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Original Article

Urodynamic findings of pediatrics with history of failed anti-vesicoureteral surgery

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Abstract: Purpose: To evaluate the role of functional bladder dysfunction in failed vesicoureteral reflux (VUR) surgery through conventional urodynamic study. Materials and Methods: This cohort study was conducted at the Labbafinejad Hospital in 2020-2022. Patients <18 years with VUR who were referred with failed surgical intervention (persistence, progression, or recurrence of reflux on the same or opposite side) were included. Demographic information (sex, urinary tract symptoms, type of surgical intervention, and side and grade of VUR) and urodynamic study UDS results were recorded and analyzed statistically. Results: 53 patients were referred with failed surgery, with an average age of 8.20 ± 3.88 and a male-to-female ratio of 0.76/1.25. Bilateral vesicoureteral reflux (VUR) was present in 47.2%. Detrusor overactivity (DO) and dysfunctional voiding (DV) were found in 41 (77.4%) and 37 (69.8%) patients. The mean maximum amplitude and frequency of DOs were 50.58 ± 43.12 and 9.02 ± 8.15. Patients with bilateral VUR had significantly higher DO (92% vs 64.2%, P = 0.022), DO amplitude (70.60 ± 40.78 vs 32.71 ± 37.43, P = 0.001), and DO frequency (11.52 ± 8.14 vs 6.79 ± 7.63, P = 0.034). Conclusion: Individuals with failed VUR surgery commonly have UDS abnormalities and it is more severe in bilateral VUR patients. It can be postulated that non-surgical management and medications may be recommended as the first approach.

Keywords: Vesicoureteral reflux, lower urinary tract dysfunction, surgery, urodynamic study

Introduction

LUTD is a condition characterized by symptoms like urgency, frequency, incontinence, straining, hesitancy, and incomplete emptying [1]. It can be diagnosed through urodynamic evaluation, radiological evidence, and functional imaging. In patients with failed VUR surgery, urodynamic studies may reveal specific changes, such as detrusor overactivity, low bladder compliance, detrusor sphincter dyssynergia, and increased post-void residual urine [2]. These dysfunctions can lead to elevated bladder pressures, exacerbating reflux and contributing to surgical failure. Possible causes include neurogenic or non-neurogenic bladder disorders, delayed bladder maturation in children, psychosocial stressors, and inadequate preoperative assessment [3]. Understanding these aspects is crucial for managing VUR and preventing surgical failure.

Lower urinary tract dysfunction (LUTD) is an umbrella term used to describe filling and voiding disorders, and if left untreated, may lead to a wide range of complications from recurrent urinary tract infections to renal impairment [4]. The coexistence between vesicoureteral reflux (VUR) and LUTD has been widely described in the literature [5]. In VUR accompanied by LUTD, the chance of spontaneous resolution of VUR is decreased, and treatment of LUTD can be helpful for the resolution of VUR [6]. The EAU guideline recommends that in children with LUTD

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along with VUR, the management of LUTD is a priority [7]. The surgical approach is reserved for those cases with LUTD intractable to medical and conservative management, recurrent febrile UTIs, worsening renal outcomes, or parental/patient preference to avoid repeated therapeutic courses [8, 9]. There are different options for surgical treatment of VUR including open, endoscopic, and laparoscopic methods. The success rate of intervention has been estimated to be 98.1%, 88%, and 83.0%, in open, laparoscopic, and endoscopic methods, respectively [10]. The presence of LUTD may significantly decrease the success rate of VUR surgery [8]. However, the role of urodynamic variables in predicting relapse after VUR surgery is controversial [11, 12]. A high rate of VUR relapse has been observed in patients with abnormal UDS results [11].

So far, not many studies have been performed on the extent and severity of urodynamic parameters disorders in patients with previously failed VUR surgery. Re-evaluating these groups of patients by UDS may improve the therapeutic approach and prevent further unnecessary invasive surgical treatments. In this cohort study, we evaluated the different parameters of UDS in referred patients with VUR who had unsuccessful surgical outcomes.

Material and methods

Study design and participants

This cohort study was conducted at the urology department of Shahid Labbafinejad Hospital during the years 2020-2022. The inclusion criteria were as follows; Age under 18 years, history of unsuccessful open VUR surgery (persistence, progression, or recurrence of reflux on the same side or opposite side), and availability of complete patient urodynamic file which was performed at least 6 months after the last surgical intervention (To eliminate the probable iatrogenic effects of any surgical intervention on the function of the bladder). The exclusion criteria were as follows: history or evidence of any congenital or acquired neurological or metabolic diseases affecting the central or peripheral nervous system and history of urologic abnormalities such as ectopic kidneys, duplex kidneys, Prune-Belly syndrome, or other non-neurologic conditions affecting the genitourinary system.

