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ARTICLE

Evaluation of boys with daytime incontinence by combined cystourethroscopy, voiding cystourethrography and urodynamics

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ABSTRACT

Objects: Approximately, 1% of school children have daytime urinary incontinence. The symptoms may be caused by an overactive bladder (OAB). In the evaluation of boys with OAB complaints, one should consider a possible urethral cause. The aim of the study was to evaluate the value of a diagnostic regime with cystourethroscopy, voiding cystourethrography (VCUG) and urodynamic pressure-flow studies in boys with OAB complaints after unsuccessful urotherapy and pharmacological therapy. **Materials and Methods:** Seventy-five boys (5–14 years old) were investigated with cystourethroscopy and within 24 h thereafter VCUG followed by urodynamic combined cystometry and pressure-flow study. All boys had daytime incontinence and urgency. **Results:** Sixty-one boys had no suspected urethral valves at cystoscopy or VCUG, and urodynamics showed no obstructed Pdet-Qmax. All 61 boys had detrusor overactivity. Two boys had late diagnosed urethral valves. In four boys, the initial cystourethroscopy was described as normal. The VCUG indicated presence of posterior urethral valves, but urodynamics showed no obstructed Pdet-Qmax. In eight boys, the initial cystourethroscopy was described as normal whereas urodynamics showed obstructed Pdet-Qmax. In four of these boys, VCUG showed abnormalities in the sphincter area but they were not described as suspected urethral valves. At repeat cystourethroscopy, urethral valves could still not be identified. Patient follow-up regarding achievement of continence after investigation guided treatment was in accordance with the literature. **Conclusions:** Boys can be safely evaluated by cystourethroscopy followed by urodynamics in search for a possible urethral problem. It is our suggestion, that VCUG can be restricted to those boys where urodynamics indicates obstruction or the findings by cystourethroscopy are uncertain.

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Introduction

Approximately, 1% of school children have daily problems with urinary incontinence, frequency and urgency [1]. Girls are affected around four times as often compared to boys [2].

The symptoms may be caused by nonneuropathic bladder-sphincter dysfunction having two main clinical expressions: dysfunctional voiding (urodynamically defined as an emptying phase abnormality with detrusor-sphincter dyscoordination impeding normal voiding) and urge syndrome or overactive bladder (OAB) (urodynamically defined as a filling phase abnormality with idiopathic detrusor overactivity throughout bladder filling) [3]. In the evaluation of boys with OAB complaints with absence of signs of spinal dysraphism, one should consider a possible urethral cause of OAB. In cases of an evident meatal stenosis or obstructive flow pattern at repeated uroflowmetry, the decision to treat the obstruction by surgery is easily taken. According to the International Children's Continence Society (ICCS), in cases where urethral obstruction is not obvious, first-line treatment should start with an understanding of the bladder and sphincter function, urotherapy [4]. Standard urotherapy includes behavioral modifications such as optimal toilet posture, timed or scheduled voids, avoidance of holding maneuvers and other lifestyle advices, but is thereafter often supported by pharmacological therapy. For those, who fail to obtain relief from OAB complaints, one should focus on a possible urethral problem. This is a relatively large group of patients because the success rate of conservative and pharmaceutical treatment of OAB rarely exceeds 50% [2]. The investigations to consider include cystourethroscopy, voiding cystourethrography (VCUG) and urodynamic pressure-flow studies. However, a consensus on evaluation strategy is not settled. All three investigations have different advantages, limitations and drawbacks. The aim of the present study was to evaluate the value of a two days diagnostic regime with cystourethroscopy, VCUG and urodynamic pressure-flow studies implemented on boys with persistent OAB complaints after unsuccessful urotherapy and pharmacological therapy.

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Materials and methods

Between 2010 and 2018, we investigated 75 boys aged 5–14 (median age 9) years old according to a prospective set-up with cystourethroscopy including application of a suprapubic catheter in general anesthesia and within 24 h thereafter VCUG followed by urodynamic combined cystometry and pressure-flow study. All boys had daily problems with urinary incontinence, urgency and eventually frequency (more than seven times per day). The median number of daily voiding was 7 and 57% (43/75) of the boys had frequency. Nocturnal enuresis, defined as bedwetting at least once a month, was also noted in 46 boys. Prior to inclusion all boys had previously tried urotherapy for a period of 3 months to 5 years (median 1 year) and the minority (23%, 17/75) had additionally included periods of anticholinergic treatment with unsatisfactorily effect. The urotherapy regime included evaluation and regular monitoring with three days frequency volume charts, uroflowmetry and bladder emptying by ultrasonography. None of the boys had any previous episodes of urinary tract infection (UTI) recorded. None of the boys had neurological symptoms or abnormalities and none had obstructive flow pattern at repeated uroflowmetry. All the boys had normal upper urinary tract estimated by ultrasound examination. The boys had follow-up for 1 month to 9 years (median 2 years and 8 months).

