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Correlation of the Proximal Urethra Diameter in Voiding Cystourethrography with the Severity of the Disease, Vesicoureteral Reflux and the Uroflowmetry Parameters in Children with Voiding Dysfunction

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What's known on the subject? and What does the study add?

The voiding dysfunction is a commonly encountered problem in children. If the patient has a history of urinary tract infection presenting with fever, a voiding cystourethrography is frequently utilized. Bladder wall irregularity, elongated bladder, widened bladder neck, and dilatation of proximal urethra can be detected in voiding cystourethrography scans of the children with voiding dysfunction. There are studies in the literature that have assessed the correlation between the dilatation of proximal urethra and voiding dysfunction. In our study, in addition to the existing literature, we analyzed the relationship between proximal urethra diameter determined in voiding cystourethrography of children with voiding dysfunction, the severity of the disease, the presence of reflux, and uroflowmetry parameters. We found that in the group with the high proximal urethra diameter, dysfunctional voiding incontinence scoring was observed to be high. However, a negative correlation was determined between high proximal urethra diameter and vesicoureteral reflux. There was no correlation between the uroflowmetry parameters, post-voiding residual urine volume and proximal urethra diameter.

Abstract

Objective: Voiding dysfunction is a commonly encountered problem in children. If a patient has a history of urinary tract infection (UTI) and presents with fever, voiding cystourethrography (VCUG) is frequently used. Proximal urethra dilatation in VCUG was determined to be an indication of voiding dysfunction. Studies in literature have been the ones assessing the correlation between the presence of proximal urethra dilatation and voiding dysfunction. In our study, however, we analyzed the relationship between the proximal urethra diameter determined in VCUG of children with voiding dysfunction, the severity of the disease, the presence of reflux, and uroflowmetry parameters.

Materials and Methods: Of the 522 VCUG-received patients 96 between the ages of 6-8 with voiding dysfunction concomitant with febrile UTI were evaluated. Dysfunctional voiding incontinence scoring (DVIS), uroflowmetry parameters, post-void residual measurements (PVR), proximal urethra diameter noted in VCUG, and presence of reflux in the patients were analysed.

Results: The mean age was 7.2±0.66. The average proximal urethra diameter was 7.6±1.8 mm. Regarding the diameter, the patients were divided into two groups: Group 1 (7.6 mm and below) and group 2 (above 7.6 mm). DVIS was higher but vesicoureteral reflux (VUR) was lower in group 2 (p=0.017, p=0.008; respectively). For uroflowmetry parameters and PVR, no significant differences were noted.

Conclusion: In the group with the high-proximal urethra diameter, DVIS was observed to be high. However, a negative correlation was determined between high-proximal urethra diameter and VUR.

Keywords: Proximal urethra diameter, VUR, uroflowmetry, dysfunctional voiding, VCUG

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Introduction

In children, voiding dysfunction (VD) is also called bladder dysfunction, and it indicates the anomalies in the filling or emptying functions of the urinary bladder (1). The International Children's Continence Society (ICCS) stated that VD should be considered in neurologically normal children aged five and above (2). VD is a frequently encountered clinical entity and is more common in girls (3).

The main symptoms of VD can be listed as urgency, frequency, daytime, and nighttime urinary incontinence. It can be diagnosed by detailed history, physical examination, voiding diary, and non-invasive methods, including urinalysis, urinary bladder ultrasound (US), and uroflowmetry (3,4).

However, voiding cystourethrography (VCUG) is performed if US findings suggest a urinary system anomaly or there is a history of recurrent urinary tract infection (UTI) (4). Bladder wall irregularity, elongated bladder, widened the bladder neck, and dilatation of proximal urethra can be detected in the VCUG scans of the children with VD (5).

Before the 1990s, proximal urethra dilatation was not considered a finding consistent with VD, especially in males without a posterior urethral valve, Prune Belly syndrome, urethral stricture, or a tumor. However, in 1992, Hausegger et al. (6) defined proximal urethral dilatation determined by VCUG as an essential finding of lower urinary tract dysfunction.

In subsequent studies, overt dilatation of the proximal urethra during voiding was termed as spinning top urethra (7). Spinning top urethra is caused by the discoordination between the external urethral sphincter and detrusor muscle, and this condition is associated with vesicoureteral reflux (VUR), UTI, and VD.

In the literature, several studies have assessed the relationship between proximal urethral dilatation and VD (6,7). Our study evaluated the relationship between proximal urethral diameter (PUD) determined in VCUG, uroflowmetry findings, the severity of VD, and the presence of VUR in children with VD.

