

Beyond the Basics: Advances in Non-invasive Diagnostics for Functional Incontinence

Jason Van Batavia, MD, MSTR, FAAP

Assistant Professor, Division of Pediatric Urology, Children's Hospital of Philadelphia, USA

ICCS Secretary General





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A reminder of 2 basic bladder functions: Storage and Voiding





(from Shweta and Swadhin Manual on Urogynecology)

Non-invasive Testing for LUT Dysfunction



- Urinalysis and Urine Culture
- Bladder and bowel diary
- LUT questionnaires, QoL assessments, Psychological screening
- Uroflowmetry +/- EMG
- Post-void residual scan
- Renal and bladder ultrasound
- Pelvic floor ultrasound
- Abdominal x-ray (KUB)



Urine Studies

- Simple and easy to obtain
- Part of initial evaluation for LUT dysfunction
- Normal in majority of patients
- Urinalysis:
 - Glucosuria -> concern for diabetes mellitus
 - Proteinuria -> concern for kidney disease
 - Low specific gravity -> concern for diabetes insipidus
 - +leuk esterase and/or nitrites -> concern for UTI
- Random urine calcium to creatinine ratio
 - >0.2 mg/mg suggests hypercalcemia -> concern for stones¹





Urine Culture



- Rule out urinary tract infection as cause of LUTD
- Recent research suggests that urine is not "sterile"
- <u>Adult women</u>: Studies have identified differences in the urinary microbiota between those with urge incontinence and those without urge incontinence
 - Urge incontinence (UI) = less Lactobacilli species, more Aerococcus and Gardnerella species¹
- Urinary microbiota may also be associated with treatment response^{2,3}
 - Adult women with UI who had fewer bacteria and less diverse bacterial community were more likely to respond to solifenacin²
 - 1. Pearce MM, et al..MBio 2014;5:01283–14
 - 2. Thomas-White KJ, et al. Int Urogynecol J 2015
 - 3. Pearce MM, AB, et al. Am J Obstet Gynecol 2015;213:e341-11

Urine Culture



• Children and adolescents also have urinary microbiota = changes with age

Journal of Pediatric Urology (2023) 19, 368.e1-368.e8

Urogenital urobiome of healthy children does not differ from that of children with bladder and bowel dysfunction

Elisabeth B. Cole^{a,*}, Mark Khemmani^b, Hui Liu^c, Thomas M. Halverson^b, Melline Fontes Noronha^b, Catherine S. Forster^a, Alan J. Wolfe^b, Nader Shaikh^a

- Clean catch urine = 16 S ribosomal RNA gene sequencing and quantitative urine culture
- 25 BBD females [mean age 8 years old] compared to 8 control females [mean age 6]
- Urogenital urobiomes of children with BBD did not differ significantly from those of asymptomatic children

Urine Culture



• Children and adolescents also have urinary microbiota = changes with age

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Urogenital urobiome of healthy children does not differ from that of children with bladder and bowel dysfunction

Elisabeth B. Cole^{*,*}, Mark Khemmani^b, Hui Liu^c, Thomas M. Halverson^b, Melline Fontes Noronha^b, Catherine S. Forster^{*}, Alan J. Wolfe^b, Nader Shaikh^{*}

Table 2	Core microbiomes of the BBD and control groups							
Group	Bladder and Bowel Dysfunction	Asymptomatic Controls						
Taxa	Peptoniphilus Porphyromonas Anaerococcus Lactobacillus Fenollaria Varibaculum Campylobacter	Peptoniphilus Anaerococcus Lactobacillus Fenollaria Finegoldia Veillonella						
	Ezakiella Ezakiella Corynebacterium Dialister Streptococcus Escherichia Schaalia Lagierella Lawsonella							

- BBD children had several additional bacteria genera/species compared to controls
 - More genera associated with opportunistic infection and/or UTI: Escherichia, Campylobacter and Streptococcus

Non-invasive Testing for LUT Dysfunction



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Bladder and Bowel Diaries

•Bladder and bowel diaries:

- Enuresis = 7-night recording of incontinence episodes and nighttime urine volume measurements
- LUT dysfunction = 48 hours of daytime frequency and volume chart [do not have to be consecutive days]
- Measured voided volumes (~15 voids)
- 7-day bowel diary with Bristol Stool Scale
 - Rome IV criteria



https://i-c-c-s.org/members/clinical-tools/



What is a normal voided volume?