At cystourethroscopy, the urethra was carefully inspected for presence of urethral valves including observation of sphincter area and posterior urethra after stop of filling inflow but during manual induced outflow by compression of the full bladder. The bladder wall was described as normal or trabeculated. Three boys with abnormal ureteral orifices or diverticula were excluded and they did not differ in terms of symptoms. Finally, a 6F duple-lumen suprapubic catheter was applied and the correct intravesical placement confirmed cystoscopically.

At VCUG, the bladder was filled with contrast medium using the 6F suprapubic catheter under fluoroscopic guidance at a slow filling rate with a maximal height of the contrast bottle of 40 cm. During voiding, steep oblique images of the lower urinary tract were taken. Findings of vesicoureteral reflux (VUR) grade 1–2 were accepted in these boys with no history of UTI. Boys with higher grade VUR were excluded.

It was noted whether the bladder wall was normal or if serration was present.

The following aspects were noticed during voiding: normal or abnormal opening of the bladder neck, indications of a posterior urethral valve with dilatation of the posterior urethra or suspicion of an obstruction in sphincter area. This last addition was introduced to distinguish pelvic floor activity from anatomic obstruction. Naturally, it was also noted if the urethra looked normal during voiding.

Medium fill water cystometry was carried out using the duple-lumen suprapubic catheter for filling and pressure measurement via connection to the transducer. A feeding tube 8F was passed intrarectally and the intra-abdominal pressure was measured. During cystometry, it was noted whether detrusor overactivity was present and if so, the amplitudes of the overactive detrusor contractions were measured. It was specially noted if the amplitudes exceeded 15 cmH_2O or in contrast if it exceeded 100 cmH_2O. Maximum cystometric bladder capacity and percentage of expected normal capacity were measured. During the pressure-flow study, the following urodynamic parameters were used for analysis: Qmax (maximum flow rate), Pdet-Qmax (detrusor pressure at Qmax) and a dynamic pressure-flow plot as generated by the MMS (Medical Measurement Systems BV, Enschede, Netherlands) software and graded as normal, equivocal or obstructed according to ICS (International Continence Society) software app on the MMS system. Due to the transurethral instrumentation performed the day before urodynamics, some urethral edema could not be excluded, and 93% (70/75) of the boys had a prepubertal urethra and were younger than 13 years old. Therefore, we did not accept the equivocal area of the ICS detrusor-flow plot, defined from an adult normal material, as obstructed.

Plain X-ray of the columna thoraco-lumbo-sacralis was performed routinely and in cases where spina bifida occulta was diagnosed, an MRI-scan of the spine was offered.

The present study follows the principles of the Declaration of Helsinki.

Results

Diagnostics

Sixty-one boys (81%, 61/75) had no suspected urethral valves at cystoscopy or VCUG and urodynamics showed no obstructed Pdet-Qmax. At cystoscopy, a trabeculated bladder was diagnosed in 29 of these boys (48%, 29/61) and serration on VCUG was also present in 16 of these boys (55%, 16/29), but also in 16 of 32 boys (50%) with normal bladder wall at cystoscopy serration on VCUG was demonstrated. Hence, the frequency of serration was identical in those with normal compared to those with trabeculated bladder wall at cystoscopy ($p=.69$ (Chi-square)). Five of the 61 boys (8%) had unilateral VUR grade II. In six of the 61 boys (10%), VCUG showed an incomplete relaxation of the sphincter area during voiding. All 61 boys had detrusor overactivity and in 93% (57/61) of the cases, the detrusor contractions exceeded 15 cmH_2O and in 12% (7/61) detrusor contractions even exceeded 100 cmH_2O (Figure 1). Further urodynamic parameters of the group are shown in Table 1.

Two boys had late diagnosed urethral valves. One of the boys was 7 years old at referral. The surgeon was at the initial cystourethroscopy uncertain about whether valves were present or not, but the VCUG indicated presence of urethral valves and urodynamics indicated obstruction (Figure 2). At repeat cystourethroscopy, posterior urethral valves were found and resected. The other boy was 8 years old at referral. The initial cystourethroscopy was described as normal, while VCUG showed abnormalities in the sphincter area and urodynamics indicated obstruction (Figure 3). At repeat cystourethroscopy, posterior urethral valves were found and resected.

