended in patients with ultrasonographic findings of bilateral high-grade hydronephrosis, duplex kidneys with hydronephrosis, ureterocele, ureteral dilatation, and abnormal bladders, because the likelihood of VUR is much higher. In patients with all other conditions, the use of VCUG to detect reflux is optional [3,26,45–47]. When infants who were diagnosed with prenatal hydronephrosis become symptomatic with UTI, further evaluation with VCUG should be considered [46].

3.2. *Siblings and offspring of reflux patients*

The screening of asymptomatic siblings and offspring of reflux patients is controversial. Some authors think that

Table 2 – Recommendations for pediatric vesicoureteral reflux screening

The parents of children with VUR should be informed that there is a high prevalence of VUR in siblings and offspring.
If screening is performed, siblings should be screened by renal ultrasonography. Voiding cystourethrography is recommended if there is evidence of renal scarring on ultrasonography or a history of urinary tract infection.
In older children who are toilet trained, there is no added value in screening for VUR.

VUR = vesicoureteral reflux.

early identification of children with VUR may prevent episodes of UTI and therefore renal scarring, while others think that screening asymptomatic individuals is likely to result in significant overtreatment of clinically insignificant VUR.

The estimate for renal cortical abnormalities is 19.3% (range: 11–54%), with 27.8% of patients in cohorts of symptomatic and asymptomatic children combined having renal damage. In asymptomatic siblings only, the rate of renal damage is 14.4% (range: 0–100%). Early screening appears to be more effective than late screening in preventing further renal damage by early diagnosis and treatment [3,5,48,49].

The lack of randomized clinical trials for screened patients to assess clinical health outcomes makes evidence-based guideline recommendations for VUR screening difficult (Table 2).

3.3. *Children with febrile urinary tract infection*

VCUG is recommended at age 0–2 yr after the first proven febrile UTI. If reflux is diagnosed, further evaluation traditionally consists of a DMSA scan. However, the scan can be reserved for high-grade VUR or VUR associated with a suggestion of abnormal renal parenchyma on the ultrasonograph, or it can be used as a baseline test to compare potential pyelonephritic consequences in the future.

An alternative top-down approach is also an option, as suggested by several studies in the literature. This approach carries out a DMSA scan first, close to the time of a febrile UTI, to determine the presence of pyelonephritis, which is then followed by VCUG if the DMSA scan reveals kidney involvement. A normal DMSA scan with no subsequent VCUG will fail to detect VUR in 5–27% of cases, with the cases of missed VUR being presumably less significant. In contrast, a normal DMSA scan with no VCUG will avoid unnecessary VCUG in >50% of individuals screened [50–53].

3.4. *Children with lower urinary tract dysfunction and vesicoureteral reflux*

Detection of LUTD is essential in treating children with VUR. It is suggested that reflux with LUTD will resolve faster after LUTD correction and that patients with LUTD are at higher risk for developing UTIs and renal scarring [54]. Alternatively, it is possible that LUTD is secondary to VUR and that treatment of VUR will therefore result in correction of LUTD. Or, it may be that there is a high coprevalence, but the treatment of one condition does not correct the other. In recent literature, no data support any of these hypotheses. Most studies are descriptive, uncontrolled, and retrospective, and the evidence quality is low.

A recent Swedish reflux study, however, has indicated that patients who have both VUR and LUTD may have a worse final outcome after treatment, including an elevated risk of kidney damage [13]. The results from the Swedish study indicate that the coexistence of both conditions should be explored in any patient who has VUR. If there are symptoms suggestive of LUTD (urgency, wetting, constipation, or holding maneuvers), an extensive history and examination, including voiding charts, uroflowmetry, and residual urine determination, will reliably diagnose underlying LUTD.

In LUTD, VUR is often low-grade and ultrasonography findings are often normal; there is no indication for performing VCUG in all children with LUTD. Instead, it would be more rational to ask all patients with LUTD if they have a history of febrile UTIs, in which case there is a greater possibility of finding VUR. However, because of the coexistence of LUTD and VUR, it is more practical to investigate any patient with LUTD and a history of febrile UTIs with a video urodynamic study, if available. Any child who fails standard therapy for LUTD should undergo urodynamic investigation. At that stage, combining a urodynamic study with VCUG is highly recommended.

4. Treatment

There are mainly two treatment approaches for patients with VUR: conservative (nonsurgical) and surgical.

