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Review Article

Tzu Chi nomograms for uroflowmetry, postvoid residual urine, and lower urinary tract function

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ABSTRACT

The objective of the article is to summarize the results of our previous reports with regard to uroflowmetry, postvoid residual urine (PVR), and lower urinary tract symptoms in healthy children in Xindian, New Taipei, Taiwan. Healthy children aged 4–12 years were enrolled and their PVR was evaluated with two sets of uroflowmetry. Those with a voided volume (VV) < 50 mL were excluded from further analysis. Bladder capacity (BC) was defined as the VV + PVR and the expected BC was defined as (age in years + 1) $\times$ 30 mL. Uroflowmetry curves were interpreted independently by two pediatric urologists. The lower value of two consecutive PVRs and the higher value of two consecutive peak flow rates (Qmax) were used to construct dual-PVR and dual-Qmax nomograms, respectively. One parent of each child completed a questionnaire on bedwetting and the dysfunctional voiding symptoms score (DVSS). A total of 1128 children (583 boys and 545 girls) with a mean age of 7.7 $\pm$ 2.2 years were eligible for analysis and construction of nomograms. On the first uroflowmetry, 960 (85.1%) children were classified as having a normal bell-shaped curve and 168 (14.9%) had a non–bell-shaped curve. An abnormal uroflow pattern was frequently observed at VV $\geq$ 100% or BC $\geq$ 115% of the expected BC. Multivariate analysis revealed that the Qmax value was significantly affected by age, VV, and sex (all $p < 0.01$). The minimally acceptable Qmax, around the 10th percentile of the dual-Qmax nomogram, was $>$ 11.5 mL/second in children aged $\leq$ 6 years and $>$ 15.0 mL/second in children aged $\geq$ 7 years. Significant variations in the PVR were observed in each individual. Multivariate studies showed that the PVR was positively associated with bladder capacity and negatively associated with age, was higher in boys than in girls, and was higher in children with abnormal uroflow patterns. For children aged $\leq$ 6 years, repetitive PVR $>$ 20 mL or $>$ 10% BC can be regarded as an elevated PVR. For children aged $\geq$ 7 years, repetitive PVR $>$ 10 mL or 6% BC can be redefined as elevated. A DVSS $\geq$ 6.66 is highly suggestive of lower urinary tract dysfunction in both sexes with good sensitivity and specificity. New nomograms for uroflowmetry, PVR, and DVSS were established for the noninvasive assessment of pediatric lower urinary tract function. Repeat tests are recommended if a single test is abnormal. Invasive videourodynamic study is recommended in cases of refractory lower urinary tract symptoms and repeat abnormal tests.

1. Introduction

Uroflowmetry and postvoid residual urine (PVR) tests serve as initial screening tools for evaluation of lower urinary tract (LUT) function in children [1,2]. The PVR has long been correlated with the occurrence and recurrence of pediatric urinary tract infection [3,4]. However, the first PVR nomogram for children was only available in 2013 [5]. The results of uroflowmetry tests show the general bladder contractility and bladder outlet resistance. The parameters generated through uroflowmetry include uroflow curves, the peak flow rate (Qmax), voided volume (VV), average flow rate, voiding time, and time to peak flow rate. Among these parameters, Qmax is the most relevant parameter for interpretation [1]. Several nomograms for Qmax in children were established almost 2 decades ago [6–8]. The commonly used Miskolc nomogram [8] for Qmax was constructed in a study in

Conflicts of interest: none.

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which 200 healthy children were enrolled, whereas 180 children were enrolled in the study of Mattsson and Spångberg [6], and 527 participated in the study of Kajbafzadeh et al [7]. All previously published nomograms used the logarithmic transformation regression model. The ranking method may reflect the true condition of healthy children, so we enrolled a large number of children to construct nomograms for the PVR and Qmax using the ranking method and compared our nomograms with previous nomograms constructed with the regression method [9]. There is significant variation in PVR and Qmax [9,10], and physicians tend to use the best values on two tests as clinically relevant [11]. Therefore, we constructed both single- and dual-nomograms for Qmax and PVR.