In four boys, the initial cystourethroscopy was described as normal. The VCUG indicated presence of posterior urethral

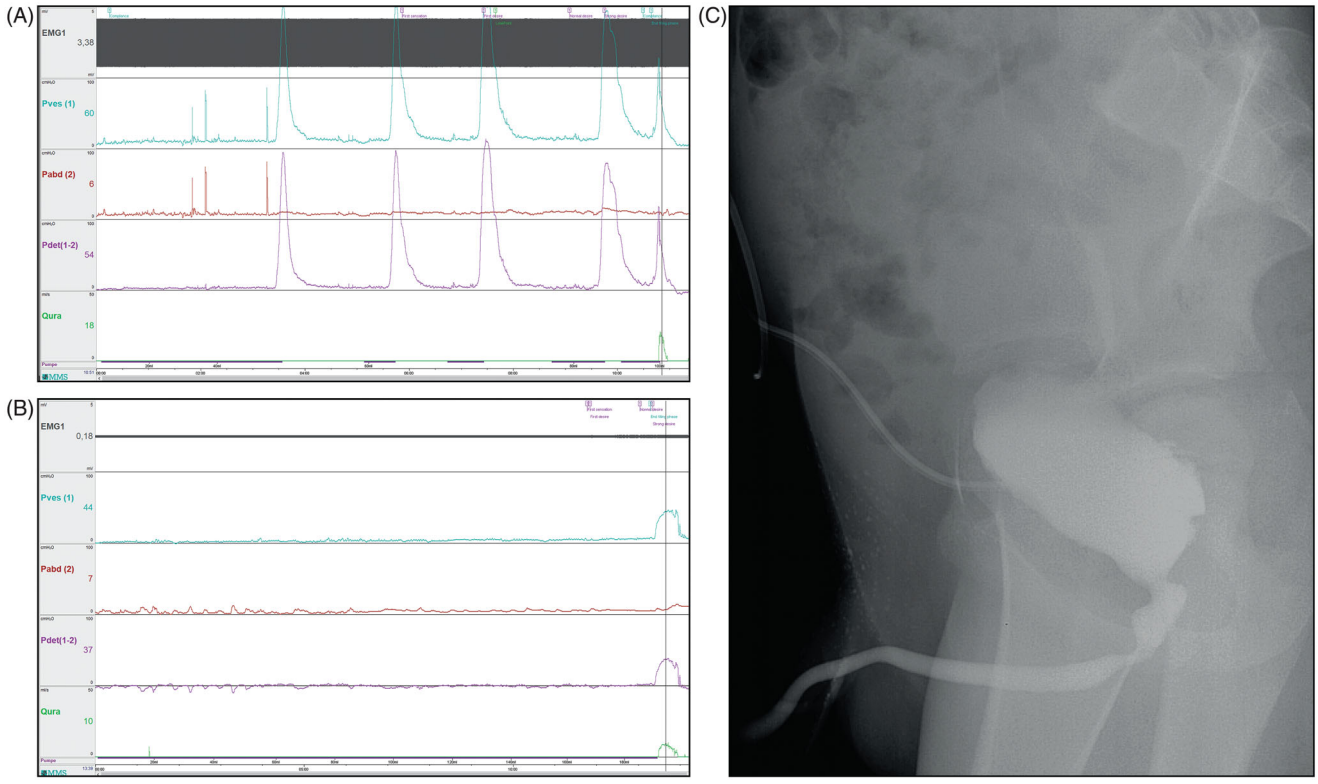

Figure 1. Urodynamic combined cystometry and pressure-flow study and VCUG in a boy with severe daily urge-incontinence at referral 8 years old. (A) Urodynamics showed overactive detrusor contractions during filling > 200 cmH_2O. Bladder capacity 38 ml, Pdet-Qmax 54 cmH_2O, Qmax 18 ml/s. (C) VCUG shows small bladder with serration and irregular posterior urethra and sphincter area. After two times transurethral Botox injections with one-year interval at 9 and 10 years of age, he has been cured now for 5 years follow-up. (B) Post treatment urodynamics showed normal cystometry and pressure-flow. Bladder capacity 116 ml, Pdet-Qmax 37 cmH_2O, Qmax 10 ml/s.

Table 1. Urodynamic parameters in 75 boys aged 5–14 years old.