Materials and Methods

This study was approved by the Ethical Review Committee of Muğla Sıtkı Koçman University (approval number: 180079). Data of the pediatric patients diagnosed with VD and who underwent VCUG during diagnostic management at our center between January 2016 and December 2020 were retrospectively reviewed. Patients with complete data without a congenital urinary tract anomaly or neurological disorder and those without occult spinal dysraphism or a history of urological surgery were included. Since patient age can affect the PUD, only patients aged between 6 and 8 were selected. Patients without urine culture, urinary US, post-voiding residual (PVR) urine volume assessment, uroflowmetry results, and a filled dysfunctional voiding and incontinence scoring system (DVIS) form were excluded. Children with monosymptomatic nocturnal enuresis were also omitted.

Data including demographic characteristics, DVIS scores, uroflowmetry results, flow pattern, PVR measured by the US, PUD measured during VCUG, and presence or absence of VUR was recorded to a database. The study population was divided into two groups based on PUD: Patients who had PUD of ≤7.6 mm were assigned to group 1, while those with PUD of >7.6 mm were included in group 2.

The DVIS scores were determined by reviewing the DVIS form completed by the children's parents or caregivers. In patients who underwent uroflowmetry testing twice or three times, mean values were calculated for each parameter. The uroflowmetry flow patterns (bell, staccato, tower, interrupted, or plateau) were identified on the basis of ICCS guidelines (2). The PVR measurements were performed by the US immediately after uroflowmetry. The mean PVR value was calculated for patients whose PVR was measured multiple times.

The same pediatric urologist performed the VCUG tests without sedation or anesthesia. Firstly, a spot X-ray was taken before the administration of the contrast medium. Subsequently, X-rays were taken during the filling and the voiding phases. The images were stored in the picture archiving and communication system (PACS). The largest PUD was measured on these anterior-posterior images in both genders, and the VUR grade was determined in patients with VUR (Figure 1).

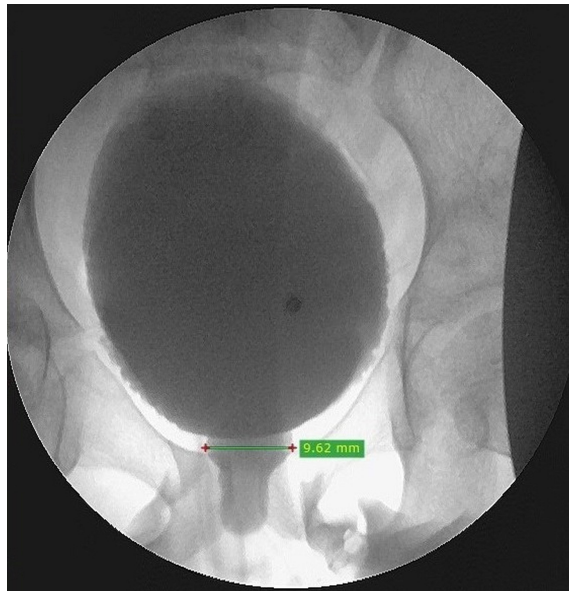

Figure 1. The measurement of proximal urethral dilatation in the voiding cystourethrography image

Statistical Analysis

The Statistical Package for Social Sciences software (SPSS for Windows, v22, IBM Corp., Armonk, NY, US) was used for all statistical analyses. Descriptive statistics were used to assess the basic characteristics. Continuous variables were expressed as mean ± standard deviations. The Student's t-test was used for comparing the groups. Categorical variables were expressed as numbers and percentages, and the chi-square test was used for comparisons between groups. Univariate and multivariate logistic regression analyses were performed to determine the predictive factors for VUR. All tests were two-sided, and the p-value was considered significant when it was less than 0.05.

Results

Our review revealed that 522 children underwent VCUG during diagnostic management of VD at our center during the study period. Among these patients, 96 were aged between 6 and 8. Six of these patients were excluded because of incomplete data, three were omitted due to monosymptomatic nocturnal enuresis, two were not included due to congenital urinary tract anomaly, and one was excluded due to the presence of a neurological disorder. Eighty-four patients who met the inclusion criteria were included.

