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Check cystoscopy in the management of anterior urethral valves in a cohort of pediatric patients

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Summary

Introduction
Anterior urethral valves (AUV) are a rare cause of lower urinary tract obstruction which could progress to renal damage, Clinical presentation varies according with patient's age and severity of obstruction, but, in most cases, diagnosis is based on voiding cysto-urethrogram (VCUG). To date, the treatment of choice is endoscopic ablation even if approved guidelines about the overall management of AUVs, including the recognition and treatment of residual valves, are not available.

Objective
We describe our protocol for AUV treatment based on primary endoscopic valve ablation followed by check cystoscopy 15 days later.

Study design
Medical records of 5 patients with AUVs admitted from 2008 to 2018 to our Pediatric Urology Unit were retrospectively reviewed. Blood tests, urinalysis, renal US and VCUG were performed in all children, while urodynamic evaluation was performed in the 3/5 patients who could void spontaneously. All patients underwent endoscopic valves ablation and after 15 days after a second look cystoscopy was performed. Follow up was based on clinical and radiological evaluation with US, urinalysis and blood tests. Postoperative non-invasive urodynamic studies were performed in the 3/5 patient toilet-trained patients and VCUG was performed in 1/5 patient.

Results
and Discussion: At primary endoscopic ablation cystoscopy revealed AUVs in the penile urethra in three patients, in the penoscrotal urethra in one case, in the bulbar urethra in another case. In 3/5 patients check cystoscopy found residual valves and a second endoscopic ablation was performed. All patients achieved symptoms release and improved urodynamic parameters. No intra or post-operative complication were reported. The assessment of residual valves is variable in literature and it is usually described for posterior urethral valves (PUVs). Few series report the use of VCUG within the first week after valve ablation, our experience instead suggests that performing a second look cystoscopy, is very effective to evaluate the presence of residual AUVs and eventually proceed with further ablation.

Conclusion
Endoscopic ablation is the gold standard treatment for AUV, but residual valves management is not clearly defined. According to our experience, a check cystoscopy 15 days after primary ablation allows to identify and treat possible residual valves showing good results in terms of safety and efficacy.

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Introduction

Lower urinary tract obstruction in children is usually due to posterior urethral valves (PUVs), while anterior urethral valves (AUVs) are the rarest entity, representing anyway the main cause of congenital obstruction of the anterior urethra. This condition is uncommon, approximately 15—30 time less frequent than PUVs, and the association of these two anomalies is extremely rare [1,2]. AUVs present frequently as a mucosal fold situated on the ventral surface of the anterior urethra, causing urethral obstruction.

In terms of anatomical location, AUVs are located more frequently at the level of bulbar urethra (40% of cases). It can be also at penoscrotal junction (30% of cases) or penile urethra (30% of cases) [3]. Undiagnosed and untreated AUVs may progress to end-stage renal disease. Nevertheless, fewer than 5% of patients with AUVs is reported to progress to renal failure [4].

Clinical presentation varies according to patient age and degree of obstruction. Severe cases may present with bilateral hydroureteronephrosis and renal failure, while UTIs, dysuria, urinary incontinence or retention, are most reported in the presence of mild obstruction.

Dagnosis is based on renal ultrasound (US), and voiding cysto-urethrogram (VCUG) which can detect most of cases. However, high degree of suspicion is often requested for a correct diagnosis and considering AUVs in differential diagnosis of lower urinary tract obstruction is recommended [5].

Most reports in literature describe series of few patients and different surgical approaches including open valves resection or endoscopic ablation [6,7]. In the last decades, cystourethroscopy with valves ablation has become the standard treatment for AUV, often allowing voiding symptoms resolution and preventing from upper urinary tract damage.

Results of valves ablation can be checked with VCUG or with a second- look cystoscopy, which permit further ablation if required. The need of a second-look cystoscopy for the detection of residual PUVs is well described in literature, supported by percentage of patients requiring further ablation as high as 78% [8]. Because of the rarity of AUVs and subsequent risk of unrecognize incomplete treatment or overtreat successful ablations, our management supports the usefulness of a second-look cystoscopy.

The paper presents our experience on the diagnosis, management and outcomes of AUVs in a series of pediatric patients, with focus on treatment and follow-up protocol, in order to optimize the management of a rare but possible cause of lower urinary tract obstruction (LUTO) and renal failure.

