

Detection of bladder trabeculation by voiding cystourethrography and sonography: observations in boys with posterior urethral valves

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To cite: Thümingner J, Haid B, Oswald J. Detection of bladder trabeculation by voiding cystourethrography and sonography: observations in boys with posterior urethral valves. *World Jnl Ped Surg* 2021;4:e000245. doi:10.1136/wjps-2020-000245

Received 1 December 2020
Accepted 10 May 2021

ABSTRACT

Background As trabeculated bladder wall is often referred to as a sign of chronically increased intravesical pressure, we investigated whether voiding cystourethrography (VCUG) or sonography reliably predicts bladder trabeculation on later urethrocystoscopy.

Methods A total of 76 consecutive patients (2012–2017) with cystoscopically confirmed posterior urethral valves (PUV) and pre-endoscopy VCUG were included. Sonography data were available for 68 of these patients. Radiological findings were reassessed and compared with endoscopic findings using Fisher's exact test and Spearman's rank assessment.

Results VCUG showed a sensitivity of 83.3% and a specificity of 30% in predicting trabeculation on a later urethrocystoscopy, with no significant difference in determining mild or severe forms ($p=0.51$). Sonography proved a sensitivity of 27.6% and a specificity of 70%, with no correlation between sonographic signs and trabeculation on cystoscopy ($r=0.1311$). In addition, vesicoureteral reflux had no significant influence as a possible pressure pop-off mechanism on the development of trabeculation in our group.

Conclusions While VCUG predicts bladder trabeculation in children with PUV with limited reliability, sonography mostly fails to detect trabeculation. Therefore, such findings should only be used with utmost caution in relation to clinical decision-making.

INTRODUCTION

Bladder trabeculation on endoscopy is a sign of detrusor hypertrophy in response to infravesical obstruction. In the pediatric population it is mainly caused by posterior urethral valves (PUV) and detrusor overactivity. Chronically increased intravesical pressure results in remodeling of the bladder wall (characterized by bladder wall hypertrophy and fibrosis) and is accompanied by decreased bladder wall compliance. Morphological changes resulting from this process are trabeculation and formation of diverticula. Trabeculations are seen on cystoscopy as a coarsely interwoven appearance to the mucosal surface formed by muscular bundles

Key messages

What is already known about this subject?

- ▶ Bladder trabeculation is often found in conjunction with bladder outlet obstruction or (neurogenic) detrusor overactivity.
- ▶ It is an important clinical finding pointing at remodeling and fibrosis of the bladder wall.
- ▶ Radiological grading systems of trabeculation for voiding cystourethrography (VCUG) have been described in the literature.

What are the new findings?

- ▶ The sensitivity of VCUG and sonography in detection of bladder trabeculation in boys with posterior urethral valve is limited.
- ▶ The presence of vesicoureteral reflux does not seem to affect the extent of bladder trabeculation in this cohort.

How might it impact on clinical practice in the foreseeable future?

- ▶ Therapeutic decisions based on the presence of bladder trabeculation should not rely on ultrasound findings.

with deposits of interstitial collagen. These underlying changes in detrusor muscle architecture occur mainly at the bladder body and less at the bladder base associated with the differential vegetative innervation.¹

In boys with vesicoureteral reflux (VUR), the stress to bladder wall and detrusor muscle might be weaker than that in boys without VUR. Nevertheless, PUV is a high-risk condition for trabeculation.²

In children, among others, partly subtle radiological sign or sonographic finding of a trabeculated bladder is of paramount importance in early diagnosis of infravesical obstruction. This might allow for timely medical (eg, anticholinergics) or surgical (eg, relief of infravesical obstruction, botulinum toxin detrusor injections) interventions aiming at



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preservation of bladder function as well as compliance and prevention of renal function loss.³

In the absence of urodynamic data, a non-invasive diagnosis of a trabeculated bladder wall might significantly influence further decision-making in a clinical setting.

This study aimed at investigating the reliability of voiding cystourethrography (VCUG) and sonography in predicting the presence of trabeculation on endoscopy.

METHODS

Patients

Data from boys with endoscopically confirmed PUV treated at a single institution (n=178) between 2012 and 2017 were reviewed. The goal was to form a high-risk group with a high prevalence of bladder trabeculation to obtain meaningful results.