In addition to Qmax, the uroflow pattern is also an important parameter. The International Children's Continence Society (ICCS) has classified uroflow patterns into bell-shaped, staccato, plateau, interrupted, and tower shaped curves [1]. Only a bell-shaped curve is regarded as normal and the prevalence of the bell-shaped curve in children varies widely from 63% to 97% [12,13]. There are few nomograms for other patterns because they have been mentioned less often in previous studies [14].

General urologists like to use symptom scores such as the International Prostate Symptom Score used in adults. Because there is no Chinese version of a questionnaire available for children with lower urinary tract dysfunction, we chose the most commonly used measurement scale, the Dysfunctional Voiding Symptom Score (DVSS), for validation [15,16]. For children with LUT symptoms, the DVSS can be used to predict the probability of LUT dysfunction and follow the treatment response.

Because the study was funded by a grant from Taipei Tzu Chi Hospital (New Taipei City, Taiwan), we called these nomograms the Taipei Tzu Chi nomograms for pediatric LUT function.

2. Enrollment of participants

The enrollment of participants is described in detail in our previous article [5]. From September, 2006 to February, 2012, all kindergartens and elementary schools in Xingdian City, Taiwan were invited to join the study. We further randomly selected classes from each grade at each elementary school. All children in the selected kindergartens were invited. The exclusion criteria were children with congenital genitourinary tract anomalies, neurological anomalies, a history of urinary tract infection, or positive nitrite or leukocyte esterase on a urine dipstick test. One parent of each child completed a questionnaire on the age, sex, body weight, height, and DVSS [15]. A uroflowmeter (UFM Master; *Medical Measurement Systems* BV, Enschede, The Netherlands) was set up in the toilets of each kindergarten and elementary school. Two sets of uroflowmetry and PVR were obtained. Boys voided in a standing position and girls in a sitting position with adequate foot support. The PVR was measured within 5 minutes after voiding with suprapubic ultrasound (LogiqBook, GE Medical Systems, Milwaukee, WI, USA), and estimated using the following equation: height × width × depth × 0.52 mL [17] only when the VV was ≥ 50 mL [18]. All uroflow patterns were reviewed and interpreted independently by two pediatric urologists in our institution [19]. The uroflow patterns were classified as bell, staccato, plateau, or interrupted. The first set of uroflowmetry curves and PVRs from each child with a VV ≥ 50 mL was included for analysis and construction of single nomograms. The higher of consecutive Qmax values and the lower of consecutive PVR values were adopted for construction of dual-Qmax and dual-PVR nomograms. During construction of the nomograms, children with repetitive abnormal flow patterns were excluded from analysis. The expected bladder capacity (EBC) for age was defined as (age in years + 1) × 30 mL [1].

3. Variability of PVR

In healthy kindergarteners, there was high variability in the PVR, and the correlation for consecutive PVR values was low in all children and negligible in the 129 children without bladder over distention (r = 0.34 and r = 0.13, respectively) [10].

Because of significant intraindividual variability in the PVR, one PVR test is not reliable for assessing pediatric voiding function. At least two PVR tests are recommended, particularly when the first PVR is abnormally high on nomograms.

4. PVR nomograms

In all children with single PVR tests, the 95th percentile of the PVR in mL was related to bladder capacity (BC), and remained constant around 16% of BC at a BC ≥ 70% of the EBC (Fig. 1). For children aged ≤ 6 years, a single PVR > 30 mL or > 21% BC, or repetitive PVR > 20 mL or > 10% BC can be regarded as elevated. For children aged ≥ 7 years, a single PVR > 20 mL or 15% BC, or repetitive PVR > 10 mL or 6% BC can be defined as elevated [5].

To interpret PVR in children, the PVR as a percentage of BC is more reliable than PVR in mL. We recommend repeat PVR tests when the initial PVR is higher than the acceptable age-specific PVR.