Material and methods

Medical records of patients with AUVs admitted from 2008 to 20198 to our Pediatric Urology Unit were retrospectively reviewed.

All patients with AUVs were included in the series. Children with associated anomalies were also analyzed. No exclusion criteria were adopted.

History, symptoms at presentation, diagnostic work-up, management and follow up data were collected.

Diagnosis was based on VCUG and cystourethroscopy for all patients.

Preoperative blood exams and urinalysis were taken. Radiological evaluation of urinary tract with US and VCUG was performed to define the level of obstruction and evaluate possible associated anomalies. Urodynamic evaluation with uroflowmetry was performed in patients who could void spontaneously.

Surgeries were performed by the two senior members of the team. Each patient was treated by a single surgeon. Valve ablation was conducted endoscopically with monopolar hook. Patients were discharged on day-2 postop on oral antibiotic prophylaxis. Indwelling urethral catheter was left in situ until the second- look cystoscopy scheduled 15 days later.

Success of treatment was defined as absence of LUTO, no clinically significative UTIs and improved urodynamic parameters.

Follow up consisted in renal US and non-invasive urodynamic evaluation with post voiding residual (PVR) assessment for toilet-trained patients. VUCG was performed in one patient with VUR. No lost at follow- up were recorded. Institutional Review Board approval was obtained.

Results

Demographic and clinical features of all patients are reported in Table 1.

Median age at surgery was 52.4 months (range 0—145 months), median weight was 15,9 kg (range 2.6—38 kg).

AUVs were diagnosed in toilet-trained children in 3/5 cases (age at diagnosis 4-5 and 11 years-old). Clinical presentation of those three patients included LUTO symptoms with dysuria, incontinence, urinary retention and recurrent UTIs. One child required preoperative positioning of a suprapubic catheter for acute urinary retention and febrile UTI. 1/5 patient had prenatal diagnosis of bilateral hydroureteronephrosis and a bilateral grade-IV VUR was diagnosed after birth. 1/5 child was born with ano-rectal malformation (recto- prostatic fistula) and on work-up bilateral hydroureteronephrosis and caudal regression syndrome were found.

Preoperative assessment was based on blood tests, urine analysis, renal US, VCUG and non-invasive urodynamic evaluation (Fig. 1).

Uroflowmetry in the 3/5 toilet-trained patients showed an obstructive pattern.

Mean Q max was 7 ml/s (range 6—8 ml/s), mean Q ave was 3.3 ml/s (range 3—4 ml/s), mean voided volume was 146,6 ml (range 135—160 ml) and mean PVR was 95,66 ml (range 14—145 ml).

Mean preoperative creatinine level was 0.49 mg/dl (range 0.3—0.7 mg/dl) (Fig. 2).

All patients underwent cystourethroscopy under general anesthesia. Antibiotic prophylaxis with cephalosporine was administered 20 min preoperatively and it was then continued at full dose during the hospitalization.

Table 1 Patients' preoperative and postoperative characteristics.

Age at Presentation	Symptoms at presentation	Preoperative diagnosis	Location of AUV	Follow-up (US in 3—6 months)	Results
12 years old	Dysuria, difficulty voiding, urinary retention.	Not identified at VCUG US Uroflow	penile	regular kidneys, regular cortico-medullar differentiation, no urinary tract dilatation	No symptoms
4 years old	Dysuria, urinary retention. Preoperative cistostomy	VCUG US uroflow	Penoscrotal	US: regular	No symptoms
5 years old	Recurrent UTI, dysuria, incontinence	VCUG US uroflow	Penile	US: regular	No simptoms no more UTIs
2 months	Recurrent UTI. Urethro-prostatic Fistula + sacral dysmorphism in caudal regression syndrome	US: Bilateral hdrouretero-nephrosys	Bulbar	US: regular kydneys, no PVR	CIC 5 times a day no UTIs
9 days	ndd	Bilateral hydroureteronephrosis at pre-natal US. VCUG: Bilat VUR grade IV, high PVR	Penile	US: regular kidneys, right pielectasia APD 6 mm. VCUG right VUR grade II	No symptoms, no PVR

A 9 and 9.5 Fr operative cystoscope with 0°camera was used in 3/5 patients and 2/5 patients respectively. Cystourethroscopy detects AUV as membranous fold obstructing the urethral lumen especially during passive urine outflow induced with Valsalva maneuver (Fig. 3).