4.1. *Conservative therapy*

The objective of conservative therapy is prevention of febrile UTI. Conservative therapy is based on the understanding that VUR can resolve spontaneously, mostly in young patients with low-grade reflux. Resolution is nearly 80% in VUR grade I–II and 30–50% in VUR grade III–V within 4–5 yr of follow-up. Spontaneous resolution is low for bilateral high-grade reflux [55].

VUR does not damage the kidney in the absence of UTI and the presence of normal lower urinary tract function. There is no evidence that small scars can cause hypertension, renal insufficiency, or problems during pregnancy. Indeed, these consequences are possible only with severe bilateral renal damage.

The conservative approach includes watchful waiting, intermittent antibiotic prophylaxis or continuous antibiotic prophylaxis (CAP), and bladder rehabilitation in patients with LUTD [54,56–59]. Circumcision during early infancy may be considered part of the conservative approach because the procedure has been shown to be effective in reducing the risk of infection in normal children [60].

Regular follow-up with imaging studies (eg, renal ultrasonography, VCUG, nuclear cystography, or DMSA scanning) is part of conservative management to monitor spontaneous resolution and kidney status. The frequency of the follow-up visits may differ; there is no validated

follow-up scheme, which mostly depends on the physician's preference. However, biannual ultrasonography of the urinary tract and annual or less frequent cystography and DMSA scanning (depending on the ultrasonographic and clinical findings) seem reasonable. Conservative management should be dismissed in all patients with febrile breakthrough infections despite prophylaxis, and intervention should be considered.

The most frequently used agents for CAP are single low doses (one-third of the treatment dose) of amoxicillin and trimethoprim (patients aged <2 mo) or trimethoprim-sulfamethoxazole or nitrofurantoin (for older infants), preferably taken at bedtime. The use of CAP and the duration of follow-up during prophylaxis in reflux patients is another area of major controversy. Although it is difficult to make definitive recommendations based on recent literature, it is clear that antibiotic prophylaxis may not be needed for every reflux patient [57,61–63].

While some trials show no benefit for CAP, especially in low grades of reflux, other trials show that CAP prevents further renal damage, especially in patients with grades III and IV reflux [64–68]. What is really difficult and risky is to select the group of patients who do not need CAP. A safe approach would be to use CAP in most instances. Decision making may be influenced by the presence of risk factors for UTI, such as young age, high-grade VUR, status of toilet training/LUTD, female sex, and circumcision status. However, recent literature does not provide any reliable information about the ideal duration of CAP in reflux patients.

A practical approach would be to use CAP until after children have been toilet trained and to make sure there is no LUTD. Active surveillance for UTI is needed after CAP has been discontinued. The follow-up scheme and the decision to perform an antireflux procedure or discontinue CAP may also depend on personal preferences and the attitude of the patient and parents. It is strongly advised that the advantages and disadvantages be discussed in detail with the family.

4.2. Surgical treatment

Surgical treatment can be carried out by endoscopic injection of bulking agents or ureteral reimplantation.

4.2.1. Subureteral injection of bulking materials

With the availability of biocompatible substances, subureteral injection of bulking materials has become increasingly popular because it is minimally invasive and is performed on an outpatient basis. Using cystoscopy, bulking materials are injected beneath the intramural part of the ureter in a submucosal location. The injected bulking agent elevates the ureteral orifice and the distal ureter so that coaptation is increased. The lumen is thus narrowed, which prevents reflux of urine into the ureter while still allowing the urine's antegrade flow. With the availability of biodegradable substances, endoscopic subureteral injection of bulking agents has become an alternative to long-term antibiotic prophylaxis and surgical intervention in the treatment of VUR in children.

Several bulking agents have been used over the past two decades. They include polytetrafluoroethylene (PTFE, or Teflon), collagen, autologous fat, polydimethylsiloxane, silicone, chondrocytes, and more recently, a solution of dextranomer/hyaluronic acid (Deflux).

The best results have been obtained with PTFE [69], but PTFE has not been approved for use in children because of concerns about particle migration [70]. Although other compounds such as collagen and chondrocytes are biocompatible, these agents have failed to provide a good outcome. Deflux was approved by the US Food and Drug Administration for the treatment of VUR in children in 2001.