5. Inter- and intraobserver agreement in the interpretation of uroflowmetry

Intraobserver agreement in interpreting each type of uroflowmetry curve and interpreting normal versus abnormal patterns

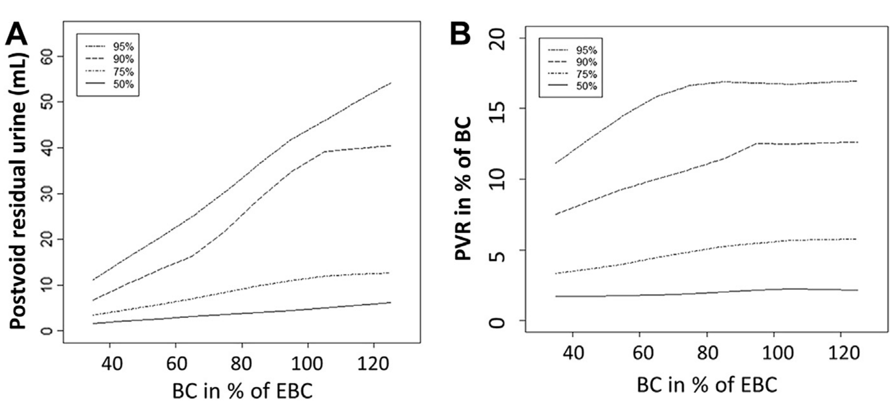

Fig. 1. Nomograms for (A) single-postvoid residual urine (PVR, mL) and (B) PVR/bladder capacity (BC, %) over bladder capacity (BC)/expected bladder capacity (EBC) in children.

Voided volume: _____mL. ☐ adequate, ☐ <50% EBC, ☐ ≥ 100%EBC.
PVR= _____mL. ☐ adequate, ☐ elevated*
Bladder capacity= _____mL. ☐ adequate, ☐ <50% EBC, ☐ ≥115% EBC.
Qmax=______mL/s. ☐ adequate, ☐ low**
Flow Pattern: ☐ normal, ☐probably normal, ☐ equivocal, ☐probably abnormal, ☐ abnormal.
Specific abnormal pattern: ☐ Tower, ☐ Staccato, ☐ Intermittent, ☐ Plateau, ☐ Obstructive, ☐ Mixed.
Conclusion: ☐ normal, ☐probably normal, ☐ equivocal, ☐probably abnormal, ☐ abnormal.
Recommendation: ☐ no further test ☐ repeat test, ☐ (video)urodynamic study

Fig. 2. Sheet for interpretation of uroflowmetry and postvoid residual urine (PVR). * PVR > 20 mL or 10% bladder capacity for children aged ≤ 6 years; PVR >10 mL or 6% bladder capacity for children aged ≥ 7 years. ** Peak flow rate (Qmax) <11.5 mL/s for children aged ≤ 6 years; Qmax <15.0 mL/s for those aged ≥ 7 years. EBC = expected bladder capacity.

were both good (κ = 0.71 and κ = 0.68, respectively). Very good interobserver agreement (κ = 0.81) was observed in the normalcy of uroflow patterns. However, there was poor interobserver agreement on the classification of the specific types of abnormal uroflowmetry curves (κ = 0.07) [19].

Based on the above findings, we concluded that uroflowmetry is a good screening tool for normalcy in kindergarten children, but is not a good tool to define the specific types of abnormal uroflowmetry. Interobserver agreement on specific types of abnormal flow pattern is low, and several potential etiologies can be present in a specific type of abnormal flow pattern. It may not be necessary to define the specific type of abnormal flow pattern in children or adults [14,20]. We recommend the method in Fig. 2 to report the results of uroflowmetry and PVR tests.

6. Uroflow patterns for healthy children

Normal bell-shaped curves were found in 85.1% of all first uroflowmetry tests in each child. For abnormal flow patterns, 18 (1.6%) were interpreted as interrupted, 45 (4.0%) as plateau, 90 (8.0%) as staccato, and 15 (1.3%) as tower shaped curves. However, only 3.8% of children had repetitive abnormal flow patterns that can be defined as abnormal.