All patients had AUVs ablation performed with monopolar hook.

Valves were located in the penile urethra in three patients, in penoscrotal urethra in one case, in bulbar urethra in another case. No associated urethral diverticulum was found; one child presented the associated PUVs.

At the second-look, 3/5 (60%) patients needed ablation of residual valves and were discharged the day after with urethral catheter for 7days. 2/5 (40%) patients did not show residual valves and did not require urethral catheter.

No intra or post-operative complications were recorded.

Mean operative time was 46 min (range 40—60 min) and 25 min (range 15—35 min) at the first and second look cystoscopy respectively.

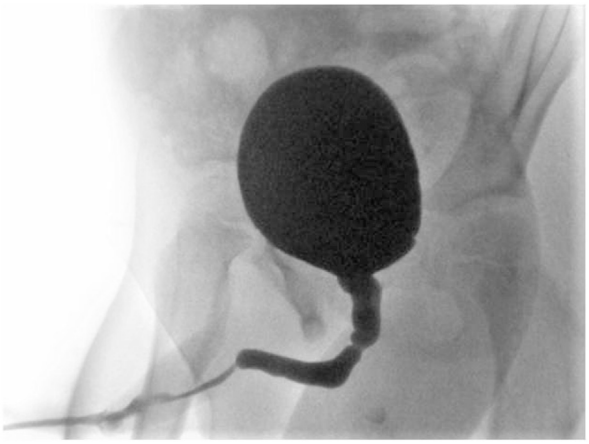

Figure 1 Preoperative VCUG.

At a mean follow-up of 43 months (range 24—72 months) the three patients with LUTO symptoms and without upper-tract anomalies, had complete symptoms relief. Their follow up consisted with US and urinalysis at 1, 3 and 6 months after the procedures for the first year, followed by clinical follow up only.

At 1 and 6 months a uroflowmetry was also performed, revealing improvement in bladder function and uroflow parameters in all, without significant PVR. Uroflowmetry at 1 month: mean Q max 14,3 ml/s (range 11—20 ml/s), mean Q ave 7.6 ml/s (range 7—8 ml/s), mean Voided Volume 219 ml (range 102—398 ml) and mean PVR 11,66 ml (range 0—20 ml).

At 6 months: mean Q max 17 ml/s (range 12—21 ml/s), mean Q ave 10,33 ml/s (range 8—12 ml/s), mean Voided Volume 245 ml (range 160—365 ml) and mean PVR 8.33 ml (range 0—15 ml)(Fig. 2B).

Mean postoperative creatinine level was 0.47 mg/dl (range 0.2—0.8 mg/dl).

The patient with VUR underwent VCUG 48 months after the ablations which revealed no left VUR and persisting right grade-II VUR. Renal US showed resolution of hydroureteronephrosis and no PVR. No more IVU or urinary symptoms were reported (Table 1).

The child with ano-rectal malformation developed neurogenic bladder needing CIC 5 times daily but the bilateral hydroureteronephrosis resolved completely.

Discussion

AUV are an uncommon cause of lower urinary tract obstruction in children and the diagnosis can be challenging [9].

This anomaly is usually located at the bulbar, penoscrotal or penile urethra, but it has been also found more distally in a juxtameatal position [10,11].