Group No. of patients	Age (years)	Max cystometric bladder capacity	% of max cystometric bladder capacity (norm)	Max amplitude of overactive detrusor contraction	Qmax	Pdet-Qmax
N = 55 (8–80)[a] No suspected urethral valves at cystoscopy, VCUG or urodynamics	9 (5–14)	127 (31–584)[a]	46 (9–146)[a]	33 (6–237)	17 (8–39)	47 (8–80)[a]
N = 6 (34–61) No suspected urethral valves at cystoscopy, VCUG or urodynamics but incomplete relaxation of the sphincter area	10.5 (6–14)	145 (43–312)	40 (20–95)	33 (8–106)	14 (8–25)	51.5 (34–61)
N = 4 (29–72) Suspected urethral valves at VCUG but not otherwise confirmed with certainty	10 (9–12)	145 (92–279)	44 (31–72)	39 (22–55)	20 (8–42)	48.5 (29–72)
N = 8 (49–250) Obstructed Pdet-Qmax but urethral valves not otherwise confirmed	10 (6–12)	105 (36–285)	34 (13–86)	45 (4–252)	7 (2–12)	105 (49–250)
N = 2 Late diagnosed urethral valves	7, 8	65, 84	27, 31	16, 54	11, 13	84, 80

Values in median and (range).
[a]This group includes one boy 10 years old with only two voluntary voidings daily, a 584 ml large bladder (146% of expected capacity) OAB, but only weak detrusor pressure (8 cmH_2O) at Qmax.

valves (Figure 4), but urodynamics showed no obstructed Pdet-Qmax. Further urodynamic parameters of the group are seen from Table 1. At repeat cystourethroscopy, urethral valves could still not be identified. However, in one of these four cases, the surgeon did a cold hook-knife cut 4 and 8 o'clock at the lower level of the colliculus guided by the VUCG, without being convinced that there were truly valves present.

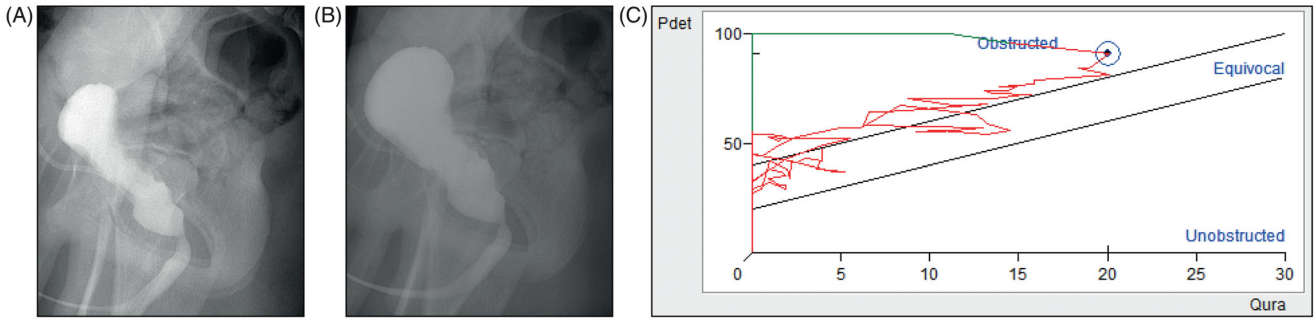

Figure 2. VCUG and urodynamics of a 7 years old boy presenting with urgency and daily incontinence. (A, B) VCUG indicated presence of urethral valves and (C) urodynamics indicated obstruction.

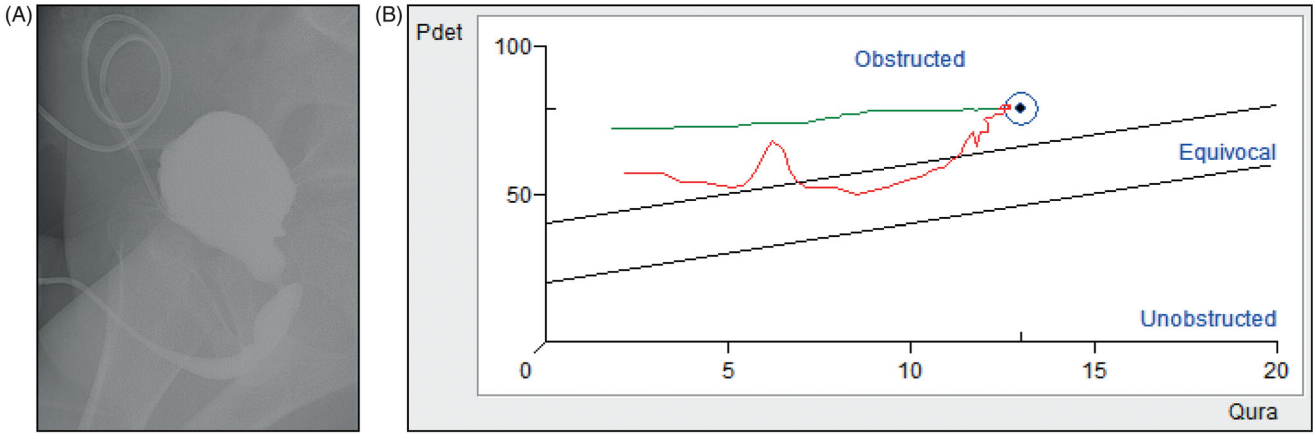

Figure 3. VCUG and urodynamics of a 8 years old boy presenting with urgency and daily incontinence. (A) VCUG indicated presence of urethral valves and (B) urodynamics indicated obstruction.