Table 3 – Recommendations for management of vesicoureteral reflux in childhood

Regardless of the grade of reflux or the presence of renal scars or symptoms, all patients diagnosed within the first year of life should be treated initially with CAP. During early childhood, the kidneys are at higher risk of developing new scars. Immediate antibiotic treatment should be initiated for febrile breakthrough infections; treatment may be parenteral in children who are not capable of taking oral medications. Definitive surgical or endoscopic correction is the preferred treatment in patients with frequent breakthrough infections [77].
Surgical correction should be considered in patients with persistent high-grade reflux (grade IV/V). There is no consensus about the timing or type of surgical correction. The outcome of open surgical correction is better than endoscopic correction for higher grades of reflux, whereas satisfactory results can be achieved by endoscopic injection in lower grades.
There is no evidence that correction of persistent low-grade reflux (grade I–III) in patients with no febrile UTI and normal kidneys offers a significant benefit. These patients may be candidates for endoscopic treatment.
In all children presenting at age 1–5 yr with dilating reflux (grade III–V), CAP is the preferred option for initial therapy. For patients with high-grade reflux or abnormal renal parenchyma, surgical repair is a reasonable alternative. In patients with lower grades of reflux and no symptoms, close surveillance without antibiotic prophylaxis may be an option.
A detailed investigation for the presence of LUTD should be performed in all children after toilet training. If LUTD is detected, the initial treatment should be directed toward LUTD.
If parents prefer definitive therapy to conservative management, surgical correction may be considered. Endoscopic treatment is an option for all children with low grades of reflux.
The traditional approach of offering initial medical treatment after diagnosis and shifting to interventional treatment in case of breakthrough infections and new scar formation must be challenged, because the treatment should be tailored to the risk group.
The choice of management depends on the presence of renal scars, the clinical course, the grade of reflux, ipsilateral renal function, bilaterality, bladder function, associated anomalies of the urinary tract, age, compliance, and parental preference [83]. Febrile UTI, high-grade reflux, bilaterality, and cortical abnormalities are considered to be risk factors for possible renal damage. The presence of LUTD is an additional risk factor for new scars.
In high-risk patients who already have renal impairment, a more aggressive, multidisciplinary approach is needed.

CAP = continuous antibiotic prophylaxis; UTI = urinary tract infection; LUTD = lower urinary tract dysfunction.

Initial clinical trials have demonstrated that this agent is effective in treating reflux [71].

In a meta-analysis [72] including 5527 patients and 8101 renal units, the reflux resolution rate (by ureter) following one treatment of grades I and II reflux was 78.5%, 72% for grade III, 63% for grade IV, and 51% for grade V. If the first injection was unsuccessful, the second treatment had a success rate of 68%, and the third treatment, 34%. The aggregate success rate with one or more injections was 85%. The success rate was significantly lower for duplicated systems (50%) compared with single systems (73%), and for neuropathic bladders (62%) compared with normal bladders (74%).

Clinical validation of the effectiveness of antireflux endoscopy is currently hampered by a lack of methodologically appropriate studies. In the most recent prospective randomized trials comparing three treatment arms (I, endoscopic injection; II, antibiotic prophylaxis; III, surveillance without antibiotic prophylaxis) in 203 children aged 1–2 yr with grade III/IV reflux, endoscopic treatment gave the highest resolution rate, 71%, compared with 39% and 47% for treatment arms II and III, respectively, at 2 yr of follow-up. The recurrence rate at 2 yr after endoscopic treatment was 20% [73]. The occurrence of febrile UTIs and scar formation were highest in the surveillance group, at 57% and 11%, respectively. New scarring occurred significantly more often in the surveillance group (11%) than in the prophylaxis group (0%) ($p = 0.0054$). Although the new scar formation rate was higher with endoscopic injection (7%) than with antibiotic prophylaxis (0%), the rate did not attain significance ($p = 0.0551$), and there was no difference between the endoscopic and surveillance groups ($p = 0.5477$) [61]. Results after longer follow-up are needed to validate this finding.

4.2.2. *Open surgical techniques*

Various intravesical and extravesical techniques have been described for the surgical correction of VUR. Although each