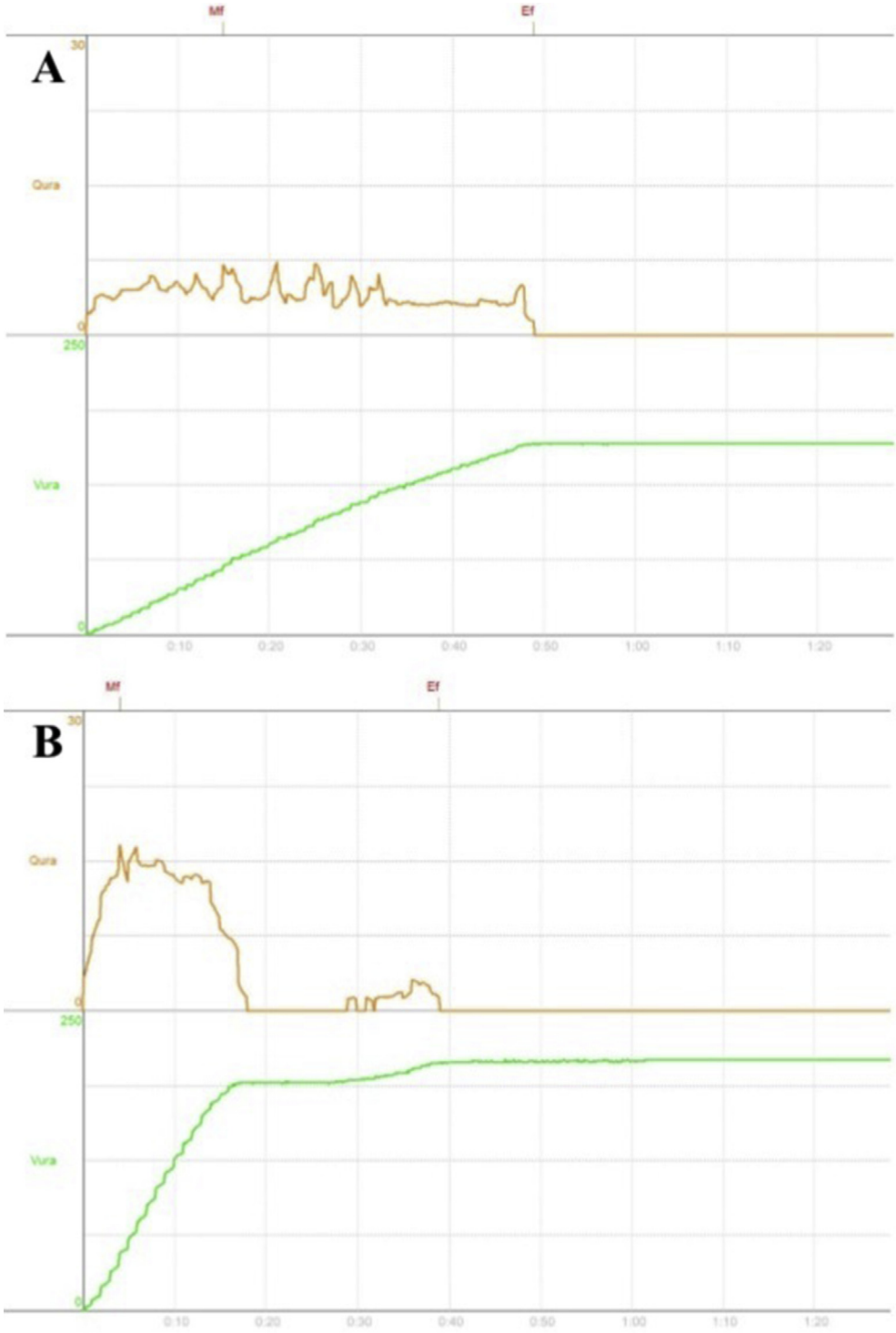

Figure 2 A: preoperative uroflowmetry; B postoperative uroflowmetry at 6 months.

The embryological mechanism leading to anterior urethral obstruction is still unclear.

Different theories were proposed, including failure of urethral duplication, unsuccessful alignment between the proximal and distal urethra, excess of tissue in the developing urethra, congenital cystic dilation of the periurethral glands and incomplete formation of the corpus spongiosum [12,13].

Associated anomalies have been rarely reported in literature. Those includes association of AUVs with hypospadias, PUV, megacystis ano-rectal malformation, Cowper's duct cyst and anterior urethral diverticulum in Prune-