PUVs were divided into 'typical' or Young type 1 and 'atypical' or Young type 3 (limited to membranes at a 12 o'clock position or localized farther distal to the verumontanum).⁴ Unequivocal membranes at a typical position associated with the verumontanum with limited extent were classified as 'abortive' PUV. As reported in the literature a sickle-shaped knife was employed during cystoscopy to examine the extent and depth of PUV.⁵

All consecutive boys who underwent first endoscopy after having undergone imaging (n=140), with all data and images relating to bladder trabeculation on VCUG and endoscopy (n=76) as well as sonography (n=68) available, were included. The exclusion criteria only pertained to availability of any radiological findings and not to clinical characteristics (eg, symptoms, age, etc). Patient characteristics are summarized in [table 1](#). Spearman's correlation and Fisher's exact test were used for statistical analysis using Prism V.6.0 (GraphPad Software, San Diego, California). The cut-off for the alpha error was defined as <0.05.

Cystoscopy

Urethroscopy was performed by five different pediatric urologists using an 8/9, 8 Fr compact pediatric

cystoscope. Findings were classified into mild and severe trabeculation according to the examiner's assessment.

Voiding cystourethrography

We perform VCUG on different indications, including febrile urinary tract infections, suspicious sonography findings (megaureters and/or hydronephrosis) and symptoms of dysfunctional micturition. The standardized procedure includes transurethral catheterization using a 4.5 Fr (<1 year of age) or a 6 Fr (>1 year of age) feeding tube. The bladder is then slowly filled with warm iodine containing contrast agent. For exclusion of anatomical anomalies, a fluoroscopic image of the pelvic region and the spine is made, followed by calibration of the fluoroscopy unit to the lowest reasonable tube tension. At least two, but if possible three, filling and voiding cycles are recorded by last image hold fluoroscopy. In boys VCUG always includes lateral imaging of the urethra and the bladder.

The pediatric urologist performing the examination primarily interpreted the images in this study. Additionally, and especially to indicate an eventual more invasive assessment by cystoscopy, pictures were demonstrated during regular conferences and discussed by multiple pediatric urologists. For the purposes of this study, all images were re-evaluated for signs of a trabeculated aspect of the bladder during filling after detailed determination of reference standards for each pathology to avoid any bias and to render the interpretation as objective as possible. Each questionable case was reviewed together with BH, who was blinded to the endoscopic findings until a clear consensus had been reached ([figure 1](#)).

Sonography

Sonography was performed by pediatric urologists with dedicated training (minimum 6 years) in urogenital sonography using state-of-the art equipment (GE Voluson, Siemens Acuson with high-resolution 6–9 MHz probes). Potential signs of detrusor alterations concordant with bladder trabeculation (thick, 'accentuated', irregularly appearing bladder wall) were recorded

Table 1 Patient characteristics (76 boys, all with endoscopic diagnostics)

	Trabeculation during cystoscopy			
	Total (n=76)	Severe (n=33)	Mild (n=33)	None (n=10)
Age at diagnosis (mon), mean/median	25.03/14.1	31.5/12	21.4/15	22.2/15.5
Age ≤3 mon at endoscopy, n	9	8	1	0
Diagnosis <12 mon of age, n (%)	25 (32.8)	16 (48.5)	8 (24.25)	1 (10)
Trabeculation on VCUG and false positives, n	62	29	26	7
No trabeculation on VCUG and false negatives, n	14	4	7	3
Bladder wall abnormalities on sonography, n	19	11	5	3
Unsuspectious bladder wall on sonography, n	49	19	23	7
Vesicoureteral reflux, n (%)	50 (65.7)	20 (60.6)	23 (69.7)	7 (70)

VCUG, voiding cystourethrography.

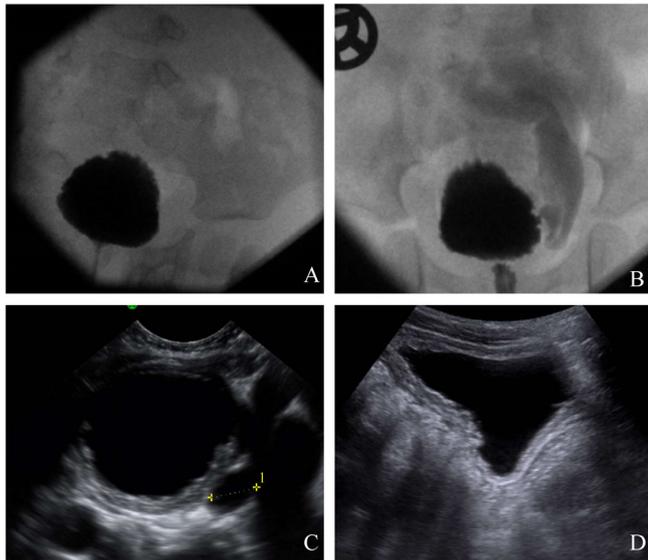


Figure 1 Radiological (A and B) and sonographic (C and D) reference images for ‘trabeculated bladder’ (all from different patients with posterior urethral valves).

with both the report as well as the images being reviewed for study-associated data assessment. Because of varying bladder filling and the inherent limitations, no bladder wall thickness measurements were performed, and the judgment whether trabeculation was suspected lay in the eyes of the sonographer (each $n > 500$ kidney and bladder ultrasound examinations per year) (figure 1).