- <u>Related to voided volumes</u>
 - Expected bladder capacity [EBC] = (age in years + 1) x 30ml
 - Validated for children 4-12 years old [reaches 390ml at 12 years]
 - Maximum voided volume (MVV) should exclude first morning void
 - Small MVV if <65% of EBC</p>
 - Large MVV if >150% of EBC
- <u>Related to urine output</u>
 - "Normal" difficult to define
 - Polyuria = 24hr total voided urine volume > 40 ml/kg body weight
 - Or >2.8L for child weighing ≥70kg
 - Nocturnal polyuria = nocturnal urine output >130% of EBC for age







The future of voiding diaries?



- Many diaries are not returned or if returned may be incomplete
- Several smart phone apps available
- Some are basic: manual entry diary for voids, bowel movements, and fluid intake

Evaluation of a Mobile Voiding Diary for Pediatric Patients with Voiding Dysfunction: A Prospective Comparative Study

Emilie K. Johnson,* Carlos R. Estrada, Kathryn L. Johnson,† Hiep T. Nguyen, Ilina Rosoklija and Caleb P. Nelson‡

From the Department of Urology, Boston Children's Hospital, Boston, Massachusetts

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- Prospective study, enrolled 83 patients with LUTD: 45 received paper diary and 38 received mobile voiding diary
- 78% completed paper diaries and 61% completed mobile diaries (p = 0.10)
- No improvement in completion rates by using mobile voiding diary

The future of voiding diaries?



- Recently, more complex smartphone apps have become available
- Some use acoustic measurement of volumes/flows no studies in pediatrics





ICCS Tools of Investigation (Austin et al 2014)



• LUT function questionnaires

- Scores allow gauge of extend of LUT dysfunction and provide method for monitoring treatment outcomes
- Recommends:
 - Dysfunctional Voiding Symptom Score (DVSS)
 - Pediatric Urinary Incontinence Quality of Life Score (PIN-Q)

<u>Psychological screening</u>

- Child Behavior Checklist (CBCL) parental questionnaire
- Short screening instrument for psychological problems in enuresis (SSIPPE)
- Can use any validated behavioral questionnaire

Non-invasive Testing for LUT Dysfunction



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ICCS Standardization: Uroflowmetry [Austin et al 2014]

• Uroflowmetry studies:

- Important non-invasive test for LUT dysfunction
- ICCS document stresses:
 - 1) Child must have adequate voided volume (>50% of expected bladder capacity for age)
 - 2) Should obtain more than 1 uroflow study to improve accuracy
- Make sure uroflow machine in private space in which patient will feel comfortable [ie, in bathroom when possible]
- Measures several important parameters (next slide)
- Addition of simultaneous EMG recording allows estimation of urethral sphincter activity
- After uroflow, obtain PVR with bladder scanner



Uroflowmetry Parameters



What information can we get?

- ✓ Flow shape
- ✓ Maximum Flow (Qmax)
- Average Flow (Qave)
- ✓ Time to Qmax
- ✓ Flow Time
- ✓ Voided Volume
- Acceleration
- ✓ Lag Time
- Pelvic Floor Activity (EMG)
- Post-voided residual (PVR)



Maximum Flow Rate (Qmax)



Most relevant quantitative parameter from uroflow to assess bladder outflow

- Sharp peaks = likely artifacts
- True Qmax = only when peak level has duration ≥2 seconds
- General rule:
 - If (Qmax)² ≥ voided volume -> probably normal Qmax