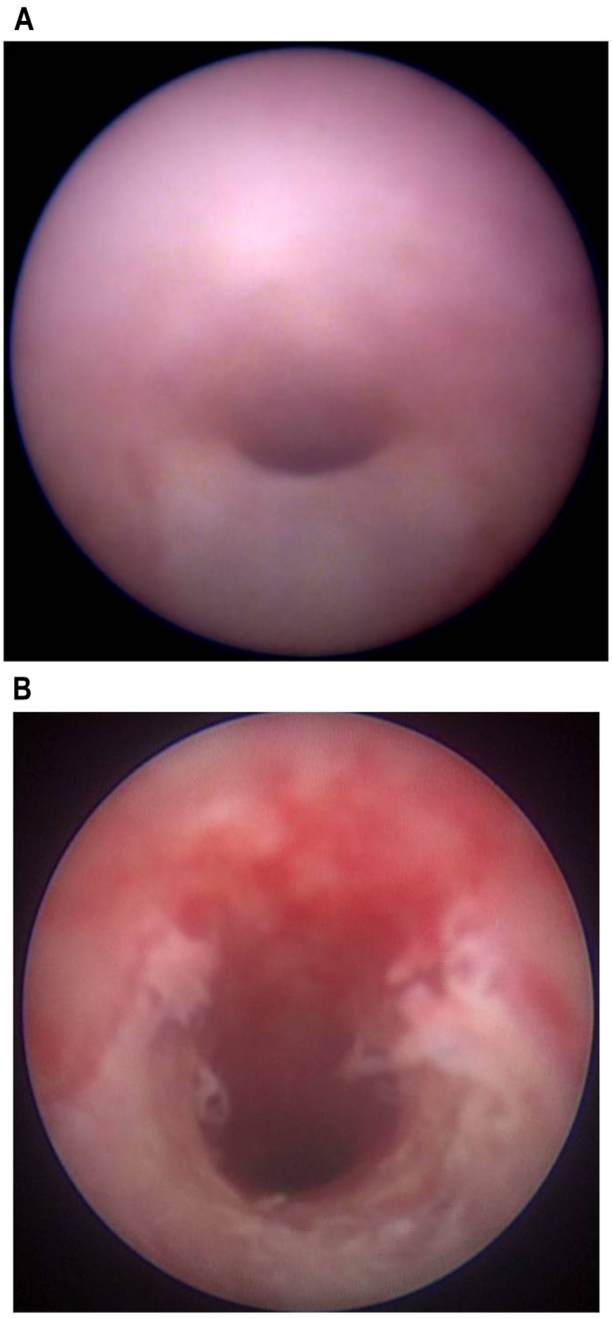

Figure 3 4y patient. A: preoperative cistoscopy; B: II look cistoscopy.

Belly syndrome [14—19] In our cohort AUVs were associated with ano-rectal malformation in one patient and PUVs in another.

AUVs may also present with anterior urethral diverticulum. The diverticula-valve pairing of the anterior urethra is estimated to be 10 times less frequent than isolated AUV [20,21].

In our series we did not find any associated anterior urethra diverticulum with AUVs, confirming its rarity.

Clinical presentation is highly variable depending on age and degree of obstruction. In newborn and infant, UTIs symptoms usually predominate. In older children AUVs can present with mild symptoms as dysuria, poor urine stream, frequency, urinary incontinence and retention [9]. Severe cases can present with bilateral hydronephrosis, progressive renal failure, bladder rupture and urinary ascites.

Late-presentation AUVs occurred in 3/5 of patient of our cohort, confirming that probably less severe anatomical variants produce a slow development of LUTO symptoms and subsequent delay in presentation and diagnosis. On the other hand, two of our patients fall within an early-presentation group where the neonatal work-up lead to prompt diagnosis.

Due to the rarity of this condition and the variability of symptoms, AUVs diagnosis is sometimes missed and some are treated as neurogenic bladder or other types of urethral stenosis, resulting in treatment delay and multiple unnecessary procedures [8].

Final diagnosis is essentially based on VCUG and cystoscopy. Renal US, uroflowmetry and cystourethroscopy also help identifying valves and possible associated anomalies.

Renal US may suggest the diagnosis of AUV through visualization of urethral dilatation and the possible impact on upper urinary tract [22].

Typical VCUG findings include a thickened wall, trabeculated bladder, dilated or elongated posterior urethra and anterior thin urethra beyond the obstruction. Cystoscopy confirms AUVs diagnosis by direct visualization of the mucosal folds and represents a tool for treatment.

Urodynamic evaluation usually detects the decrease in the urine outflow with increased urethral resistance. Bladder-sphincter dysfunction and dyssynergia are also reported [5].

Three of our patients presented an obstructive pattern at the preoperative uroflowmetry with high PVR, but no cases of bladder-sphincter dyssynergia was found.

