Voiding efficiency and urodynamic parameters in pediatric patients with posterior urethral valves

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ABSTRACT

Objective. To describe the differences between voiding efficiency (VE) and other parameters of non-invasive urodynamic studies between patients with a history of posterior urethral valves (PUV) and patients without anatomical alterations of the lower urinary tract.

Materials and methods. A retrospective case-control study was carried out from 2012 to 2022. Cases with a PUV history and controls without anatomical urethral alterations were included. Clinical variables, classic urodynamic parameters, lag time, and VE were collected. Student's t-test, Mann-Whitney U test, and Kruskal-Wallis' test were used to compare quantitative variables, whereas the chi-squared test was employed to compare qualitative variables.

Results. N= 100 (n= 50 cases and n= 50 controls). Age: 7.8 ± 3.73 years. The case group had greater postvoiding residual volume (9 ml vs. 3 ml; p= 0.025) and a longer lag time (3.7 ± 5.41 s vs. 2.6 ± 1.80 s; p= 0.006), as well as less VE (93.8% vs. 98%; p= 0.020), than the control group.

Conclusions. In patients with a history of PUV, alterations in urodynamic studies were more frequent than in controls. Voiding efficiency is an easily measurable urodynamic parameter that has not been implemented in regular practice in pediatric patients yet. Our data demonstrates that VE can be lower in PUV patients than in patients without anatomical urethral alterations.

KEY WORDS: CAKUT; Posterior urethral valves; Urodynamics; Voiding efficiency.

EFICIENCIA VESICAL Y PARÁMETROS URODINÁMICOS EN PACIENTES PEDIÁTRICOS CON VÁLVULAS DE URETRA POSTERIOR

RESUMEN

Objetivos. Describir las diferencias entre la eficiencia vesical (EFV) y otros parámetros de estudios urodinámicos no invasivos entre pacientes con antecedentes de válvulas de la uretra posterior (VUP) y pacientes sin alteraciones anatómicas del tracto urinario inferior.

Material y método. Estudio caso-control retrospectivo entre 2012 y 2022. Se incluyeron casos con antecedente de VUP y controles sin alteración anatómica uretral. Se recogieron variables clínicas, parámetros urodinámicos clásicos, Lag time, y EFV. En el análisis comparativo fue empleado el t-test, U de Mann-Whitney y Kruskal-Wallis para variables cuantitativas y Chi-cuadrado para cualitativas.

Resultados. N= 100 (n= 50 casos y n= 50 controles). Edad 7,8 ± 3,73 años. El grupo de casos presentó mayor residuo postmiccional (9ml *vs* 3ml; p= 0,025) y Lag Time (3,7 ± 5,41 s *vs* 2,6 ± 1,80 s; p= 0,006), así como menor EFV (93,8% *vs* 98%; p= 0,020) que los controles.

Conclusiones. Los pacientes con antecedentes de VUP presentan alteración en estudios urodinámicos con más frecuencia que controles. La eficiencia vesical es un parámetro urodinámico de fácil obtención y no implementado en la práctica habitual en pacientes pediátricos. Nuestros datos muestran que la EFV que puede estar disminuida en los pacientes con VUP al compararla con pacientes sin alteración anatómica uretral.

PALABRAS CLAVE: Válvulas de uretra posterior; Eficiencia vesical; Estudio urodinámico no invasivo

INTRODUCTION

Posterior urethral valves (PUV) are the most frequent cause of lower urinary tract obstruction in male newborns[1-3]. Survival has improved in the last decades, but prognosis in terms of renal function remains stable, with 20-60% developing chronic renal disease (CRD) and 11-50% developing terminal CRD[4].

Optimization of voiding dysfunction, which is present in 75% of PUV patients, is the only factor that could improve renal failure progression[2,4-9]. Physiopathology is related to morphological and biochemical bladder changes as a result of maintained urinary flow obstruction. This causes loss of bladder elasticity, alteration of accommodation, and increased retrograde pressure on the upper urinary tract[6].