All investigators and clinicians interpreting the sonography and VCUG images were board-certified urologists with a special training in fluoroscopy and sonography diagnostics. Radiologists are not involved in diagnostic image interpretation in these modalities in our country.

RESULTS

On endoscopy, 66 of 76 (86.8%) boys showed bladder wall trabeculation (50% mild and 50% severe).

Voiding cystourethrography

Review of the preoperative VCUG images revealed signs of trabeculation in 62 (81.6%) boys. Compared with endoscopy, 7 (11.2%) were false positive, whereas 11 (17.7%) were false negative, showing mild ($n=7$, 11.2%) or severe ($n=4$, 6.5%) trabeculation on endoscopy. These results translate into a sensitivity of 83.3% and a specificity of 30%.

Of the 33 patients with mild trabeculation on cystoscopy, 26 (78.8%) showed trabeculation on VCUG. Of the 33 patients with severe trabeculation on cystoscopy, 29 (87.8%) showed trabeculation on VCUG. There was no significant difference in radiological detection rate comparing mild versus severe trabeculation (Fisher’s exact test $p=0.51$, 95% CI 0.72 to 1.11).

Spearman’s rank assessment showed no correlation between expression of trabeculation on cystoscopy and VCUG (Spearman’s rank $r=0.12$, 95% CI -0.12 to 0.34).

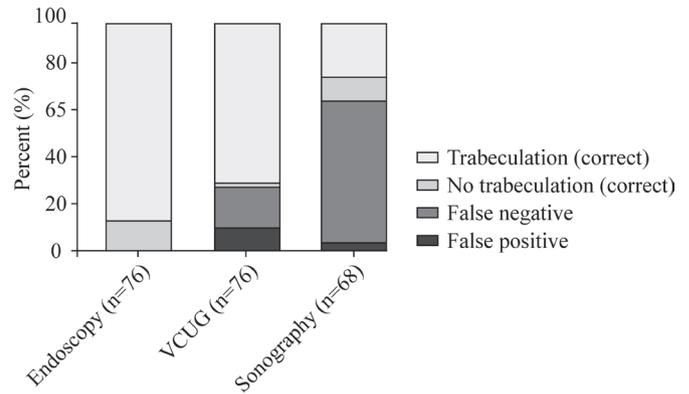


Figure 2 Percentage of correctly predicted trabeculation/ no trabeculation, false negatives and false positives for either method (VCUG, voiding cystourethrography). VCUG yielded three true negatives (no trabeculation), resulting in a very thin red bar that is hardly visible.

Furthermore, there was no correlation between severity of trabeculation on cystoscopic findings and trabeculation on VCUG (Spearman’s rank $r=0.16$, 95% CI -0.076 to 0.38) (figure 2).

Additionally, we investigated our patients concerning VUR. Of the 76 boys, 50 (65.8%) demonstrated VUR on VCUG (33 unilateral, 17 bilateral). A total of 43 (86%) of these also showed trabeculation on endoscopy (20 severe and 23 mild).

In the group with unilateral reflux ($n=33$), 28 (84.8%) patients had a trabeculation confirmed during cystoscopy (16 severe and 12 mild), and in patients with bilateral reflux ($n=17$) 15 (88.2%) showed trabeculation (4 severe and 11 mild). Of the boys without VUR ($n=26$), 23 (88.5%) showed trabeculation (13 severe and 10 mild). There was no significant difference in trabeculation comparing VUR versus no VUR (Fisher’s exact test $p=1$). Also, there was no significant difference in the incidence of severe and mild trabeculation comparing VUR versus no VUR (Fisher’s exact test $p=0.61$).

Sonography

On sonography, 19 of 68 (27.9%) boys had bladder wall abnormalities concordant with a possible bladder trabeculation. Among these, 16 (84.2%) showed a trabeculated bladder wall on endoscopy, while 3 (15.8%) turned out false positive. In total, 42 (61.7%) were false negative, showing mild ($n=23$) or severe ($n=19$) trabeculation on endoscopy, translating to a sensitivity of 27.6% and a specificity of 70%.

A total of 5 (15.15%) boys with endoscopically mild trabeculation and 11 (33.3%) with severe trabeculation showed corresponding sonographic signs of possible bladder wall changes (Fisher’s exact test $p=0.15$, 95% CI 0.10 to 1.18).

No correlation between conspicuous sonography findings and trabeculation on cystoscopy was found (Spearman’s rank $r=0.13$, 95% CI -0.12 to 0.36) (figure 2).