The mean age of the patients (n=84) was 7.2±0.66 [minimum (min): 6-maximum (max): 8] years. Among these patients, 48 (57.1%) were girls, while 36 (42.9%) were boys. The mean PUD was 7.6±1.8 (min: 4-max: 12) mm. There were 40 (47.6%) patients in group 1, while group 2 consisted of 44 (52.4%) patients. There was no significant difference between the groups regarding gender distribution (p=0.705). There were more female patients than male patients in both groups. The mean DVIS score was significantly higher in group 2 than in group 1 (17.4±5.9 vs. 13.9±7.19; p=0.017). The overall rate of VUR was 31% in the entire cohort (n=26). Our comparative analysis revealed that the rate of VUR was significantly higher in group 1 than in group 2 (45% vs. 18.2%; p=0.008). The mean voided urine volume, max flow rate, and PVR was similar between the two groups (p=0.236, p=0.381, p=0.460, respectively). No significant difference between the groups was noted regarding the flow pattern (p=0.09). However, staccato and tower type flow patterns were encountered at higher rates in group 2 without reaching the level of significance (Table 1).

The univariate analysis elucidated that the VUR rate was negatively correlated with PUD; the rate of VUR was higher in patients with relatively shorter PUDs with an adjusted odds ratio (AOR) of 0.61 [AOR 95% confidence interval (CI): 0.61 (0.43-0.86), p=0.005]. Multivariate analysis confirmed the negative correlation between these two parameters (i.e., PUD and VUR) [AOR (95% CI): 0.36 (0.21-0.59), p=0.001]. These analyses also showed that female gender and DVIS scores were associated with the presence of VUR [AOR (95% CI): 4.33 (1.09-17.2), p=0.03, and AOR (95% CI): 1.46 (1.12-1.65), p=0.002)] (Table 2).

Discussion

The VD is widely ascribed to poor voiding habits, the etiology of proximal urethral dilatation -a common finding in these patients- has not been fully clarified yet. However, it was

Table 1. Comparison of the parameters between the two groups

	Group 1* n=40 (47.6%)	**Group 2* n=44 (52.4%)**	**p-value**
Gender			
Boy (n, %)	18 (45%)	18 (40%)	0.705
Girl (n, %)	22 (55%)	26 (60%)	
DVIS	13.9±7.19	17.4±5.9	**0.017**
VUR+ (n, %)	18 (45%)	8 (18.2%)	**0.008**
Mean Q_{max} (mL/sec ± SD)	16.1±6.34	17.3±6.02	0.381
Mean voided volume (mL ± SD)	192±80.3	213±80.3	0.236
Flow pattern			
Staccato (n, %)	9 (22.5%)	14 (31.8%)	0.090
Tower (n, %)	9 (22.5%)	15 (36.1%)	
Interrupted (n, %)	6 (15%)	8 (18.2%)	
Bell (n, %)	15 (37.5%)	5 (11.4%)	
Plateau (n, %)	1 (2.5%)	3 (4.5%)	
Mean PVR (mL ± SD)	16.4±14.5	17.3±12.8	0.460

*Group 1: Proximal urethral diameter ≤7.6 mm, Group 2: Proximal urethral diameter >7.6 mm, SD: Standard deviation, PVR: Post-void residual measurements, DVIS: Dysfunctional voiding incontinence scoring, VUR: Vesicoureteral reflux

Table 2. Univariate and multivariate analyses of potential prognostic factors for vesicoureteral reflux

Parameters OR (95% CI)		Univariate		Multivariate	
		p-value	OR (95% CI)	p-value	
Proximal urethral diameter (mm)	≤**7.6** >**7.6**	Ref. 0.61 (0.43-0.86)	**0.005**	Ref. 0.36 (0.21-0.59)	**0.001**
Gender	**Male** **Female**	Ref. 4.33 (1.09-17.2)	**0.03**	Ref. 1.35 (0.82-8.3)	0.12
Dysfunctional voiding score		1.46 (1.12-1.65)	**0.002**	1.12 (0.94-1.36)	0.08

OR: Odds ratio, CI: Confidence interval

postulated that, in these children, the voluntary contractions during voiding led to the contraction of the distal urethral sphincter and a subsequent pressure increase in the proximal urethra. The increased pressure, which persists until the relaxation of the external urethral sphincter relaxes, also affects the proximal urethra. At this stage, the proximal urethra starts to dilate for compliance. This dilatation appears as an infundibular-shaped tube in VCUG (Figure 1) (7-9).

It was reported that PUD is more common in girls than in boys (7,9). Urethral sphincters are looser in girls than in boys. Besides, the bladder neck's anatomical features in males also contribute to the difference in the proximal urethral dilatation rates between male and female children (9). In line with these data, among the patients with VD who underwent VCUG, proximal urethral dilatation was encountered 6-fold more frequently in girls than in boys (7,9). As such, in our study, there were more girls than boys in both groups. This finding was more prominent in group 2 than group 1. However, no significant difference was detected between the groups concerning gender distribution (p=0.705). These findings may be due to the small patient number in our study.