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Urodynamic studies (UDS) provide with objective information regarding the bladder's functional condition. Therefore, they are considered as a key tool in the assessment of lower urinary tract dysfunction[9,10]. According to the International Children's Continence Society (ICCS)'s recommendations, urine flow test with electromyography (UFT + EMG) should be the primary non-invasive study when facing a suspected voiding dysfunction[10,11]. However, no non-invasive urodynamic parameters with a prognostic implication in PUV patients have been reported so far.

Voiding efficiency (VE) is the bladder's capacity of conducting a complete and effective voiding, based on the relationship between bladder contractility and urethral resistance[12-14]. Even though VE is not commonly assessed in the pediatric population, it does offer certain advantages as it can be easily achieved and calculated from non-invasive UDSs[12-14].

The objective of this study was to establish the differences in non-invasive urodynamic parameters, including VE, between patients with a history of PUV and controls without anatomical urethral alterations.

MATERIALS AND METHODS

A retrospective case-control study was carried out at La Fe Polytechnical University Hospital from 2012 to 2022.

Inclusion criteria in the case group was history of PUV with at least two records of UFT + EMG and a minimum follow-up of 1 year. In the control group, criteria were male sex, age under 14 years, lack of anatomical alteration of the lower urinary tract (LUT), two records of UFT + EMG, and a minimum follow-up of 1 year. 1 control per case was selected for comparative analysis purposes.

Variables collected were demographic (age), clinical (urinary incontinence (UI), filling symptoms, voiding, and drug treatment), analytical (creatinine levels and alteration of renal function), and radiological (increased bladder thickness (≥ 3 mm), ureterohydronephrosis (UHN), vesicoureteral reflux (VUR), and alterations of renal uptake at scintigraphy). Renal function was assessed based on plasmatic creatinine concentration and glomerular filtration rate (GFR) as calculated using Schwartz formula[15].

UFT+EMG was carried out using the MMS V8.17I (24.9.2010) device. Classic parameters were achieved according to ICCS recommendations[10]. Urine flow curve pattern was characterized as bell-shaped, tower-shaped, staccato/irregular, interrupted, or plateau. Quantitative parameters collected included peak flow (Qmax), voiding time, and voiding volume. Qmax was converted to percentile according to three nomograms published (Miskolc, Gupta, and Tzu Chi) to make determination more robust, since there is no predetermined nomogram available in pediatrics[16.17].

Following UFT, all patients underwent ultrasonography to measure postvoiding residual volume (PVRV). Age-expected bladder capacity (AEBC) and VE were measured[10,13,14]. Additionally, even though it is not a commonly used urodynamic parameter, the flow index (FI) was reported as it is more accurate and reproducible than Qmax, and it is independent from voiding volume and PVRV[18]. EMG was conducted in all patients to calculate lag time, with values between 2 and 6 seconds being regarded as normal.

The IMB SPSS V 23.0 software was used for statistical analysis purposes. The Kolmogorov-Smirnoff test was used to identify variables with a normal distribution. Student's t-test was employed to compare parametric quantitative variables. Mann-Whitney U test and Kruskal-Wallis' test were used for non-parametric quantitative variables. The chi-squared test was employed for qualitative variables. Statistical significance was established at $p<0.05$.

RESULTS

100 patients were included. The sample consisted of 50 cases with PUV and 50 controls with no urethral pathology. Mean age was 7.8 ± 3.73 years, and follow-up was 3.5 ± 2.29 years. Mean age in the PUV group was lower (6.9 (4.5-10.6) vs. 9.4 (7.7-12.1) years) (p= 0.006) (Table 1).

The most frequent baseline pathology in controls was monosymptomatic enuresis (56%), followed by voiding dysfunction (16%), repeated infections (16%), and urinary incontinence (12%).