Data collection

53 patients were included and their demographic information including age and sex, urinary tract symptoms, and laterality and grade of VUR before surgery were recorded. The basic information of the patients including the surgical report documents and urodynamic study files and reports were evaluated. Additional information was collected by direct contact with the patients/parents or through recorded medical documents. In the different medical centers in our area, the dominant open surgical approach is the modified trigonoplasty (Gil-Vernet) method (an intra-vesical approach that leaves the extra vesical neurovascular supply intact) [13]. The patients were routinely followed up after operation with urine analysis and culture monthly, an ultrasound scan in the first month, and repeated every 3 months. Prophylactic antibiotics are not stopped until radionuclide cystography is performed and confirmed reflux improvement. Post-operative recommendations include bladder and bowel programs as a routine in our center. In all patients, a direct radionuclide cystography was performed 6 months after the operation, and persistence of VUR with the same pre-operative grade, upgrades, or de novo contralateral VUR in unilateral cases was considered as surgical failure. Downgrading of VUR (from a high to low grade) in asymptomatic patients with sterile urine was considered a surgical response. In all failed cases, UDS was performed regardless of whether or not performed before the initial intervention. The postoperative urodynamic parameters were also recorded from the documented files (**Table 1**).

Studied variables/outcome parameters

In the filling phase of UDS bladder capacity, bladder compliance, and presence or absence of detrusor overactivity (DO) or leakage, number and maximum amplitude of DOs, and in the voiding phase voiding pressure at the maximum flow rate, the pattern of the void, Qmax, electromyography (EMG) status, and post-void residual volume (PVR) were evaluated. Normal bladder volume was calculated with the formula (age × 30) + 30. Values of ≤15 ml/cm H_2O were considered as decreased bladder compliance [14]. DO was described as any involuntary Detrusor contraction with the calculated

Table 1. Urodynamic findings in patients with history of failed antireflux surgery

Detrusor overactvity	77.4%
Decreased capacity	35.8%
Decreased compliance	62.3%
High pressure voiding	60.4%
Dysfunctional voiding	69.8%
Detrusor overactivity in patients with bilateral vesicoureteral reflux vs unilateral cases	92% vs 64.2%, P = 0.022
Amplitude of detrusor overactivities in patients with bilateral vesicoureteral reflux vs unilateral cases	70.60 ± 40.78 vs 32.71 ± 37.43, P = 0.001
Frequency of detrusor overactivities in patients with bilateral vesicoureteral reflux vs unilateral cases	11.52 ± 8.14 vs 6.79 ± 7.63, P = 0.034

Table 2. Demographic factors, symptoms, and characteristics of vesicoureteral reflux before surgery

Variable		
Sex M/F n (%)	23 (43.4%)/30 (56.6%)	
Age (Year)	8.20 ± 3.88	
Laterality	Unilateral	28 (52.8%)
	Bilateral	25 (47.2%)
Grade	2	5 (9.4%)
	3	22 (41.5%)
	4	19 (35.8%)
	5	7 (13.2%)
Renal parenchymal Scar	Normal	14 (26.4%)
	Unilateral	28 (52.8%)
	Bilateral	11 (20.8%)
Symptoms	UTI	48 (90.6%)
	Urgency	32 (60.4%)
	Frequency	40 (75.5%)
	Incontinence	14 (26.4%)
	Enuresis	28 (52.8%)

increase in pressure equal to or >15 cm H_2O in consecutive filling cycles. Qmax values of >11.5 mL/s in children aged ≤6 years and >15.0 mL/s in those aged ≥7 years were considered normal. In the case of PVR, in children ≤6 years, a repetitive PVR of >20 ml or >10% bladder capacity was regarded as high, and in those aged ≥7 years, a repetitive PVR of >10 ml or 6% bladder capacity was considered as high. It should be noted that bladder capacity and compliance were calculated regardless of reflux effect and urine volume which escaped to the upper urinary system (which may have resulted in false higher calculation in both capacity and compliance in some cases). In terms of voiding pressure, the following normal values were considered; in infants median of 100 cm H_2O in males and 70 cm H_2O in females, and 1 to 3-year-old children, 70 cm H_2O in males and 60 cm H_2O in females. EMG results were interpreted in two patterns: coordinated and dis-coordinated. Based on EMG activity in the voiding phase; dysfunctional voiding was defined as any sphincter activity during the voiding phase leading to reduced or interrupted urinary flow [15-17].