It was previously reported that urgency (87.3%), frequency (81.8%), daytime incontinence (76.3%), and enuresis (47.2%) were the most frequently encountered symptoms in patients with VD, and there was a significant correlation between the presence of these symptoms, VD and proximal urethra dilatation (4). In some other studies, it was noted that the most common symptom was urgency, and it was present in 52-87% patients with VD (3,10). These studies also reported that daytime and nighttime incontinence could be detected in up to 77% of these patients. We use the DVIS system defined by Akbal et al. (11) for scoring the VD. Our comparative analysis revealed that the mean DVIS score was significantly higher in group 2 (i.e., patients with relatively higher PUD) than in group 1 (i.e., patients with relatively lower PUD) (p=0.0017). We also found that PUD and DVIS scores (i.e., the severity of disease) were correlated with each other.

UTI and VUR can accompany VD (11). High intravesical pressure in patients with VD leads to ischemia in the bladder mucosa. Both ischemia and the urine returning to the bladder from the urethral meatus and transferring bacteria to the bladder increase UTI risk (12). It has been demonstrated that high intravesical pressures in patients with VD amplify the risk of VUR and its severity (6). It was reported that in patients with VUR and overactive bladder, gradually increasing pressure resulting from the resistance of the pelvic floor and external urethral sphincter to the involuntary contractions increases the risk of renal damage (6). In a study including 121 patients, Kibar et al. (7) determined that the rate of VUR was 81% in patients diagnosed with spinning top urethra. In another study, it was reported that 12.7% of the patients with VD had VUR by VCUG (4). However, the rate of VUR in patients with proximal urethral dilatation was not analyzed.

Our study found a negative correlation between the PUD and VUR by univariate and multivariate analyses. These analyses also showed that VUR was more frequently encountered in girls with high DVIS. We postulate that an increase in the PUD and urethral compliance reduces both the intravesical pressure and intramural pressure in the urinary bladder. Besides, an insufficient increase in PUD can lead to a rise in bladder pressure and the risk of VUR.

Staccato and tower type flow patterns detected in uroflowmetry tests are considered to be diagnostic of VD (3). In our study, there was no association between PUD and voiding patterns. However, staccato and tower patterns were detected more frequently in group 2.

It was reported that the mean PVR was significantly higher in patients with VD and proximal urethral dilatation than in healthy persons (13). In our study, there was no difference between the two groups regarding mean PVR (p=0.46). The difference between the PUDs did not lead to a significant difference between the groups regarding flow patterns and PVR.

The ideal method for diagnosing VD is urodynamic testing (5). However, some parameters obtained by VCUG can reduce the number of patients undergoing this invasive procedure. Kakizaki et al. (5) reported that an inner external urethral sphincter diameter of less than 3 mm measured during the voiding phase of VCUG indicated detrusor-sphincter incoordination. They stated that urodynamic testing was necessary for these patients.

This study has set a cut-off value using the data obtained from VCUGs performed in children without VD. They also showed that in 96% children with normal voiding, the external urethral sphincter's inner diameter was determined to be 3 mm and above in VCUG (5).

In our study, we did not determine a cut-off value for PUD to indicate VD. This limitation was because it was a retrospective study, and it was not appropriate from an ethical perspective to perform VCUG in healthy children to measure PUD. Besides, only children aged between 6 and 8 were included in our study.

Some studies showed that the possibility of urodynamically diagnosed overactive bladder was relatively high in children who had symptoms of VD and VCUG findings were consistent with trabeculation, spinning top urethra, and the low bladder capacity in the urinary US (4,14). These studies reached an actual diagnosis without performing invasive urodynamic tests.

Conclusion

The determination of age-specific cut-off values for PUD in VCUG by prospective studies can open up new perspectives for assessing children with VD. We suggest that the utilization of parameters including PUD, bladder wall thickness, bladder capacity, symptom scores, and uroflowmetric parameters can reduce the need for performing invasive urodynamic procedures to diagnose VD.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Ethical Committee of Muğla Sıtkı Koçman University (approval number: 180079).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.T., İ.A., S.C.K., N.C., H.Ş., Concept: H.T., İ.A., Design: H.T., İ.A., Data Collection or Processing: S.C.K., N.C., H.Ş., Analysis or Interpretation: H.T., İ.A., Literature Search: S.C.K., N.C., H.Ş., Writing: H.T., İ.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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