Ultrasonography of Bladder Dysfunction in Children: Does Sex Affect the Measurements and Diagnosis?

Çocuklarda Mesane Disfonksiyonunun Ultrasonografisi: Cinsiyet Ölçümler ve Tanıda Etkili mi?

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Abstract

Aim: Although evaluating bladder dysfunction in children with ultrasonography is feasible, effects of sex differences on the bladder wall measurements and diagnosis are still unknown. This study aimed to measure bladder dysfunction parameters in children by ultrasonography and determine the possible effects of sex on the diagnostic performance.

Materials and Methods: The study included 64 children diagnosed with bladder dysfunction (female/male: 46/18; age: 7.8±2.5, 4–16 years) and 11 healthy children (female/male: 7/4; age: 9.9±4.4, 4–17 years). The anterior, posterior and both lateral walls of the bladder were measured using US before and after urinating. The full-to-empty ratios (FER) of wall thickness were calculated. Statistical data analysis and receiver operating characteristic analysis were performed, and the measurements were evaluated for sex-based differences.

Results: Intergroup data analysis showed that the FER was consistently different between the patients and healthy children, but not between the two sexes. The FER cut-off thresholds (with sensitivity and specificity values) for anterior, posterior, right lateral, and left lateral detrusor were 0.321 (75%, 73%), 0.401 (70%, 63%), 0.328 (73%, 65%), and 0.321 (75%, 65%) mm, respectively. The detrusor thicknesses varied between females and males within each group irrespective of whether the bladder was full or empty. The same was also true for the FER.

Discussion and Conclusion: Ultrasound-based FER measurement of bladder wall thickness is significantly useful in the diagnosis of bladder dysfunction, irrespective of sex.

Keywords: bladder dysfunction; children; full-to-empty ratio; sex difference; ultrasonography

Öz

Amaç: Çocuklarda mesane disfonksiyonunu ultrasonografi ile değerlendirmek mümkün olmakla birlikte, cinsiyet farkının mesane duvarı ölçümleri ve tanı üzerindeki etkileri halen bilinmemektedir. Bu çalışmanın amacı, çocuklarda mesane disfonksiyonu parametrelerini ultrasonografiyle ölçmek ve cinsiyetin tanı performansına olası etkilerini belirlemektir.

Gereç ve Yöntemler: Çalışmaya mesane disfonksiyonu tanılı 64 çocuk (kız/erkek: 46/18; yaş: 7,8±2,5, 4–16 yıl) ve sağlıklı 11 (kız/erkek: 4/7; yaş: 9,9±4,4, 5–17 yıl) çocuk dahil edildi. Anteriyor, posteriyor ve her iki lateral mesane detrusor duvarı işeme öncesi ve sonrası ölçüldü. Mesane boş ve dolu iken alınan detrusor duvar kalınlık ölçüm oranları hesaplandı. Veriler istatistiksel olarak analiz edildi; alıcı işlem karakteristik analizi yapıldı ve ölçümlerdeki cinsiyete dayalı farklılıklar değerlendirildi.

Bulgular: Gruplar arası verilerin analizinde dolu/boş mesane detrusor duvar kalınlık oranlarında sağlıklı ve hasta grup arasında anlamlı farklılıklar saptanırken, cinsiyet ile ilişki izlenmedi. Dolu/boş mesane detrusor kalınlığı için eşik değerleri (sensitivite ve spesifite ile birlikte) anteriyor, posteriyor, sağ lateral ve sol lateral detrusor için sırasıyla 0,321 (%75, %63), 0,401(%70, %63), 0,328 (%73, %65), 0,321 (%75, %65) mm olarak bulundu. Detrusor kalınlığı mesanenin dolu ya da boş olmasından bağımsız, her grup içinde kız ve erkek cinsiyet arasında değişkenlik gösterdi. Aynı durum dolu/boş mesane detrusor kalınlık oranları için de geçerliydi.