Statistically significant differences were found in the clinical situation of patients (Table 1). 22 (44%) cases and 37 (74%) controls remained asymptomatic during follow-up. In the remaining ones, the most frequent symptom was urinary incontinence (56% of cases and 26% of controls), followed by filling symptoms (34% and 26%, respectively). Regarding drug treatment, there were no differences between both groups in the use of anticholinergics or alpha-blockers. In terms of radiological variables, statistically significant differences were found in the four parameters assessed – increased bladder thickness, UHN, VUR, and low uptake at scintigraphy. 44.44% of the PUV cases had alteration of renal function. In the control group, renal function was normal in all cases (Table 1).

In the case group, normal UFT curve patterns were less frequent [33 (66%) vs. 15 (30%); p= 0.001]. In the PUV group, the plateau curve with prolonged flow was more frequent (Fig.1). No differences were found in terms of EMG alteration [3 (6%) vs. 6 (12%); p= 0.185) or FI (0.7 vs. 0.8; p= 0.01]. PUV patients had lower Qmax percentiles in the three nomograms employed – Miskolc p30 vs. p60 (p= 0.001), Gupta p20 v p50 (0.003), and Tzu Chi p30 vs. p50 (p= 0.025). PVRV was higher (9 ml vs. 3 ml; p= 0.025) and lag time (3.7 ± 5.41 s vs. 2.6 ± 1.80 s; p= 0.006) was

Table 1. Baseline characteristics of both groups.

Variable	*Cases (PUV) n= 50*	*Controls n= 50*	*p value*
Age (years)	6.9 (4.5-10.6)	9.4 (7.7-12.1)	0.006
Symptoms			0.03
• UI	28 (56%)	13 (26%)	
• Filling	17 (34%)	13 (26%)	
• Voiding	10 (20%)	10 (10%)	
Treatment			0.65
• Anticholinergics	18 (36%)	20(40%)	
• Alpha-blockers	1 (2%)	2 (4%)	
Altered bladder morphology	24 (48%)	3 (6%)	0.000
UHN			0.000
• Unilateral	16 (32%)	1 (2%)	
• Bilateral	16 (32%)	1 (2%)	
VUR			0.003
• Unilateral	9 (18%)	0	
• Bilateral	4 (8%)	0	
Scintigraphy (low uptake)			0.000
• Unilateral	25 (50%)	0	
• Bilateral	12 (24%)	1 (2%)	
Altered renal function	20 (40%)	0	0.000

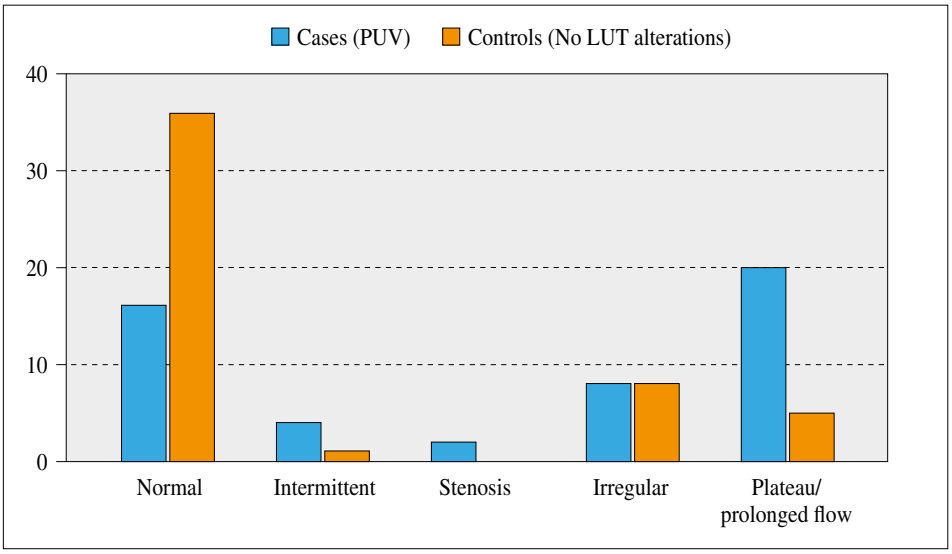

Figure 1. Morphology of the urine flow test curve. Comparison between groups.

longer in the case group. Similarly, VE in the case group was lower than in the control group [93.8% (86.0-98.1) vs. 98% (93.1-100); p= 0.02] (Table 2).