DISCUSSION

While clinically important, trabeculation of the bladder wall cannot be reliably detected or excluded with non-invasive methods, with sonography being inferior to VCUG. There have been several attempts to establish grading systems for trabeculation on VCUG. Selby *et al*⁶ developed one for VCUG images in children with neurogenic bladder. They accomplished a strong inter-rater and intrarater reliability, but did not reference these results to endoscopy findings.⁶

In the pediatric age group, however, the early detection of changes relating to the compliance and function of the detrusor muscle might be crucial.⁷ In children, the presence of severe bladder trabeculation is related to infravesical obstruction, influencing clinical decision-making.⁸ Similarly, in adults trabeculation on endoscopy has been clearly proven to be correlated with bladder outlet obstruction in the context of prostatic hyperplasia.⁹ Bloom *et al*¹ showed a distinct pattern of trabeculation on cystography in 72% (similar to the 86.6% in our study) of a group of boys with severe PUV (n=47), but they did not correlate the imaging findings to endoscopy.

In adults with neurogenic bladder disease as a high-risk factor for increased intravesical pressure, the correlation between VCUG and endoscopy was moderate, comparable with our findings. Limited by the different etiology, endoscopically proofed trabeculation correlated with urodynamic signs of obstruction.¹⁰ Jung *et al*¹⁰ used a grading system for VCUG in adults which had been established by Cho *et al*¹¹ in 2013, and they demonstrated its clinical significance when matching urodynamic results with the fluoroscopic grades of trabeculations.

Interestingly, signs of ‘trabeculation’ as seen on VCUG despite the possibility of false positive findings seem to correlate with the presence of otherwise unsuspected PUV.³

In our study no significant difference in endoscopically confirmed trabeculation was found comparing patients with VUR and without VUR. In patients with bilateral VUR, trabeculation was as common (>80%) but mostly mild compared with boys with unilateral VUR or no VUR. This might be taken as a hint for a potential pressure pop-off with implications to bladder dynamics similar to that described in the past for (contralateral) kidney function.^{2 12} In line with these findings, a recent study showed no benefit for long-term renal function through a possible pop-off mechanism through VUR.¹³ D’Oro *et al*¹⁴ investigated a group of boys with PUV and pressure pop-offs and came to the conclusion that the pop-off mechanism does not have a significant benefit to bladder outcomes but merely indicates more severe bladder dysfunction. VUR—independent of infravesical obstruction—might be connected to bladder dysfunction and, hypothetically, also contribute to detrusor hyperactivity and consequent trabeculation as well.¹⁵

Our study is limited by the lack of urodynamic data that are not available for most of our patients. According to previous literature urodynamic measurements might be

a good way to predict the development of trabeculation in cases with chronically increased intravesical pressure. However, in our particular group of pediatric patients, it is questionable whether an additional invasive examination can be justified.

Furthermore, the assessment of images and endoscopy relied on the two investigators’ experience, as no validated systems in children were available. Image interpretation by (pediatric) urologists is standard in our country; radiologists are usually not involved, and there is no reason to believe that their interpretation might have been different. Nevertheless, we cannot exclude that, especially pertaining to ultrasound with a higher interobserver variability, there might have been a higher detection rate with the examinations having been performed by even more experienced specialists. Moreover, radiation-saving VCUG technique and therefore relatively low image quality might account for some false negative findings in this series. The exclusion of a relatively large number of patients based on the availability of images and the sequence of examinations conducted does not affect the results of this study as still consecutive patients are included.

In conclusion, VCUG has a moderate sensitivity (83.3%) and a low specificity (30%) to reliably predict or exclude bladder trabeculation in children with PUV as seen on endoscopy. Sonography is even less reliable (sensitivity 27.6%, specificity 70%). ‘Trabeculation’ as often described on VCUG and sonography should be incorporated into clinical decision-making only with utmost scrutiny with ‘negative’ sonography findings being not able to rule out even severe trabeculation on endoscopy. Cystoscopy seems to be the only reliable method to investigate trabeculation of the bladder wall in high-risk children.

Acknowledgements We thank Franz Zimmermann for critical reading of the manuscript.

Contributors TJ contributed to conceptualization, methodology, formal analysis, data curation and writing—original draft. BH was involved in conceptualization, methodology, formal analysis, resources, data curation, writing—review and editing project, administration. JO contributed to conceptualization, writing—review and editing, supervision.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol of this retrospective study is in accordance with the ethical standards of the institutional research committee (Gemeinsame Ethikkommission der Barmherzigen Schwestern+Barmherzige Brüder, EKS 38/17, approved on November 2, 2017) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animals were involved in this research.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are stored by the authors and their institutions and are available upon reasonable request.

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