Because good detrusor contractility in children may overcome bladder outlet resistance, the Qmax may not be so reliable in children [21]. Therefore, some pediatric urologists consider the uroflow pattern to be a more important parameter than the Qmax. Although abnormal flow patterns are not a guarantee of an underlying abnormality, they serve as a guide to the existence of a specific condition [1]. In healthy children, the uroflow pattern is regarded as smooth and bell shaped. Among healthy children, the proportion of bell shaped curves ranges widely from 63% to 97.2% [12,13,22]. Possible explanations for the discrepancy may be an unclear definition for bell-shaped curves by the ICCS, interpretation by different observers, differences in voided volume, and difference in baseline characteristics of the participants enrolled.

7. The effects of bladder capacity on interpretation of uroflowmetry and PVR

Qmax and PVR are dependent on bladder capacity and voided volume [23,24]. Based on the receiver operating characteristic curve for abnormal uroflowmetry or an elevated PVR,

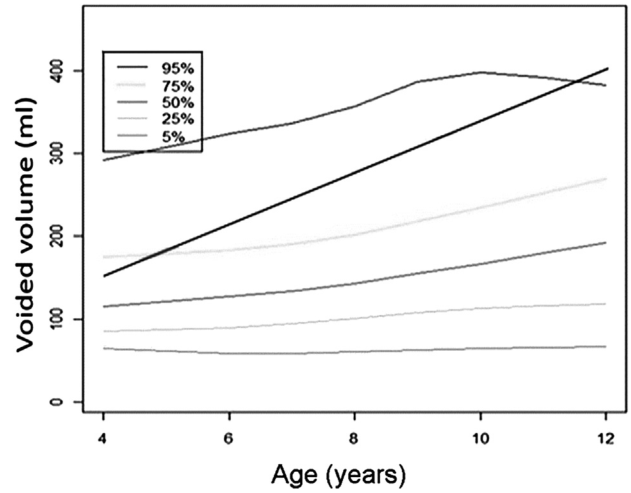

Fig. 3. Nomogram for voided volume during uroflowmetry tests. The black line represents the expected bladder capacity for age [(age in years +1) × 30 mL].

bladder capacity ≥ 115% EBC and VV ≥ 100% EBC were regarded as urinary bladder over distension [23,24]. There were statistically more elevated PVR (> 20 mL) values, and more non–bell-shaped uroflowmetry curves in voidings with bladder over distension. The Qmax also decreased at extreme bladder over distension. The VV increased as age increased, whereas the rate of bladder over distention, and VV > 100% EBC decreased with age (Fig. 3).

The parameters generated through uroflowmetry tests were dependent on the VV [25]. According to the 1998 ICCS guidelines [18], uroflowmetry with a VV > 50 mL is regarded as relevant for interpretation. Yang et al [26] found that uroflowmetry with a VV < 50% EBC yielded variable results. The interpretation of uroflowmetry should be made only when VV is > 50 mL, or > 50% of EBC. We were the first to define the upper limit of the VV for interpretation in uroflowmetry. An optimal bladder capacity between 50% and 115% EBC for children aged 4–6 years is recommended for interpretation of uroflowmetry and PVR. As children grow, their bladder capacity increases. The optimal bladder capacity for older children needs to be investigated.

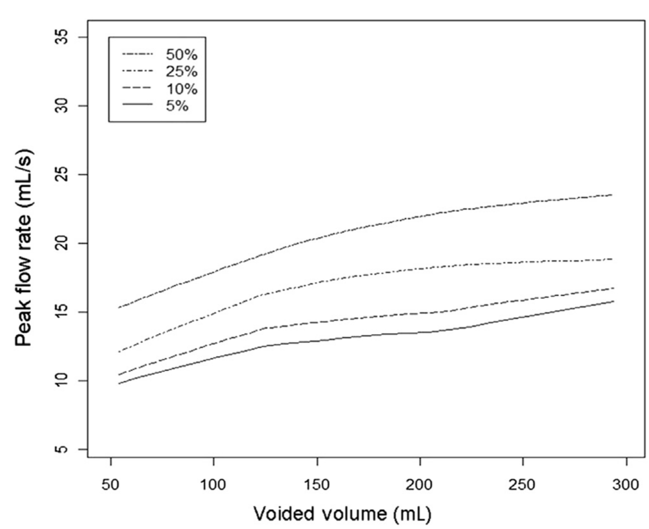

Fig. 4. Dual nomogram for peak flow rate (Qmax, mL/second) over voided volume (mL) in uroflowmetry tests.