Table 4 – Management and follow-up according to different risk groups

Risk groups	Presentation	Initial treatment		Follow-up
High	Symptomatic male or female patients after toilet training, with high-grade reflux (grade IV/V), abnormal kidneys, and LUTD	Initial treatment is always for LUTD; intervention may be considered in cases of recurrent febrile infections or persistent reflux	Greater possibility of earlier intervention	More aggressive follow-up for UTI and LUTD; full reevaluation after 6 mo
High	Symptomatic male or female patients after toilet training, with high-grade reflux (grade IV/V), abnormal kidneys, and no LUTD	Intervention should be considered	Open surgery has better results than endoscopic surgery	Postoperative VCUG on indication only; follow-up of kidney status until after puberty
Moderate	Symptomatic male or female patients before toilet training, with high-grade reflux and abnormal kidneys	CAP is the initial treatment; intervention may be considered in cases of BT infections or persistent reflux	Spontaneous resolution is higher in males	Follow-up for UTI/ hydronephrosis; full reevaluation after 12–24 mo
Moderate	Asymptomatic patients (PNH or sibling), with high-grade reflux and abnormal kidneys	CAP is the initial treatment; intervention may be considered in cases of BT infections or persistent reflux		Follow-up for UTI/ hydronephrosis; full reevaluation after 12–24 mo
Moderate	Symptomatic male or female patients after toilet training, with high-grade reflux and normal kidneys with LUTD	Initial treatment is always for LUTD; intervention may be considered in cases of BT infections or persistent reflux	In case of persistent LUTD despite urotherapy, intervention should be considered; the choice of intervention is controversial	Follow-up for UTI, LUTD, and kidney status; full reevaluation after successful urotherapy
Moderate	Symptomatic male or female patients after toilet training, with low-grade reflux and abnormal kidneys with or without LUTD	Choice of treatment is controversial; endoscopic treatment may be an option; LUTD treatment should be given if needed		Follow-up for UTI, LUTD, and kidney status until after puberty
Moderate	All symptomatic patients with normal kidneys, with low-grade reflux and LUTD	Initial treatment is always for LUTD		Follow-up for UTI and LUTD
Low	All symptomatic patients with normal kidneys, with low-grade reflux with no LUTD	Either no treatment or CAP	If no treatment is given, parents should be informed about risk of infection	Follow-up for UTI
Low	All asymptomatic patients with normal kidneys and low-grade reflux	Either no treatment or CAP in infants	If no treatment is given, parents should be informed about risk of infection	Follow-up for UTI

LUTD = lower urinary tract dysfunction; UTI = urinary tract infection; VCUG = voiding cystourethrography; CAP = continuous antibiotic prophylaxis; BT = breakthrough; PNH = prenatally diagnosed hydronephrosis.
A *symptomatic patient* is a patient with febrile UTI (upper tract involvement) or with marked findings of afebrile UTI confined to the bladder (ie, malodorous or discolored urine with or without voiding difficulties). An *asymptomatic patient* is a patient with none of these findings.

method has specific advantages and complications, all the techniques share the basic principle of lengthening the intramural part of the ureter by submucosal embedding of the ureter. All the techniques have been shown to be safe, with a low rate of complications and excellent success rates (92–98%) [74].

The most popular and reliable open procedure is the Cohen cross-trigonal reimplantation. The main concern with this procedure is the difficulty of accessing the ureters endoscopically if needed when the child is older. Alternatives are suprahiatal reimplantation (Politano-Leadbetter technique) and infrahiatal reimplantation (Glenn-Anderson technique). If an extravesical procedure (Lich-Gregoir technique) is planned, cystoscopy should be performed preoperatively to assess the bladder mucosa and the position and configuration of the ureteral orifices. In patients with bilateral reflux, an intravesical antireflux procedure may be considered, because simultaneous bilateral extravesical reflux repair carries an increased risk of temporary postoperative urine retention [75]. All surgical procedures offer very high and similar success rates for correcting VUR.

4.2.3. Laparoscopy

A considerable number of case series with transperitoneal extravesical and pneumovesicoscopic intravesical ureteral reimplantations have showed the feasibility of the technique. Today, both conventional and robot-assisted laparoscopic approaches yield outcomes comparable to their open counterparts in terms of successful resolution of reflux. Further studies are needed to define the costs and benefits of both approaches.

The major shortcoming of the new techniques seems to be the longer operative times, which bar their wider acceptance. Also, laparoscopic approaches are more invasive than endoscopic correction, and the advantages over open surgery are still debated. Therefore, at present, a laparoscopic approach cannot be recommended as a routine procedure. It can be offered to parents as an alternative in centers with sufficient experience [60,76–82].

Table 3 summarizes the recommendations for management of VUR in childhood. Table 4 summarizes the management of different risk groups.

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Study concept and design: Tekgül.
Acquisition of data: Tekgül.
Analysis and interpretation of data: Tekgül.
Drafting of the manuscript: Tekgül, Hoebeke, Kočvara, Nijman, Stein, Dogan, Radmayr, Riedmiller.
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