Statistical analysis

Data analysis was carried out using IBM SPSS 27.0 software (IBM Corp., Armonk, NY, USA). Quantitative variables were reported by mean ± standard deviation and qualitative variables by number and percentage. Data normality was checked by the Kolmogorov-Smirnov test. To compare qualitative variables between two groups, a chi-square test was used, an independent t-test was used to compare parametric quantitative variables, and a Mann-Whitney U test was used to compare non-parametric quantitative variables. A significance level of 0.05 was considered.

Results

This study included 53 failed surgical interventions with a mean age of 8.20 ± 3.88. There were 23 (43.4%) boys and 30 (56.6%) girls with an M/F ratio of 0.76:1. 25 (47.2%) patients had bilateral VUR. **Table 2** demonstrates patients' demographic data and information related to the patient's condition and symptoms before surgery.

DO and DV were found in 41 (77.4%) and 37 (69.8%) of patients respectively. The mean ma-

Table 3. UDS findings of included patients

No DO & DV		2 (3.8%)
DO		41 (77.4%)
DV		37 (69.8%)
DO + DV		27 (50.9%)
Capacity	Low	19 (35.8%)
	Normal	26 (49.1%)
	High	8 (15.1%)
Decreased compliance		33 (62.3%)
Leakage in filling phase		14 (26.4%)
High-pressure voiding		32 (60.4%)
High PVR		16 (30.2%)
Coexistence of DO and high-pressure voiding		63.4%
Coexistence of DV and high-pressure voiding		87.5%
Mean maximum amplitude of detrusor instabilities (Cm H_2O) ± SD		50.58 ± 43.12
Mean number of detrusor instabilities in filling phase ± SD		9.02 ± 8.15

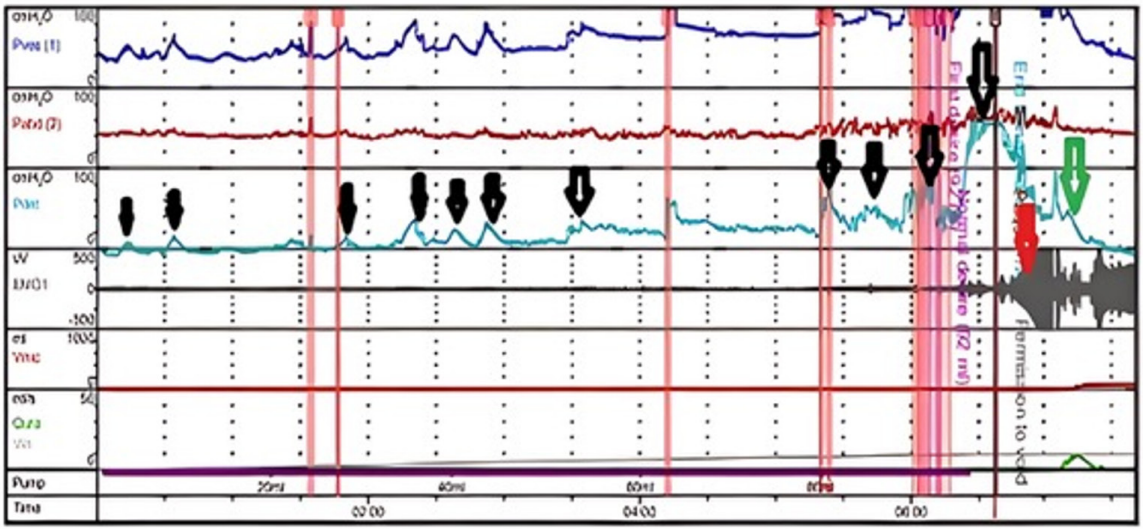

Figure 1. Urodynamic graph of a 7-year-old girl with a history of failed anti-vesicoureteral reflux surgery: black flashes show detrusor overactivities in the filling phase (11 episodes with mean amplitude of 46.3 cm H_2O). Red flash shows dis-coordinated sphincter in the voiding phase. capacity <10 cc, compliance is low <3 cc/cm H_2O, Qmax is low = 10 and Pdet/Qmax is 50 cmH_2O (green flash).

ximum amplitude of DOs was 50.58 ± 43.12 with a minimum of 0 and a maximum of 150 (**Table 3**). The mean number of DOs was 9.02 ± 8.15, with a minimum of 0 and a maximum of 40 (**Figure 1**).