Tartışma ve Sonuç: Ultrasonografi ile saptanan dolu/boş mesane detrusor kalınlık oranları, mesane disfonksiyonu tanısına cinsiyetten bağımsız olarak katkı sağlamaktadır.

Anahtar Sözcükler: cinsiyet farkı; çocuk; dolu–boş oranı; mesane disfonksiyonu; ultrasonografi

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INTRODUCTION

Bladder dysfunction is defined as impaired coordination between the detrusor muscle and urinary sphincter, and is a common problem in children. Incomplete voiding of the bladder raises the intravesical pressure and consequently thickens the bladder wall. Depending on its origin, the dysfunction is classified as a neurogenic, nonneurogenic, or anatomically-related abnormality (1). When undiagnosed or untreated, it may lead to urinary retention, urinary tract infection, vesicoureteral reflux, irreversible bladder dysfunction and, ultimately, nephropathy (2). Infection due to urinary retention creates inflammation and increases the detrusor muscle activity. Detailed anamnesis and physical examination forms the basis of diagnosis. However, biochemical and microbiological urine sample analysis may also be necessary. For morphologic evaluation, urodynamic flow test is typically performed. An abnormal pattern is associated with increased detrusor thickness (3). This procedure is invasive and takes a long time. Alternatively, safer approaches are preferable, provided robust diagnosis of bladder dysfunction is feasible (4). As it is noninvasive and easily practiced, studies lately focused on the applicability and success of ultrasonography (US) in the diagnosis of voiding dysfunction (5,6). However, it alone does not provide sufficient information for the diagnosis because detrusor thickness varies significantly from child to child. The full-to-empty ratio (FER) of detrusor thickness was suggested as a plausible diagnostic factor (6), but it is yet to be addressed how the FER is affected by anatomical differences in each sex. This study was performed to investigate this effect.

MATERIALS AND METHODS

Patients

The study protocol was approved by the Institutional Ethical Committee (29/09/2017-E.53603 and no: 53043469-050.04.04). Informed consent was obtained from the families of the children. Subjects with a history of bladder surgery or known bladder anomalies were excluded. The diagnosis was made based on the dysfunctional voiding and incontinence scoring system (7). Detailed history-taking, physical examination, and neurologic evaluation were also performed for each child. The additional checkups included urinalysis, uroflow test, and urine culture when infection was suspected. Finally, a total of 64 children diagnosed with the condition underwent US scans, and 11 healthy children were included as the control group.

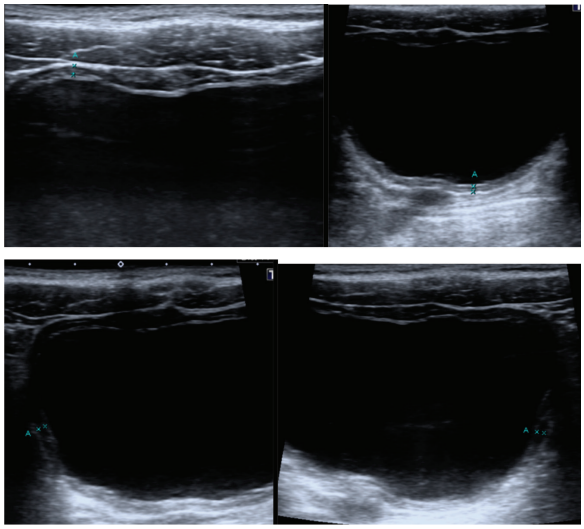

Figure 1. Transverse view of the bladder shows example measurements from the anterior (upper right), posterior (upper left), right lateral (upper right), and left lateral (upper left) bladder walls.