In another group, the initial cystourethroscopy was likewise described as normal in eight boys. In all cases, urodynamics showed obstructed Pdet-Qmax. Further urodynamic parameters of the group are seen from Table 1. In four of these boys (50%, 4/8), VCUG showed abnormalities in the sphincter area but they were not specifically described as suspected urethral valves (Figure 5). At repeat cystourethroscopy, urethral valves could still not be identified.

Fifteen of the 75 boys (20%) had an occult spina bifida (L5, S1) demonstrated on X-ray and MRI-scans of the spine were normal in all 17 cases examined.

Follow-up

The two boys who had transurethral valve resection were both continent at follow-up 2 and 6 years postoperatively. Both had supplementary pharmacological treatment.

The 10-year old boy with infrequent voiding, large bladder capacity, OAB but straining and weak Pdet-Qmax improved on urotherapy and Xatral treatment during the 1-year follow-up.

Included in the group of 61 boys with no suspected urethral valves at cystoscopy or VCUG and where urodynamics showed no obstructed Pdet-Qmax, there were 10 boys (median age 8 years, range 6–10) at diagnostics who had later transurethral Botox® injections in detrusor within the follow-up period of median 3.5 (range 2–8.5) years. The amplitudes of the overactive detrusor contractions at urodynamics were similar in the 10 boys who received Botox® treatment compared to those 51 who did not (median 31 cmH_2O, range 10–237 versus 33 cmH_2O, 6–143, respectively) (p=.78 (Mann–Whitney)). Botox® treatment was settled, in consultation, by patients and parents because other pharmaceutical treatment with different drugs had been unsuccessful.

Four boys became continent after one Botox® treatment, three boys after two treatments and one boy after three treatments. However, three of those boys did still occasionally have nocturnal enuresis. Two of the boys have still incontinence problems after 1 and 4 treatments at 2 and 3 years of follow-up, respectively.

The remaining 62 boys of the total material had urotherapy combined with individual continuous pharmaceutical treatment including drugs as tolterodin, mirabegron, fesoterodin, oxybutynin, solifenacin and desmopressin. The design of the present study did not allow to evaluate the results of specific pharma regimens, however, at end of follow-up 47% (29/62) were cured and continent day and night. Another 10% (16/62) became day-time continent but had persistent nocturnal enuresis.

Discussion

Our study shows that the majority of boys (87%, 65/75; 95%CI: 77–93) with OAB complaints, normal upper urinary tract, absence of evident meatal stenosis or obstructive flow