DISCUSSION

Voiding dysfunction in PUV patients has been associated with a 1.15- to 8.9-fold risk of developing CRD. Therefore, optimizing bladder dynamics is regarded as a key objective to improve prognosis[19-22]. Apart from contributing to renal function deterioration, voiding dysfunction is symptomatic in 13-38% of PUV patients, with a negative impact on quality of life[1,23]. Consequently, considering that urodynamic alterations usually occur before clinical alterations, urodynamic assessment of all patients with a history of PUV, including asymptomatic ones, is recommended[9,23-25]. In our experience, of the 22 asymp-

Table 2. UFT + EMG urodynamic parameters.

Variable	*Cases (PUV) n= 50*	*Controls n= 50*	*p value*
Altered urine flow test	33 (68.6%)	15 (31.3%)	0.001
Continuous urine flow test	41 (49.4%)	42 (50.6%)	0.500
Interrupted urine flow test	9 (52.9%)	8 (47.1%)	0.500
Altered EMG	3 (3.33%)	6 (66.6%)	0.185
AEBC (%)	65.8 ± 39.02	63.8 ± 46.60	0.764
Qmax	12.5 (10-19)	16 (12.5-21.5)	0.010
• Miskolc nomogram	p30 (25-50)	p60 (50-75)	0.001
• Gupta nomogram	p20 (10-25)	p50 (25-75)	0.003
• Tzu Chi nomogram	p30 (25-50)	p50 (25-75)	0.025
FI	0.7 (0.5-0.8)	0.8 (0.6-1.0)	0.010
Lag time (s)	3.7 ± 5.41	2.6 ± 1.80	0.006
PVRV (ml)	9 (1.8-23.5)	3 (0-11.3)	0.025
VE (%)	93.8 (86.0-98.1)	98 (93.1-100)	0.02

EMG: Electromyography; AEBC: Age-expected bladder capacity (Age + 1) x 30; FI: Flow index; PVRV: Postvoiding residual volume; VE (%): Voiding efficiency.

tomatic cases, only 10 had a normal UFT, whereas the remaining 12 (54.55%) had urodynamic study alterations.

According to the literature, PUV patients have an altered urine flow test curve. The normal curve was more frequent in the control group, whereas the case group had a higher percentage of plateau curve instances (n= 20; 40%)[26,27]. Age-adjusted Qmax percentiles were lower in the case group. No differences were found in terms of FI, with a mean of 0.7 in the case group and 0.8 in the control group. Considering that FI< 0.7 suggests a flat curve, whereas values between 0.71 and 1.25 correspond with a bell-shaped curve[26], our results suggest that a flattened curve is more likely in the case group, even if this difference was not statistically significant. Consistent with other studies, PVRV was higher and lag time was longer in patients with a history of VUP[22,26].

Lag time is an emergent parameter indicating a potential alteration in the opening of the bladder neck. Currently, the clinical use of lag time is not widespread as it is difficult to calculate, it is variable, and it requires EMG, but it provides useful information in the assessment of patients with LUT dysfunction. Patients with bladder dysfunction have been observed to have longer lag times[26], consistent with our sample. As it is the case in previous studies, PVRV was higher in PUV patients than in controls[22,26]. However, this parameter is highly variable and little concordant in various measurements, both inter- and intra-individual, since it depends on pre-voiding volume, which explains why some studies show divergent results[22].