Ultrasonography

US was carried out by an experienced pediatric radiologist working in the field for 6 years. The bladder examination was performed in the supine position through the suprapubic area using 7–12 MHz linear array probe attached to Aplio 500 (Toshiba, Japan) US scanner. When the subject was older than 14 years of age, the probe was switched to 1.9–6 MHz, wide-banded matrix convex transducer. Bladder wall thickness was measured between the two hyperechogenic lines representing the adventitia and mucosa (Figure 1). Thicknesses at the anterior, posterior and both lateral sections were recorded separately when the bladder was full and empty, as described by Muller et al. (8). The state of fullness was determined as the time when the child was significantly in need of urinating. The empty status was considered after two micturations separated by 10 minutes apart. The children diagnosed with neurogenic bladder required clean intermittent catheterization (CIC). Full bladder measurements of these children were performed in the morning before CIC, and empty bladder measurement was performed after removing the catheter.

Table 1. Ultrasound-based measurements of regional detrusor thicknesses from full and empty bladders. Comparison of intragroup sex differences.

		Healthy children			Patients		
		Female	Male	p	Female	Male	p
		Median (min.–max.)	Median (min.–max.)		Median (min.–max.)	Median (min.–max.)	
Anterior	Empty (mm)	3.4 (2.5–4.1)	4.5 (2.2–6.3)	0.182	3.9 (2.0–7.9)	3.7 (0.3–7.5)	0.611
	Full (mm)	1.0 (0.9–1.2)	1.3 (0.8–1.7)	0.106	1.7 (0.6–3.6)	1.6 (0.8–2.7)	0.432
	FER	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.705	0.4 (0.1–1.0)	0.4 (0.2–4.0)	0.881
Posterior	Empty (mm)	3.4 (2.5–3.8)	4.0 (2.7–5.6)	0.131	4.1 (2.4–7.5)	4.0 (1.5–6.6)	0.771
	Full (mm)	1.2 (0.9–1.5)	2.0 (1.0–3.5)	0.215	2.0 (0.8–4.0)	2.0 (1.2–3.9)	0.389
	FER	0.3 (0.2–0.4)	0.3 (0.2–0.7)	0.850	0.4 (0.1–1.2)	0.5 (0.5–1.2)	0.748
Lateral right	Empty (mm)	3.8 (2.5–4.1)	4.4 (2.6–6.4)	0.155	4.1 (2.0–8.9)	4.0 (1.1–8.4)	0.575
	Full (mm)	1.2 (0.9–1.5)	1.5 (0.8–2.2)	0.295	1.8 (1.0–3.6)	1.7 (1.0–3.5)	0.312
	FER	0.3 (0.2–0.4)	0.3 (0.2–0.5)	0.925	0.4 (0.1–1.0)	0.5 (0.1–1.7)	0.935
Lateral left	Empty (mm)	3.4 (2.5–4.1)	4.4 (2.6–6.1)	0.131	4.0 (2.1–8.2)	4.0 (1.3–6.4)	0.929
	Full (mm)	1.0 (0.9–1.2)	1.5 (0.8–2.4)	0.154	1.8 (1.0–3.6)	1.7 (0.9–3.8)	0.427
	FER	0.3 (0.2–0.4)	0.3 (0.2–0.5)	0.705	0.4 (0.2–1.5)	0.4 (2.0–1.3)	0.575

Statistical analysis

The measurements were analyzed using SPSS software (v. 21.0). Data distribution was assessed by the Kolmogorov–Smirnov test. When the data did not follow normal distribution, the Mann–Whitney U test was used for intra- and intergroup comparison for sex differences. Also, ROC (receiver operating characteristic) analysis was performed and threshold values were determined for the variables that had the potential of serving as a diagnostic biomarker of voiding dysfunction. When a significant cut-off value was observed, sensitivity and specificity were also specified. A 5% type-1 error level was used to infer statistical significance.