Table 1
Summary of normal reference values of pediatric lower urinary tract function.

Parameters		
Age, y	4–6	7–12
PVR, % of bladder capacity	<10	<6
PVR (mL)	<20	<10
Flow pattern	Bell-shaped	Bell-shaped
Qmax (mL/s)	>11.5	>15.0
Optimal bladder capacity, % expected bladder capacity	50–115	To be determined

PVR = postvoid residual urine; Qmax = peak flow rate.

8. Age- and sex-specific Qmax nomogram

The 5th, 10th, 25th, and 50th percentiles in the overall dual-Qmax were 12.1 mL/second, 14.0 mL/second, 17.3 mL/second, and 20.8 mL/second, respectively. The Qmax increased as age and voided volume increased. Dual-Qmax nomograms on voided volume are shown in Fig. 4. Girls had a higher Qmax than boys. [9] For practical use, we suggest a minimally acceptable Qmax, i.e., around the 10th percentile of the dual-Qmax nomogram, of $>$ 11.5 mL/second in children aged $\leq$ 6 years and $>$15.0 mL/second in children aged $\geq$ 7 years.

Among the parameters generated from uroflowmetry, Qmax is regarded by the ICCS as the most relevant variable when assessing bladder outflow [1]. Therefore, Qmax plays an important role in monitoring the effectiveness of medical and surgical treatment for voiding dysfunction. Surgeons usually use Qmax as a parameter for bladder outlet obstruction in children undergoing hypospadias repair [11]. Some surgeons have adopted the higher value of consecutive Qmax values to make this diagnosis. Therefore, children with two uroflowmetry tests with VV $>$ 50 mL were enrolled for dual-Qmax nomograms.

The ICCS considers a Qmax (mL/s) larger than the square root of the VV (mL) as within normal limits [1]. The results of current nomograms were in line with that rule. Actually, a Qmax equal to the square root of the VV is generally between the 10th and 25th percentiles of Qmax nomogram, and the value would be close to the 25th percentile at large VV in both boys and girls.

9. Validation of a Chinese version DVSS

We enrolled 60 children from pediatric urology clinics who had a diagnosis of dysfunctional voiding according to ICCS guidelines [20]. We also randomly selected 235 healthy children from the community as a control group. In this age- and sex-matched study, we found that the DVSS was reliable with good validity. We chose a cut-off point of 6.66 with 81.67% sensitivity and 82.67% specificity to diagnose dysfunctional voiding. The DVSS showed good test–retest reliability [16].

The validated Chinese version of the DVSS can be used to screen children in the community and pediatric clinics. Patients can be followed with the DVSS to evaluate their response to medical and surgical treatment.

10. Limitations

The parameters of uroflowmetry, PVR, and DVSS may differ in different geographic areas, ethnic groups, and sexes and depend significantly on the VV and age. Therefore, external validation of the current nomograms in the other ethnic groups is warranted. Despite the fact that the DVSS is one of the most commonly used questionnaires for pediatric dysfunctional voiding, it lacks items related to extraordinary urinary frequency, enuresis, and fecal soiling, which may compromise content validity.

11. Conclusion

New nomograms for the DVSS, PVR, and uroflowmetry have been established for the noninvasive assessment of pediatric lower urinary tract function and are summarized in Table 1. Repeat tests are recommended if a single test is abnormal. Invasive video-urodynamic study is recommended in cases of refractory LUT symptoms and repeat abnormal tests. The Chinese version of the DVSS can be used to screen and monitor treatment response for LUT dysfunction in children.

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