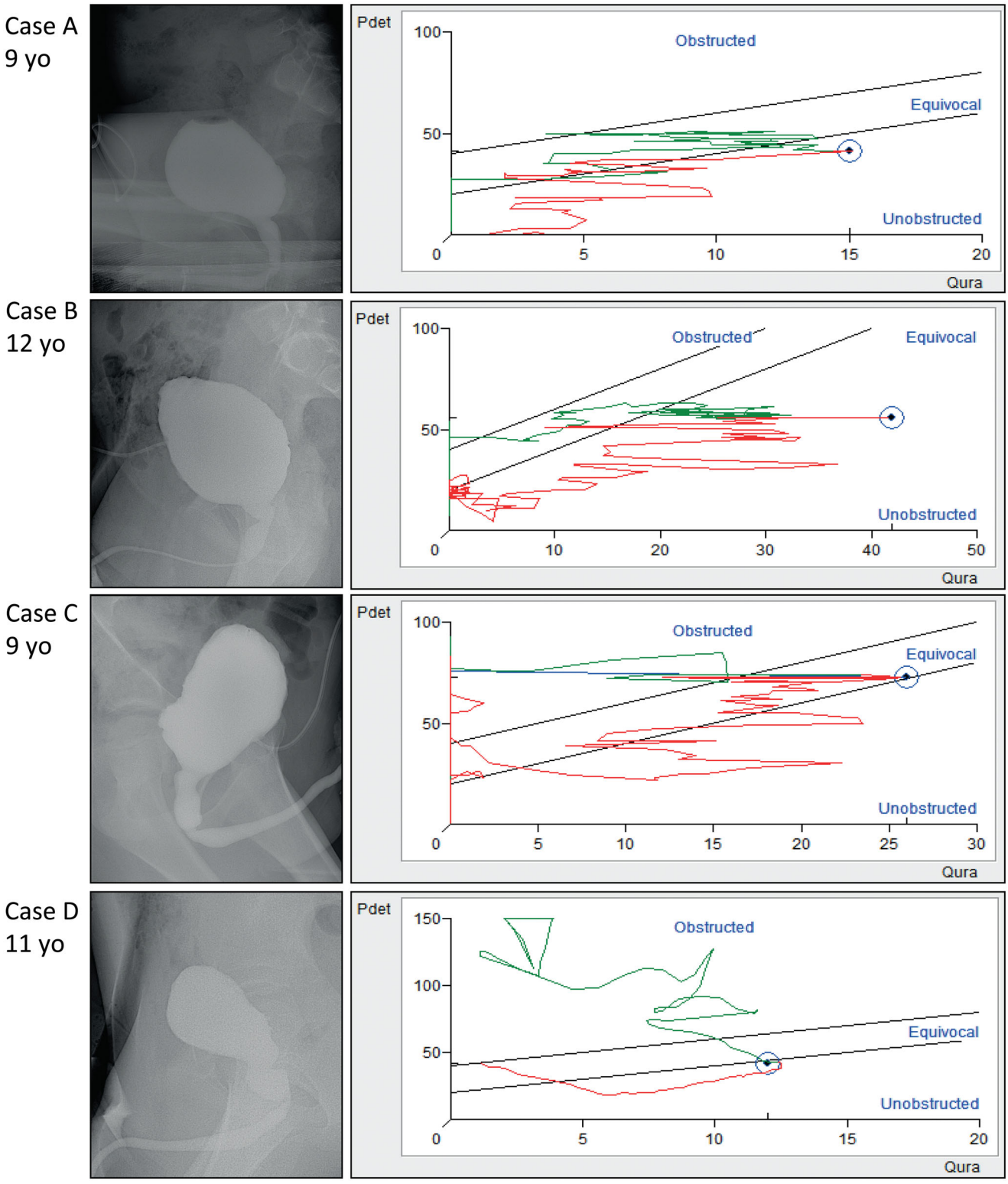

Figure 4. VCUG and urodynamics in four boys where the initial cystourethroscopy was described as normal. The VCUG indicated presence of posterior urethral valves but urodynamics showed no obstructed Pdet-Qmax. At repeat cystourethroscopy of case A, a cold hook-knife cut 4 and 8 o'clock at lower level of the colliculus guided by the VCUG was performed, without the surgeon being convinced that there were truly valves present.

pattern at repeated uroflowmetry and no history of UTI, can be safely evaluated by cystourethroscopy followed by urodynamic combined cystometry and pressure-flow study in search for a possible urethral problem. In our study, VCUG did not add diagnostic information to these patients in general, and VCUG can be restricted those boys where urodynamics indicated obstruction or the findings by cystourethroscopy and/or urodynamics are equivocal or uncertain. This means that the majority of the boys can avoid radiation. Ozen et al. [5] similarly questioned the need for VCUG. They evaluated VCUG and cystourethroscopy in 17 boys diagnosed with late-presented (mean age 7.35 years)