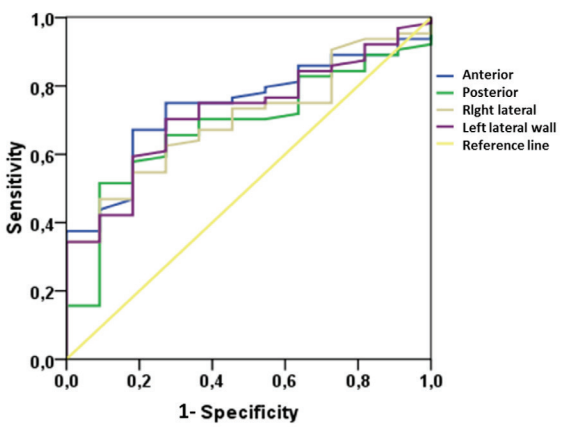

Figure 2. Receiver operating characteristic curve governing the FER measurements.

RESULTS

The sex ratio and age variations of the children included were 46/18 (female/male) and 7.8±2.5 (4–16) years in the dysfunctional voiding group and 7/4 (female/male) 9.9±4.4 (4–17) years in the control group. The ultrasound-based measurements of wall thickness from different segments of the bladder are listed in Table 1. Intergroup comparison indicated that detrusor thicknesses varied between females and males within each group irrespective of whether the bladder was full or empty. The same was also true for the FER. Intergroup differences in sex were not statistically significant, except for the anterior, posterior and lateral right walls of the full bladder as well as the anterior FER in healthy females (Table 2).

When the data from both sexes were combined together under each group and the intergroup comparison was made, the FER readings were determined to be significantly different between the patient and control groups (Table 3). Thus, ROC analysis was only performed on this ratio for all wall segments (Figure 2). For predicting children with dysfunctional voiding, the FER cut-off estimates and the corresponding (sensitivity and specificity) values were determined from the curves in Figure 2 as 0.321 (75%, 73%) for the anterior, 0.401 (70%, 63%) for the posterior, 0.328 (73%, 65%) for the right lateral, and 0.321 (75%, 65%) for the left lateral wall segments.

Table 2. Intergroup sex differences and bladder wall thicknesses.

		Female			Male		
		Healthy children Median (min.–max.)	Patients Median (min.–max.)	p	Healthy children Median (min.–max.)	Patients Median (min.–max.)	p
Anterior	Empty (mm)	3.4 (2.5–4.1)	3.9 (2–7.9)	0.316	4.5 (2.2–6.3)	3.7 (0.3–7.5)	0.250
	Full (mm)	**0.9 (0.9–1.2)**	**1.7 (0.6–3.6)**	**0.004**	1.3 (0.8–1.7)	1.6 (0.8–2.7)	0.347
	FER	**0.2 (0.2–0.4)**	**0.4 (0.1–1)**	**0.089**	0.3 (0.2–0.4)	0.4 (0.2–4.0)	0.155
Posterior	Empty (mm)	3.4 (2.5–3.8)	4.1 (2.4–7.5)	0.217	4.0 (2.7–5.6)	3.9 (1.5–6.6)	0.808
	Full (mm)	**1.2 (0.9–1.5)**	**1.9 (0.8–4)**	**0.006**	1.7 (1.0–3.5)	1.9 (1.2–3.9)	0.301
	FER	0.3 (0.2–0.4)	0.4 (0.1–1.2)	0.108	0.3 (0.2–0.7)	0.5 (0.5–1.2)	0.380
Lateral right	Empty (mm)	3.8 (2.5–4.1)	4.1 (2.0–8.9)	0.604	4.4 (2.6–6.4)	4.0 (1.1–8.4)	0.250
	Full (mm)	**1.2 (0.9–1.5)**	**1.8 (1–3.6)**	**0.014**	1.5 (0.8–2.2)	1.7 (1.0–3.5)	0.543
	FER	0.3 (0.2–0.4)	0.4 (0.1–1.0)	0.180	0.3 (0.2–0.5)	0.5 (0.1–1.7)	0.155
Lateral left	Empty (mm)	3.4 (2.5–4.1)	4.0 (2.1–8.2)	0.508	4.4 (2.6–6.1)	3.8 (1.3–6.4)	0.289
	Full (mm)	1.0 (0.9–1.2)	2.0 (1–3.6)	0.154	1.5 (0.8–2.4)	1.7 (0.9–3.8)	0.427
	FER	0.3 (0.2–0.4)	0.4 (0.2–1.5)	0.705	0.3 (0.2–0.5)	0.4 (2.2–1.3)	0.575

Table 3. Intergroup comparisons of bladder wall thicknesses.