VE is regarded as a representative parameter of bladder voiding. Its main advantage lies in the fact it can be achieved from non-invasive UDSs, since it is more representative when calculated without a bladder probe[12]. In addition, it considers pre-voiding volume, which reduces variability. Even though it is easy to calculate, it is not widely used, and the literature regarding the pediatric population is scarce. VE had not been previously used in pediatric PUV patients, but given the physiopathological similarity between these patients and adult patients with benign prostate hyperplasia, we believe VE assessment could be useful. VE was lower in PUV patients than in controls without anatomical urethral alterations. Some of the VE limitations reported include the absence of clinical significance of VE levels in pediatrics and the lack of correlation between VE levels and urodynamic diagnosis[14].

The primary limitation of this study lies in its retrospective, single-center nature. Regarding the choice of the control group, a 1:1 ratio with the case group was used. This decision was based on the availability of controls with adequate characteristics under similar conditions, and also on the need for a well-balanced, manageable analysis. We acknowledge that a greater ratio could have increased statistical power, but our decision was explained by the limitations in the access to homogeneous controls. The choice of patients apparently with no organic pathology as part of the control group was based on the need for a reference clinical standard free from structural urethral alterations. However, this approach may have magnified the differences between both groups. If a control group with characteristics more similar to the case group (for instance, patients with minor organic pathologies) had been selected,

the differences observed could have been less, primarily involving the magnitude of the parameters assessed, but not necessarily their direction. This should be regarded as a methodological limitation that could be dealt with in future studies. No VE cut-off point from which associated clinical progression is worse was achieved, and there are no pediatric literature references assessing this. Therefore, we consider adding this parameter in future investigations.

In conclusion, altered non-invasive UDSs are more frequent in pediatric PUV patients than in controls without anatomical LUT alterations. VE is an easily measurable parameter that shows worse results in PUV patients, similarly to lag time and PVRV.