Although signs and symptoms are well described, no specific protocol on AUVs management has been widely adopted so far, with several studies reporting their own different strategies. Treatment initially included open valves resection and urethral reconstruction. However, over the past two decades, endoscopic valves ablation with electrocautery, resecting hook or, more recently, with holmium laser has become the procedure of choice. In most patients this procedure allows to achieve good results with lower complications over dilatation maneuvers or open surgical approach [3,23].

In unstable patients, e. g infant with febrile UTI, suprapubic catheter or temporary diversion with cystostomy can be considered instead of immediate endoscopy [12,24].

The assessment of residual valves is variable in literature. Few series report the use of VCUG within the first week after valves ablation [1,23].

Our experience suggests that the second look cystoscopy is very effective to evaluate the presence of residual valves and proceed with further ablation. Check cystoscopy is a reasonable part of many protocols for the treatment of PUVs, because of the low positive predictive value of the VCUG alone in excluding residual valve tissue.

Smeulders et al. showed that the presence of PUVs remnants at post-operative VCUG positively predicted further valve ablation in only 60% of patients. In the same

way, 50% of patients with valves resolution at VCUG needed further ablation [25].

In their series of 50 patients Nawaz et al. also found residual PUVs in 78% of patients, suggesting second- look cystoscopy after primary endoscopic ablation as a useful procedure [8].

VCUG represents the investigation of choice for urethral anomalies. However, inadequate transit of contrast through the anterior urethra may alter its appearance, as argued by Gobbi et al. and Kajbafzadeh et al. [5,17]. The possibility of a false negative VCUG has also to be considered, especially if the association of.

AUVs and PUVs exist, as reported by Kehiani et al. In this scenario, AUVs are usually an incidental finding during cystourethroscopy for PUVs ablation [26].

Our experience suggests thatdefinitive treatment of AUVs can benefit of a second look cystoscopy which effectively evaluate the presence of residual valves.

In our series, 60% of patients required remnant leaflets ablation suggesting that the first attempt was not completely successful. Due to the rarity of the condition, it appears difficult to build up the experience required to understand when the procedure is complete. Subsequently, the planned check-cystoscopy allows the surgeon to first perform a cautious and safer resection, knowing the possibility to leave minor remnant. Mali et al. reported the 20% of patients in their series with residual AUVs at check cystoscopy, recommending the second-look as a regular part of AUVs management [4].

Among the surgical complications reported, in literature, mostly from open procedures, scrotal urinoma/hematoma, post-operative urethral strictures, and urethracutaneous fistula are the most common [23]. In our series we did not record any intra or postoperative complication, after both first and second- look cystoscopy. It has been suggested that careful ablation with re-resection should avoid the urethral strictures caused by a more aggressive primary treatment [25].

Finally, some authors evaluated urodynamic patterns in patient with AUVs before and after treatment showing that transurethral ablation of AUVs effectively solves obstruction and relieves the symptoms [18]. Our uroflowmetry studies throughout the follow-up showed an improvement in bladder capacity and urine steam as well as urinary continence, in line with other series [5].

Our study presents some limitations as the retrospective nature of the review and the small sample of patients. The cohort of patients is not homogeneous by age and type of presentation and more than one surgeon was involved in the patients' care. Moreover, due to rarity of the condition we decided to include also patients with significative comorbidities which might have influenced the short and long-term outcome.

However, a standardized management protocol is described, and follow-up shows its efficacy in preventing recurrence and renal damage.

Conclusions

Children with clinical presentation compatible with LUTO and UTIs should be carefully evaluated, considering AUV in differential diagnosis.

VCUG is strongly suggested in the diagnostic algorithm and a high grade of suspicion is required.

Endoscopic ablation is the gold standard treatment for AUV, but residual valves diagnosis and management are not still defined. According to our experience an accurate management including check cystoscopy after 15 days allows to identify residual valves and set the appropriate treatment without increasing the risk of complications. This approach permits a more careful initial treatment, eventually leaving minimal residual valves for a safer delay ablation.

Authorship

CC, MCC designed the study, acquired and analyzed data.
AM, LL, GB, SS revised critically the article.
MT, AE, LM finally approved the version to be submitted.

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Conflict of interest

None.

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