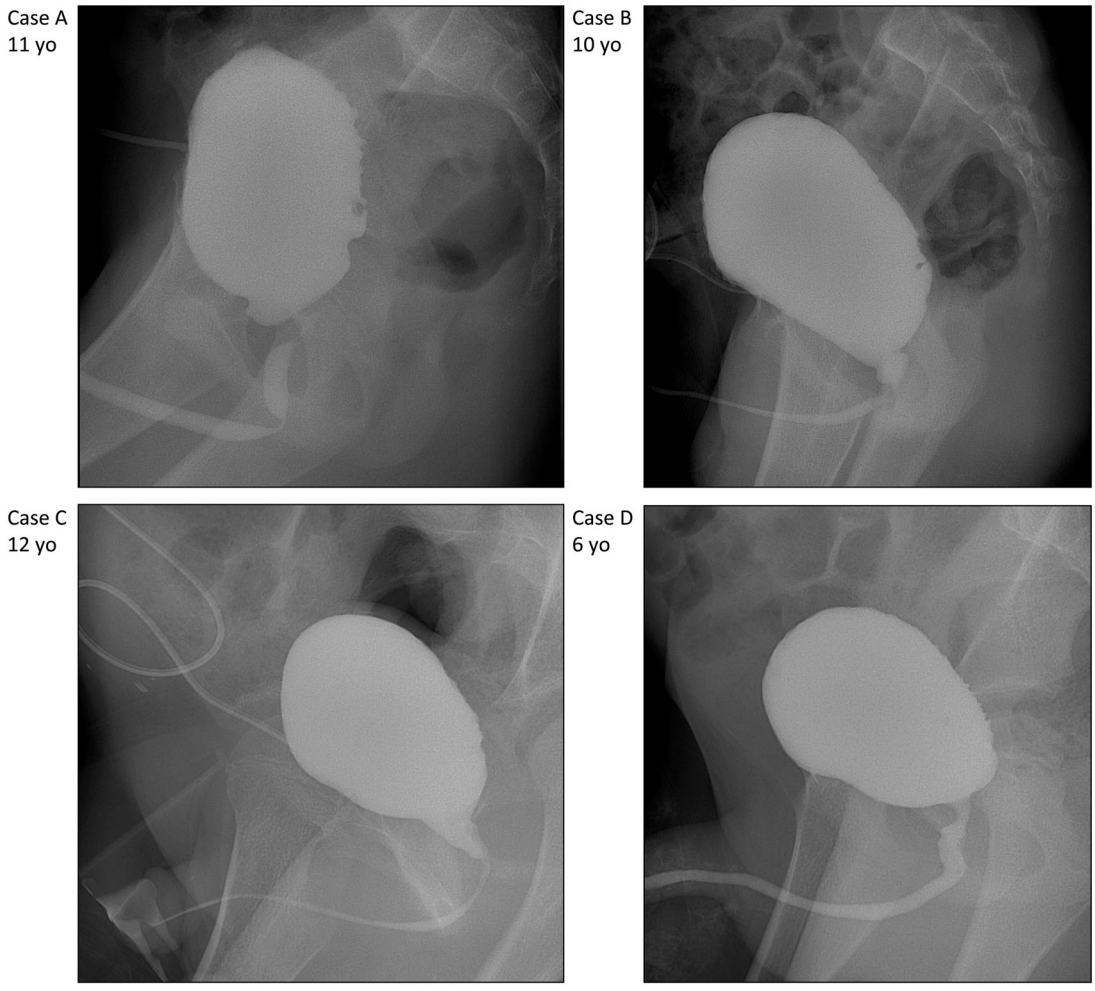

Figure 5. In eight boys, the initial cystourethroscopy was described as normal. In all cases, urodynamics showed obstructed Pdet-Qmax. In four of these boys, VCUG showed abnormalities in the sphincter area but they were not specifically described as suspected urethral valves. At repeat cystourethroscopy urethral valves could still not be identified. The VCUGs of the latter four boys are presented here.

posterior urethral valves. They concluded that cystourethroscopic examination should be preferred to diagnose posterior urethral valves regardless of VCUG results [5]. However, the authors main objective in that study referred to the normal appearing urethra on VCUG in 35% of the cases where posterior urethral valves were diagnosed by cystourethroscopy. de Kort et al. [6] did also evaluate the reliability of VCUG to diagnose infravesical obstruction in 72 boys. The VCUGs were assessed by two pediatric radiologists and two pediatric urologists. The kappa values for agreement among observers regarding an abnormal prostatic urethra, visible urethral obstruction and obstruction in the sphincter area were only 0.35, 0.33 and 0.26, respectively.

However, cystourethroscopic examinations of the urethra also have their limitations. de Jong et al. [7] let 25 experienced pediatric urological surgeons observe video fragments of cystourethroscopy in boys. For most of these boys, a strong suspicion of urethral obstruction had been present; however, some were controls. The video fragments stopped when an incision seemed about to be made, using the endoscopic hook on, or behind, 17 folds/valves. The pediatric urological surgeons were then asked whether they would have incised these folds/valves. Agreement of >80% was observed for 12 of the 17 questions. Of the 17 cases, five yielded agreement of 50–75%. Only in one case, 100% agreement was reached. This study illustrates some of the controversies in diagnosis of especially late-presented posterior urethral valves. In our series, four cases had a cystourethroscopy described as normal, but the VCUG indicated presence of posterior urethral valves. Theoretically, we might have overlooked urethral valves even though cystourethroscopy was repeated based on the VUCG findings. When dealing with a potential infravesical obstruction in boys it is evident from the literature, that feelings and traditions play a significant role. Some see structures, where others do not. Some of the aforementioned eight cases shown in Figures 4 and 5 might eventually represent Cobb's collar or Moormann's ring which is a stricture of the bulbar urethra often un-recognized but having considerable relevance urologically [8]. According to Dewan et al. [9], Cobb's collar is not a valve but a congenital stricture and distinct from the congenital obstructive posterior urethral membrane by the fact that it is not associated with the verumontanum. A few years later, Dewan et al. [10] re-defined the bulbar urethral narrowings such as Cobb's collar and Moormann's ring by using videorecorded cystoscopy. de Jong et al. [11] from the Utrecht group found and