REFERENCES

1. Tang LF, Bi YL, Fan Y, Liu Y, Sun YB, Wang AL. Posterior urethral valves with lower urinary tract symptoms: Perspective on urodynamics. J Invest Surg. 2021;34(10):1066-71.
2. Massaguer C, Martín-Solé O, Pérez-Bertólez S, Tarrado X, García-Aparicio L. Pop-off mechanisms as protective factors against chronic renal disease in children with posterior urethral valves. Cir Pediatr. 2022; 35(4): 180-6.
3. Sarhan OM, Wadie B, Al-Kawai F, Dawaba M. Bladder function in children with posterior urethral valves: impact of antenatal versus postnatal diagnosis. Int Braz J Urol. 2022; 48(1): 78-86.
4. Ansari MS, Nunia SK, Bansal A, Singh P, Sekhon V, Singh D, et al. Bladder contractility index in posterior urethral valve: A new marker for early prediction of progression to renal failure. J Pediatr Urol. 2018; 14(2): 162.e1-e5.
5. Ansari MS, Gulia A, Srivastava A, Kapoor R. Risk factors for progression to end-stage renal disease in children with posterior urethral valves. J Pediatr Urol. 2010; 6(3): 261-4.
6. Desai D, Duffy PG. Posterior urethral valves and other urethral abnormalities. En: Wilcox D, Thomas DFM, editores. Essentials of Pediatric Urology. 3ª ed. CRC Press; 2022. p. 115-8.
7. Long Christopher J, Bowen DK. Predicting and modifying risk for development of renal failure in boys with posterior urethral valves. Curr Urol Rep 2018; 19(7): 55.
8. Romero RM, Roldán S. Actualización en válvulas de uretra posterior. Cir Pediatr. 2018; 31(1): 1-7.
9. Vaze PG, Saha S, Sinha R, Banerjee S. Urodynamics in posterior urethral valve: Pursuit of prognostication or optimisation. J Pediatr Urol. 2021; 17(1): 111.e1-e8.
10. Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the International Children's Continence Society. Neurourol Urodyn. 2016; 35(4): 471-81.
11. Wenske S, Van Batavia JP, Combs AJ, Glassberg KI. Analysis of uroflow patterns in children with dysfunctional voiding. J Pediatr Urol. 2014; 10(2): 250-4.
12. Valentini FA, Marti BG, Zimmern PE, Robain G, Nelson PP. Comparison of bladder voiding efficiency in women when calculated from a free flow versus an intubated flow. Bladder. 2018; 27(4): e36.
13. Bosch JL, Kranse R, van Mastrigt R, Schröder FH. Dependence of male voiding efficiency on age, bladder contractility and urethral resistance: development of a voiding efficiency nomogram. J Urol. 1995; 154(1): 190-4.
14. Valentini FA, Marti BG, Robain G, Zimern PE, Nelson PP. Is bladder voiding efficiency useful to evaluate voiding function in women older than 65 years? Prog Urol. 2019; 29(11): 567-71.
15. Schwartz GJ, Furth SL. Glomerular filtration rate measurement and estimation in chronic kidney disease. Pediatr Nephrol. 2007; 22(11): 1839-48.
16. Gupta DK, Sankhwar SN, Goel A. Uroflowmetry nomograms for healthy children 5 to 15 years old. J Urol. 2013; 190(3): 1008-13.
17. Yang SS, Chiang IN, Hsieh CH, Chang SJ. The Tzu Chi nomograms for maximum urinary flow rate (Qmax) in children: comparison with Miskolc nomogram. BJU Int. 2014; 113(3): 492-7.
18. Franco I, Franco JA, Nussenblatt B. Can the idealized voider derived flow indexes be a measure of voiding efficiency and how accurate are they? Neurourol Urodyn. 2018; 37(6): 1913-24
19. Polak-Jonkisz D, Rehan LR, Fornalczyk K, Hackemer P, Zwolińska D. Valve bladder syndrome in children: On the trail of the best strategies to prevent chronic kidney disease. Adv Clin Exp Med. 2017; 26(8): 1293-300.
20. Klaus R, Lange-Sperandio B. Chronic kidney disease in boys with posterior urethral valves–pathogenesis, prognosis and management. Biomedicines. 2022;10(8):1894.
21. El Desoky SM, Banakhar M, Khashoggi K, Zaher ZF, Kari JA. Voiding dysfunction in children causes, management, and prognosis: A single-center retrospective study. Saudi Med J. 2021; 42(8): 869-77.
22. Capitanucci, ML, Marciano, A, Zaccara, A, La Sala, E, Mosiello, G, De Gennaro, M. Long-term bladder function followup in boys with posterior urethral valves: comparison of noninvasive vs invasive urodynamic studies. J. Urol. 2022; 188(3): 953-7.
23. De Gennaro M, Capitanucci ML, Mosiello G, Caione P, Silveri M. The changing urodynamic pattern from infancy to adolescence in boys with posterior urethral valves. BJU Int. 2000; 85(9): 1104-8.
24. Ghanem MA, Wolffenbuttel KP, De Vylder A, Nijman RJ. Long-term bladder dysfunction and renal function in boys with posterior urethral valves based on urodynamic findings. J Urol. 2004; 171(6): 2409-12.
25. Radmayr C, Bogaert G, Burgu B, Dogan,HS, Nijman JM, Quaedackers J, et al. EAU Guidelines on Paediatric Urology. Edn. Presentado en EAU Annual Congress Milan 2023. Disponible en: https://uroweb.org/guidelines/paediatric-urology/chapter/the-guideline.
26. Fuentes M, Magalhães J, Barroso U. Diagnosis and management of bladder dysfunction in neurologically normal children. Front. Pediatr. 2019; 25(7): 298.
27. Hennus PM, van der Heijden GJ, Bosch JL, de Jong TP, de Kort LM. A systematic review on renal and bladder dysfunction after endoscopic treatment of infravesical obstruction in boys. PLoS One. 2012; 7(9): e44663.