BJU International

The Tzu Chi nomograms for maximum urinary flow rate (Q_{max}) in children: comparison with Miskolc nomogram

Stephen S. Yang*[†], I-Ni Chiang^{‡§}, Cheng-Hsing Hsieh*[†] and Shang-Jen Chang*[†]

*Division of Urology, Taipei Tzuchi Hospital, The Buddhist Tzuchi Medical Foundation, New Taipei, [†]Medical College of Buddhist Tzu Chi University, Hualien, [‡]Department of Urology, National Taiwan University Hospital, and [§]Medical College of National Taiwan University, Taipei, Taiwan

Different between



Age groups	4–6 y	ears	7-9 y	ears	10–12 years						
percenne	Single (<i>n</i> = 186)	Dual (<i>n</i> = 138)	Single (<i>n</i> = 257)	Dual (<i>n</i> = 199)	Single (<i>n</i> = 140)	Dual (n = 115)					
5th	8.6	10.4	11.9	12.9	12.3	14.0					
10th	10.0	11.6	12.0	14.8	14.0	15.4					
5th	12.2	13.3	15.7	17.6	17.3	18.6					
50th	15.0	16.3	19.8	21.6	21.5	23.3					

Age groups	4-6 y	ears	7-9 y	ears	10–12 years						
percentile	Single (<i>n</i> = 201)	Dual (<i>n</i> = 147)	Single (<i>n</i> = 221)	Dual (<i>n</i> = 187)	Single (<i>n</i> = 123)	Dual (n = 102)					
5th	9.5	11.0	12.0	12.1	13.9	16.5					
10th	11.3	12.0	13.4	15.3	16.1	17.6					
25th	13.5	14.8	17.1	18.8	20.1	21.4					
50th	16.3	17.2	20.4	23.1	24.5	26.6					



Depends on voided volume





Important in evaluating patients' evolution



Uroflow Patterns/Shapes



- ICCS (Austin et al, 2014) recognizes:
 - Bell-shaped curve
 - Tower-shaped curve
 - Plateau-shaped curve
 - Staccato-shaped curve
 - Interrupted-shaped curve

Smooth/continuous flows Fractionated flows



Bell-shaped curve: Suggests normal, healthy child

L L



Flow Full Scale 40 ml/s



Tower-shaped curve: sudden high-amplitude of short duration







• Suggests = overactive bladder

Staccato-shaped curve: irregular and fluctuating but flow is continuous (never reaches 0)





- Fluctuations = larger than the square root of the max flow rate
- Suggests = dysfunctional voiding

Interrupted-shaped curve: discrete peaks with spikes similar to staccato but times of 0 flow between peaks







- Suggests = underactive bladder (Valsavla voiding)
- Can also be seen with dysfunctional voiding





Plateau-shaped curve: flattened, low-amplitude prolonged flow curve



• Suggests = bladder outlet obstruction





• Uroflow curve pattern in and of itself is not DIAGNOSTIC of a specific LUT condition!



Table 2

0.01-0.2 0.21-0.4 0.41-0.6 0.61-0.8 0.81-1.0

Uroflow Patterns/Shapes



Journal of Pediatric Urology (2023) 19, 546-554

Is it time to reconsider how we document pediatric uroflow studies?: A study from the SPU Voiding Dysfunction task force

Jason P. Van Batavia ^{a,*}, Hans G. Pohl^b, Walid A. Farhat^c, George Chiang^d, Ahmad BaniHani^e, Therese Collett-Gardere^f, Israel Franco^f

- Included 119 uroflow studies from 5 sites across the USA
- Rated by 7 "experts" in LUTD

Table 3Kappa values for inter-rater agreement using various methods for defining uroflow curve patterns: ICCS definition,BTP (bell, tower, or plateau), and smooth vs. fractionated classification.