Bladder wall		Healthy children Median (min.–max.)	Patients Median (min.–max.)	p
Anterior	Empty (mm)	4.1 (2.2–6.3)	3.9 (0.3–7.9)	0.970
	Full (mm)	1.1 (0.8–2.3)	1.7(0.6–3.6)	0.002
	FER	**0.3 (0.2–0.4)**	**0.4 (0.1–4.0)**	**0.011**
Posterior	Empty (mm)	3.8 (2.5–5.6)	4.0 (1.5–7.5)	0.579
	Full (mm)	1.4 (0.9–3.5)	1.8 (0.8–4.5)	0.005
	FER	**0.4 (0.2–0.7)**	**0.5 (0.1–1.2)**	**0.054**
Lateral right	Empty (mm)	4.1 (2.5–6.4)	3.8 (1.1–8.9)	0.564
	Full (mm)	1.3 (0.8–2.2)	1.8 (1.0–3.7)	0.010
	FER	**0.3 (0.2–0.5)**	**0.5 (0.1–1.7)**	**0.034**
Lateral left	Empty (mm)	4.1 (2.5–6.1)	3.8 (1.3–8.2)	0.590
	Full (mm)	1.2 (0.8–2.4)	1.6 (0.9–3.8)	0.011
	FER	**0.3 (0.2–0.5)**	**0.4 (0.2–1.4)**	**0.019**

DISCUSSION AND CONCLUSION

Voiding dysfunction is a common problem of childhood caused by various factors (1). Evaluations based on voiding habits and uroflow tests have an important place in the diagnosis. Urodynamic tests involve invasive and expensive procedures conducted by qualified staff (4). As time constraints and radiation exposure are of main concerns, less invasive approaches are sought after. Image-based information gained from the urinary bladder wall has been proposed for visualizing the pathophysiology of the disease and monitoring the treatment success (9).

Ultrasonography imaging is a noninvasive, easily accessed and cost-effective method increasingly used for the assessment of voiding dysfunction. Increased bladder wall thickness in children with myelodysplasia was noted as a risk factor for upper urinary tract damage (10). The bladder detrusor thickness alone has a limited contribution to the diagnosis of voiding dysfunction (11,12). Such thickness measurements were reported to have low specificity in the evaluation, but the FER revealed more reliable information about the deformation of the bladder detrusor, and thereby may be valuable in voiding dysfunction detection. Our results were similar to this assertion as the FER was found to be significantly higher in the dysfunctional voiding group. This result was attributed to the deformation and loss of compliance in the bladder wall. When the healthy female and male children were

compared, bladder wall thickness was significantly higher in males than in females. This finding was in agreement with the literature and associated with the maximum detrusor pressure and higher urethral resistance in females (6).

Bladder wall thickness varies considerably depending on factors such as bladder capacity, size differences, and inability to standardize the fullness description. Therefore, determining a single cut-off value regarding the overall bladder detrusor thickness between the measurements from the healthy children and patients was quite difficult. Nevertheless, cut-off values for the individual segments of the wall were feasible. The cut-off estimates in this study had low specificity and sensitivity, and also were compatible with those reported in the literature (6).

This study has several limitations. First, subject enrollment was limited in both groups. Secondly, the sex ratios of the groups were not similar. The other limitations included a varying degree of perception of bladder fullness among the children, inability to provide the preferred amount of fullness in especially younger children, and the use of convex probe in children older than 14 years of age.

As an indirect US-based measurement from the detrusor wall, the FER provides significant contribution to the diagnosis of bladder dysfunction, and sex does not appear to play a role in this process in spite of the anatomical differences.

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