In a subgroup analysis according to bilateral vs unilateral VUR patients, bilateral VUR patients had significantly higher DO (92% vs 64.2%, P = 0.022), DO amplitude (70.60 ± 40.78 vs 32.71 ± 37.43, P = 0.001), and DO frequency (11.52 ± 8.14 vs 6.79 ± 7.63, P = 0.034) (**Table 4**; **Figure 2**).

Discussion

The current cohort study was designed to assess the UDS of VUR patients who had unsatisfactory surgical results. The goal was to identify risk variables that could interfere with treatment outcomes and to prevent more unnecessary surgical interventions.

Table 4. Subgroup analysis between unilateral and bilateral VUR group

		Unilateral (n = 28)	Bilateral (n = 25)	*P*-value
Age		7.71 ± 4.21	8.76 ± 3.47	0.333
Sex M/F		15/13	8/17	0.166
Grade	2	5/28 (17.8%)	0/25 (0%)	0.169
	3	11/28 (39.2%)	11/25 (44.0%)	
	4	9/28 (32.1%)	10/25 (40.0%)	
	5	3/28 (10.7%)	4/25 (16.0%)	
DO		18/28 (64.2%)	23/25 (92.0%)	0.022
DV		20/28 (71.4%)	17/25 (68.0%)	0.786
Abnormal UDS (DO+DV)		27/28 (96.4%)	24/25 (96.0%)	0.935
DO amplitude (Mean ± SD)		32.71 ± 37.43	70.60 ± 40.78	0.001
DO frequency (Mean ± SD)		6.79 ± 7.63	11.52 ± 8.14	0.034
Low compliance		17/28 (60.7%)	16/25 (64.0%)	0.805
Leakage		6/28 (21.4%)	8/25 (32.0%)	0.534
High-pressure voiding		15/28 (53.5%)	17/25 (68.0%)	0.400

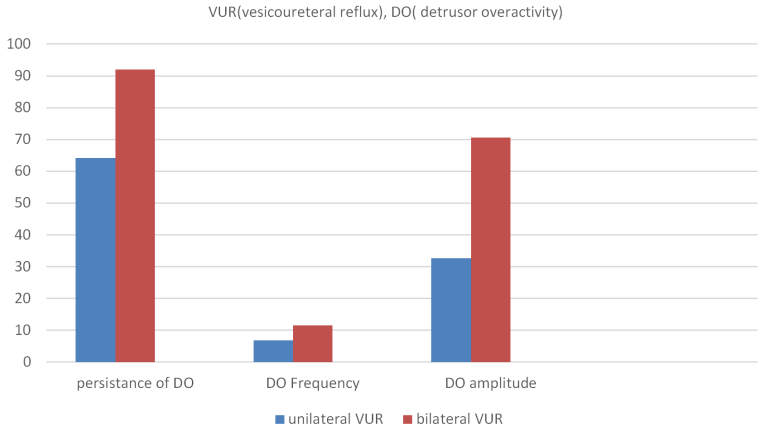

Figure 2. Subgroup analysis according to unilateral vs. bilateral VUR.

Bilateral VUR patients showed significantly greater DO, DO amplitude, and DO frequency in our population's urodynamic analysis. The majority of patients experienced DO, high-pressure voiding, and DV. DO patients had a higher frequency of high-pressure voiding. DV was more common in individuals with high-pressure voiding, and leakage was more common in those with DO. Various patient-related and intraoperative parameters are linked to VUR surgery surgical outcomes [18]. The existence of LUTS is one of the most important criteria linked with the efficacy of VUR treatment [19]. Initial diagnosis of LUTS is based on history taking. The presence of symptoms such as daily incontinence, enuresis, and holding maneuvers in the child's history suggests the possibility of concurrent LUTS. However, taking into account that history taking from children, especially children who are not toilet trained, sometimes its existence is not recognized before surgery. Due to the probability of damage to the ureterovesical nerve and/or disturbed bladder dynamics, de novo LUTD may occur in patients with bilateral high-grade reflux without LUTD before a ureteroneocystostomy [20].

In our study UDS was performed at least 6 months following surgery, therefore the acute iatrogenic effects of surgery on the bladder wall layers and function are almost negligible. Furthermore, because the surgical approach was intravesical (Gil-Vernet trigonoplasty technique), there is a low risk of iatrogenic damage to the extravesical neural plexus supplying the lower urinary tract, and the success rate of this surgical method in the treatment of VUR has been reported to be greater than 90% in previous studies [13]. In our modified surgical method, the medial wall of the intravesical ureter is dissected and released from the muscular layer of trigone (without incising and weakening the muscles) and brought together in the midline, the ureters slide above the trigonal muscles and the intravesical length of ureters increase in both sides simultaneously. According to this approach, each ureter is the anchor of the other one as well, so de novo VUR on the opposite side after surgery raises the probability of lower urinary tract dysfunction.