		shape description	5 disparate readers ICCS kappa ^a	5 disparate readers BTP kappa ^a	5 disparate readers smooth/fractionated ^a
Fleiss Multi	-rater kappa classification.	ICCS			
	Interpretation	Bell-shaped	0.35	0.21	
	Poor agreement	Interrupted	0.29		
0	Slight agreement	Plateau	0.37	0.42	
0	Fair agreement	Staccato	0.46		
0	Moderate agreement	Tower	0.42	0.37	
0	Substantial agreement	Smooth vs. Fractionated			
0	Atmost perfect agreement	Fractionated			0.70
		Smooth			0.70
		overall agreement	0.34	0.28	0.70
		n	119	119	72

a: Fleiss kappa for multi-raters.

Flow Index (FI)



- Subjectivity in the interpretation of flow curves
- Great variability Inter and Intra observer

Torrens M & Abram P, 1979; Van de Beek et al., 1977; Chang & Yang, 2008; Kanematsu A et al., 2010; Vijverberg MA, 2011; Netto et al., 2019; Van Batvia et al., 2023

- Qmax and Qave calculations do not include bladder volume during voiding
- Uniform and objective referential pattern
- Helps predict the type of curve and voiding characteristics

Flow Index (FI)





A Quantitative Approach to the Interpretation of Uroflowmetry in Children

Israel Franco,^{1*} Stephen Shei-Dei Yang,² Shang-Jen Chang,² Brandon Nussenblatt,³ and Jacob A. Franco⁴

Analyzed 1,258 uroflow curves in healthy children

Estimated Flow Index

Male $Q_{ave} = 3.412+0.052(TBC) - 0.0000061(TBC)^2$ Male $Q_{max} = 11.26+0.0701(TBC)-0.0000513(TBC)^2$ Female $Q_{ave} = 3.37+0.048(TBC)-0.0000354(TBC)^2$ Female $Q_{max} = 10.723+0.073(TBC)-0.0000423(TBC)^2$

Flow Index (FI) =

Qmax / Expected Qmax

Qave / Expected Qave

TBC = Voided Volume + Post Void Residual

Allows comparison of uroflow parameters independent of voided volume and age

Flow Index (FI)





A Quantitative Approach to the Interpretation of Uroflowmetry in Children

Israel Franco,¹* Stephen Shei-Dei Yang,² Shang-Jen Chang,² Brandon Nussenblatt,³ and Jacob A. Franco⁴

Cut-off Values

	Girls 🌳
Plateau	≤ 0.741
Bell	0.741 to 1.133
Tower	≥ 1.33

	Boys ð
Plateau	≤ 0.735
Bell	0.735 to 1.285
Tower	≥ 1.285

Simultaneous EMG during Uroflow



- Electromyography unit should have:
 - High sampling rate and broad sensitivity
 - High quality audio monitor
- Methods:
 - Needle electrodes
 - External patches electrodes
 - Peri-anally at 3 and 9 o'clock around anal sphincter
- Measure pelvic floor activity = surrogate for external urethral sphincter
- Optional if dual channel: addition of patch electrodes on abdomen to measure abdominal straining



Why should you include EMG with uroflow?



- Provides additional value that can support or contradict the diagnosis of specific LUT condition:
 - 1) Activity of pelvic floor/sphincter during void
 - Differentiate fractionated uroflow (staccato or interrupted) secondary to active external urethral sphincter or abdominal straining



ICCS Recognized LUT Daytime Conditions



(Austin et al, Jurol 2014)



Active EMG during void = Dysfunctional Voiding



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Active EMG during void = Dysfunctional Voiding (

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Active EMG activity during void = dysfunctional voiding



Why should you include EMG with uroflow?