resected urethral valves or flap valves in 43% of 180 boys diagnosed with OAB complaints aged between 5 and 16 years, which is a much higher proportion than 3% resected in our group. However, in another study, the Utrecht group compared the long-term effect of their strategy regarding low threshold endoscopic desobstruction versus a conservative treatment regime performed in Rotterdam on urine incontinence and urgency in boys with persistent OAB symptoms [12]. Although, the baseline characteristics of the boys with persistent OAB symptoms from the two centers were similar, 88% had urethral valve resection in Utrecht compared to 11% in Rotterdam [12]. The latter figure is within the 99%CI resected in our material. There were no differences between the results of treatment in the two centers after a mean follow-up of 5 years of the boys concerning dryness at daytime, dryness day and night and presence of urgency and frequency [12]. In Utrecht suspicion of an infravesical obstruction included a urodynamically high-voiding pressures (>55 cm H_2O), which we find quite low according to the aforementioned reasons seen in our method paragraph [12]. Such value would also have been accepted as normal in previously published pediatric normal materials [13–15]. In a urodynamic study from 2016 comprising 54 boys with late diagnosed urethral valves aged 6–13 years [16], the preoperative mean Pdet-Qmax was 66 H_2O. This figure seems higher than the Pdet-Qmax of the boys we did not consider to be obstructed but also somewhat lower than the Pdet-Qmax in the boys, which we defined as urodynamically obstructed. Unfortunately, the ICCS does not set up specific urodynamic criteria for bladder outlet obstruction except that detrusor pressure is elevated during voiding [17]. The number of repeat cystoscopy was very high, namely 14/75 cases including the two cases with valves. This leads to the question if it might have been good to do urodynamics and possible VCUG first and reserve cystoscopy for unclear cases. Furthermore, one may of course also question the possible impact of a transurethral procedure followed shortly by the two other procedures and especially in case of urodynamics. The order of investigations is affected by local logistics and traditions. Applying catheterization for these elective interventions without general anesthesia is not well accepted anymore. To avoid repetitive episodes of general anesthesia, the present program was the standard. As previously mentioned, the transurethral instrumentation performed the day before urodynamics, could induce some urethral edema that may influence urodynamic findings. However, for example by applying a transurethral catheter in local analgesia before urodynamics the increase in detrusor pressure in cmH_2O during micturition equals the fall in Qmax in ml/s. The effect of the catheter is to occlude part of the cross-sectional area of the urethra and so raise the pressure corresponding to a given open cross-sectional area by $H \times$Acat, where Acat is the cross-sectional area of the catheter and H is the distensibility of the urethra [18]. Regarding urodynamic evaluation in children with OAB it is well accepted that neither detrusor overactivity nor increased pelvic floor activity during voiding correlated with treatment outcome [2]. Standard treatment could be the first choice in urge syndrome as well as in dysfunctional voiding, reserving urodynamic studies for patients in whom this first approach fails. Our study was not designed to evaluate the results of oral pharmaceutical drug therapy. However, our results were in accordance with the literature anyway [2]. Furthermore, we found urodynamics useful to discriminate between boys who had overactive detrusor contractions secondarily related to infravesical obstruction and boys who had an idiopathic overactive detrusor, as seen in 93% of the 61 boys where there were no suspected urethral valves at cystoscopy or VCUG and urodynamics showed no obstructed Pdet-Qmax. Ten of these boys had transurethral Botox® injection therapy, whereof eight seemed to benefit from the treatment. Our results are in accordance with the literature, where the materials of boys having transurethral Botox® injections indicated by idiopathic OAB are sparse [19–21].

Conclusions

In the evaluation of boys with OAB complaints who are refractory to urotherapy and standard pharmaceutical drug therapy, one should consider a possible urethral cause of OAB. The boys can be safely evaluated by cystourethroscopy followed by urodynamic combined cystometry and pressure-flow study in search for a possible urethral problem. It is our suggestion, that VCUG can be restricted to those boys where urodynamics indicates obstruction or the findings by cystourethroscopy are uncertain.

Disclosure statement

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