Even without taking into account the effect of VUR on the escaped volume of urine into the upper urinary system (as there is no video urodynamic facility in our center), decreased bladder capacity and compliance were observed in

35.8% and 62.3% of the patients, respectively which is noteworthy. This important finding indicates that if the amount of estimated liquid volume which escaped to the ureter is subtracted, the number of cases with decreased bladder capacity and compliance will most likely be higher.

The high incidence of UDS abnormalities identified in patients with failed VUR surgery in the current study suggests that more diagnostic options should be considered in failed cases before proceeding to another invasive or less invasive surgical approach. In patients with voiding dysfunction, bladders usually exhibit events of strong DOs. The failure to relax external urethral sphincter muscular tonicity, which is also required for effective voiding, can also cause voiding dysfunction [21].

Some experts have suggested that VUR may be an acquired condition. High intravesical pressure can cause UTI, damaging intravesical anatomy and reflux [22, 23]. In children with VUR, a crucial part of the assessment is to examine the bladder for residual urine, increased bladder wall thickness and trabeculation, urinary incontinence, or any other proof of detrusor-sphincter dyssynergia [21]. In a previous study, 57% of infants with VUR had abnormal UDS [24]. The results of our study are almost similar to this study.

The relationship between the existence of voiding dysfunction and the outcomes of VUR surgery is described in the literature, however, existing data on the extent and severity of urodynamic parameters disorders in patients with failed VUR surgery is limited [11]. It is widely accepted that re-implantation of the ureter into the bladder in children with significant voiding dysfunction accompanies a high risk of failure [25]. Neo et al. evaluated the impact of dysfunctional voiding on the setback of ureteral reimplantation for primary reflux. In 10 children with initial failure without a clear predisposing factor, all urodynamic evaluations performed were dissonant. Also, all patients had disturbances in the detrusor muscle and voluntary urethral sphincter function [26]. In our study, about 77% of patients had DV, which shows the importance of this urodynamic disorder. In a study conducted by Basiri et al., in all cases with reflux relapse who underwent UDS after the failure of the surgery, an abnormality was reported [11]. Furthermore, a failure rate of 30% was reported by Allen for reflux surgery in children with dis-coordinated voiding [21]. On the other hand, in a study conducted by Lavelle et al., 24 of 52 patients undergoing an endoscopic procedure had voiding dysfunction. They found no significant difference in the cure rate among patients with and without voiding dysfunction [27]. Overall, it seems necessary that in children with a failed VUR surgery, a urodynamic assessment be performed to diagnose dysfunctional voiding. Early diagnosis of children with voiding dysfunction and VUR may elevate the chance of resolution with non-operative management or create circumstances that increase the success rate of surgical treatment [26]. Another study by Sharifiaghdas and et al. found that in the urodynamic study of patients with vesicoureteral reflux, the most common pathological finding was detrusor overactivity (DO), identified in 64.3% of patients, followed by dysfunctional voiding (DV) in 50.3% patients. Children with VUR grades II and III had more abnormal urodynamic findings than those with grades IV and V. Detrusor overactivity (DO) was more common in children under 10 with unilateral, lower-grade VUR, while detrusor underactivity (DV) was more prevalent in children over 10 with bilateral, higher-grade VUR. Additionally, children with abnormal urodynamic findings experienced higher rates of lower urinary tract symptoms (LUTS), bowel and bladder dysfunction (BBD), and urinary tract infections (UTIs) [16]. In comparison to this study, our study had a lower percentage of DO, but a higher percentage of DV.

There are some limitations to this study. The most important is the lack of pre-operative urodynamic study. However the recommended indications for pre-op UDS are limited according to the literature. We did not have a comparison group (e.g., a group without a failed surgery), which limits the ability of a provider to apply this to a more general population of children with VUR and the number of patients was limited, hence, its results should be evaluated by further studies.

Conclusion

Individuals with failed VUR surgery commonly have UDS abnormalities. This raises the caution for immediate further surgical approach. It can be postulated that conservative manage-

ment such as pelvic floor therapy and medications may be considered as the first approach, and invasive surgical interventions are reserved for intractable failed cases.

Disclosure of conflict of interest

None.

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