- Provides additional value that can support or contradict the diagnosis of specific LUT condition:
 - 1) Activity of pelvic floor/sphincter during void
 - Differentiate fractionated uroflow (staccato or interrupted) secondary to active external urethral sphincter or abdominal straining
 - 2) Calculation of EMG lag time

PELVIC FLOOR EMG LAG TIME





Pelvic floor EMG lag time



- Defined as the time interval from pelvic floor relaxation and the start of urine flow
- Normal 2-6 seconds
 - Based on: 28 children without daytime LUTS
 - PNE or VUR
 - Mean EMG lag time = 3.6 seconds
 - SD = 2.0
 - Range = 1.5 to 6 seconds



ICCS Recognized LUT Daytime Conditions

(Austin et al, Jurol 2014)







Prolonged EMG Lag Time





Prolonged EMG Lag Time >6 seconds

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PRIMARY BLADDER NECK DYSFUNCTION IN CHILDREN AND ADOLESCENTS I: PELVIC FLOOR ELECTROMYOGRAPHY LAG TIME—A NEW NONINVASIVE METHOD TO SCREEN FOR AND MONITOR THERAPEUTIC RESPONSE

ANDREW J. COMBS,* NEIL GRAFSTEIN,† MARK HOROWITZ* AND KENNETH I. GLASSBERG‡ From the Divisions of Pediatric Urology, State University of New York Downstate Medical Center, Brooklyn and Children's Hospital of New York-Presbyterian (Weill-Cornell and Columbia University Divisions), New York, New York

- All 22 children with VUDS confirmed PBND had prolonged EMG lag time (mean 23.9 seconds)
- 17 normal children on VUDS had normal EMG lag times (mean 1.5 seconds)

ICCS Recognized LUT Daytime Conditions (Austin et al, Jurol 2014)



Urinary urgency, usually with frequency and nocturia, with or without urinary incontinence, in absence of UTI; usually 2/2 detrusor overactivity











Short Pelvic Floor Electromyographic Lag Time: A Novel Noninvasive Approach to Document Detrusor Overactivity in **Children with Lower Urinary Tract Symptoms**

Andrew J. Combs, Jason P. Van Batavia, Mark Horowitz and Kenneth I. Glassberg*

From the Division of Pediatric Urology, Morgan Stanley Children's Hospital of New York-Presbyterian, Columbia University Medical Center and Division of Pediatric Urology, State University of New York Downstate Medical Center (MH), New York, New York



Short Pelvic Floor Electromyographic Lag Time: A Novel Noninvasive Approach to Document Detrusor Overactivity in Children with Lower Urinary Tract Symptoms

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Purpose: Noninvasive uroflow with simultaneous electromyography can measure electromyographic lag time, ie the interval between the start of pelvic floor relaxation and the start of urine flow (normally 2 to 6 seconds). Intuitively one would expect that in patients experiencing urgency secondary to detrusor overactivity the lag time would be short or even a negative value. We studied whether short electromyographic lag time on uroflow with electromyography actually correlates with documented detrusor overactivity on urodynamics. Materials and Methods: We reviewed 2 separate and distinct cohorts of 50 neurologically and anatomically normal children with persistent lower urinary tract symptoms who were evaluated by uroflow with simultaneous electromyography and videourodynamics. Group 1 consisted of 30 boys and 20 girls (mean age 7.8 years, range 4 to 19) selected based on electromyographic lag time of 0 seconds or less on screening uroflow with electromyography who subsequently underwent videourodynamics. Group 2 consisted of 14 boys and 36 girls (median age 8.4 years, range 5 to 18) selected based on the presence of detrusor overactivity on videourodynamics whose screening uroflow with electromyography was then reviewed. Correlations between short electromyographic lag time and videouro-

Results: For group 1 urodynamics confirmed the presence of detrusor overactivity in all patients with an electromyographic lag time of 0 seconds or less. For group 2 mean ± SD electromyographic lag time was 0.1 ± 1.7 seconds, and 35 patients (70%) with urodynamically proved detrusor overactivity had a lag time of 0 seconds or less. Conclusions: In patients with lower urinary tract symptoms an electromyographic lag time of 0 seconds or less is 100% predictive of detrusor overactivity. This short electromyographic lag time has 100% specificity and 70% sensitivity for diagnosing detrusor overactivity (88% if less than 2 seconds). Thus, diagnosing the presence or absence of detrusor overactivity in most children with lower urinary tract symptoms and a quiet pelvic floor during voiding can be done reliably via uroflow with simultaneous electromyography.

Key Words: electromyography; lower urinary tract symptoms; urinary bladder, overactive; urination disorders; urodynamics

DIAGNOSIS of a nonneurogenic lower uri- nary tract condition based solely on	vasive testing that provides useful jective information can be invaluable
symptomatology is often misleading	making a more accurate diagnosis,
and can result in less efficacious or	lecting patients who would benefit fr
even inappropriate therapy. ^{1,2} Nonin-	more invasive testing, enhancing th

		0022-5347/13/1896-2282/0	http://dx.doi.org/10.1016/j.juro.2013.01.011
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dynamically proved detrusor overactivity were analyzed.

Cohort #1: Sensitivities of Each Analyzed Shortened EMG Lag Time for DO









- Defined as the time interval from pelvic floor relaxation and the start of urine flow
- Normal 2-6 seconds
- Prolonged EMG lag time >6 seconds
 - Think: primary bladder neck dysfunction
- Shortened EMG lag time <2 seconds
 - Think: detrusor overactivity (overactive bladder)

Why should you include EMG with uroflow?



- Provides additional value that can support or contradict the diagnosis of specific LUT condition:
 - 1) Activity of pelvic floor/sphincter during void
 - Differentiate fractionated uroflow (staccato or interrupted) secondary to active external urethral sphincter or abdominal straining
 - 2) Calculation of EMG lag time
- Can be used in follow up to monitor treatment success or need for additional therapy

Uroflow/EMG to monitor treatment success



- Utility of repeat uroflow/EMG studies during treatment
- Resolution of active EMG during voiding after biofeedback
 - Can sometimes uncover shortened EMG lag time
- Monitor EMG lag time with pharmacologic therapy

Non-invasive Testing for LUT Dysfunction



- Urinalysis and Urine Culture
- Bladder and bowel diary
- LUT questionnaires, QoL assessments, Psychological screening
- Uroflowmetry +/- EMG
- Post-void residual scan
- Renal and bladder ultrasound
- Pelvic floor ultrasound
- Abdominal x-ray (KUB)



Pelvic Floor Ultrasound



Figure 2. Photographs of sagittal plane taken with ultrasound probe on urethral meatus. S = symphysis; U = urethra; R = rectum. (A) Situation at rest. (B) Paradoxical reaction during contraction of pelvic floor muscles, showing important backward displacement of urethra and bladder neck, widening of bladder neck, and shortening of urethra.

- Non-invasive visualization of pelvic floor movement during voiding
- Two methods have been described:
 - <u>1) Perineal dynamic ultrasound</u> (De Jong et al [Uretcht] Urology 2007)
 - Paradoxical pelvic floor movement associated with dysfunction voiding in children
 - Abnormal movement resolved with successful biofeedback

- <u>2) Dynamic pelvic floor transabdominal ultrasound (DFU)</u>

(Godbole et al, J Ped Urol 2013)

- 100 healthy children evaluated
- Normal reference ranges generated for: direction of, distance of, and endurance of pelvic floor movements
- No studies published using this technique in children with LUT dysfunction

Take Home Messages



- Non-invasive diagnostics in the evaluation (and follow up) of children with LUT dysfunction must include urine studies, bladder/bowel diaries, questionnaires/QoL assessments, uroflowmetry +/- EMG
- Uroflowmetry studies can provide a variety of important micturition parameters; however, there is poor inter-rater reliability
- Ensuring child has adequate bladder volume and obtaining multiple studies can help increase accuracy
- Ways to standardize interpretation include considering:
 - Uroflow pattern = Smooth or Fractionated
 - Flow rates = Flow Index

THANKS Questions???

Email: vanbatavij@chop.edu Whatsapp: +1 267 608 5467

