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Detrusor wall thickness compared to other non-invasive methods in diagnosing men with bladder outlet obstruction: A prospective controlled study

W. ElSaied , A. Mosharafa , H. ElFayoumy *, M. ElGhoniemy , A. Ziada , H. ElGhamrawy , A. Ibrahim , M. Abdel-Azim

Kasr Al Aini Hospital, Cairo University, Cairo, Egypt

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Abstract
Introduction: The current study aims to compare the diagnostic accuracy of detrusor wall thickness to other noninvasive, tools, using pressure flow studies as a reference, in the assessment of bladder outlet, obstruction among men presenting with lower urinary tract symptoms.
Patients and Methods: Men aged 50 or older presenting with lower urinary tract symptoms were evaluated for bladder outlet, obstruction using detrusor wall thickness (measured by a transabdominal 7.5 MHz ultrasound) and, other non-invasive tools (namely uroflowmetry, post-void residual, and prostate volume), and the results were compared to pressure flow study.
Results: Detrusor wall thickness ranged from 0.7 mm to 7 mm (mean ± SD of 2.39 ± 1.64 mm), and 21 patients, were classified as obstructed (thickness ≥ 2 mm). Based on pressure flow study 23 patients had, bladder outlet obstruction. Detrusor wall thickness had the highest accuracy (88.0%), the highest, specificity (92.6%) and the highest positive predictive value (90.5%) among the non-invasive tests.

Abbreviations: BOO, bladder outlet obstruction; BWT, bladder wall thickness; DRE, digital rectal examination; DWT, detrusor wall thickness; IPSS, international prostate symptoms score; LUTS, lower urinary tract symptoms; PFS, pressure flow study; PSA, prostate specific antigen; PVR, post void residual; Q-ave, average flow rate; Q-max, maximum flow rate.

* Corresponding author at: 52-A Cournish Al Maadi, 2nd floor, Apartment 21, 11431 Cairo, Egypt. Tel.: +20 1223239100; fax: +20 33052200.
E-mail address: hany.elfayoumy@kasralainy.edu.eg (H. ElFayoumy).

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Conclusions: Detrusor wall thickness measurement can be used to diagnose and quantify bladder outlet obstruction, non-invasively in men with lower urinary tract symptoms, with an accuracy approaching that of the standard pressure flow studies.

Introduction

Bladder outlet obstruction (BOO) is an underlying cause for Lower Urinary Tract Symptoms (LUTS) in a significant proportion of men presenting with these commons symptoms [1]. While pressure flow studies (PFS) are considered the gold standard for diagnosing and quantifying BOO [2], urologists in their routine clinical practice frequently rely on less invasive methods (such as urinary flow rate, post-void residual [PVR], and prostate volume) to assess BOO. During the last decade, there has been a renewed interest in evaluating the accuracy and usefulness of non-invasive methods based on ultrasound measurements in assessing BOO. In the current study, we compare the diagnostic accuracy of Detrusor Wall Thickness (DWT) to other non-invasive tools and to PFS (as a reference) in the assessment of BOO in men presenting with LUTS.

Patients and methods

Between March 2008 and December 2008, 500 men aged 50 years or older, presenting to the Urology clinic at our institution with LUTS, were considered candidates for the study. An initial evaluation consisted of complete history (with International Prostate Symptoms Score [IPSS] determination) and physical examination (including Digital Rectal Examination [DRE]), Prostate Specific Antigen (PSA), urine analysis, and serum creatinine. The following patients were excluded: patients receiving treatment for BOO/LUTS, prior lower urinary tract or prostate surgery, urethral stricture, and suspected prostate cancer based on DRE or elevated PSA >4 ng/dL.

After obtaining the internal review board approval for the study and after informed consent, eligible patients (50) were enrolled and were further evaluated by transabdominal ultrasound. The bladder was scanned at capacity (patient feeling strong desire to void) using a 3.5 MHz probe to measure inner bladder dimensions, then detrusor wall thickness was measured using a 7.5 MHz probe at the anterior wall,dome and whenever possible right and left lateral walls and trigone, taking the average of three points about 1 cm apart for each section. The detrusor layer is identified as the central hypoechoic layer of the bladder wall, bounded by the thin hyperechoic layers representing the mucosa (with the submucosa) and subserosal tissues. Prostate volume was then estimated using the ellipsoid formula: antero-posterior height x transverse width × cephalo-caudal length x Piπ/6. (above 25 g considered abnormal). A free uroflowmetry was then obtained (patients considered obstructed based on flow rate if they showed maximum flow rate [Q-max] of less than 10 ml/sec or average flow rate [Q-ave] of less than 7 ml/min). A post-void scan with a 3.5 MHz probe was then obtained and a post-void residual urine volume of >50 ml considered abnormal.

At a second visit (1–2 weeks later), all patients had a urodynamic study performed according to "good urodymanic practice" standard of the International Continence Society [3], and interpreted by an investigator blinded to the results of the other performed tests. Pressure flow studies (PFS) were reported using the standard International Continence Society (ICS) nomogram, and Bladder Outlet Obstruction Index (BOOI) was calculated according the formula: BOOI = PdetQmax – 2(Qmax). Patients were divided according to the pressure flow study (PFS) analysis into obstructed (BOOI of 40 cm H_2O or greater) and non-obstructed.

The data was analyzed using SPSS software version 12. For quantitative variables, the range, mean, median and standard deviation were calculated. For categorical variables, the number and percent distribution were calculated. For each diagnostic parameter the sensitivity, specificity, positive and negative predictive values, and likelihood ratios for positive/negative tests were calculated.

Results

Fifty patients aged 53–76 years (mean age 61.7) were enrolled in the study. Table 1 details the results of the initial evaluation, ultrasound findings, and uroflowmetry for the patients. Detrusor Wall Thickness (DWT) was determined at capacity, with all patients having a bladder volume of >250 ml at capacity. DWT measurements showed minimal differences between the sections of the bladder wall where measurements were performed (anterior wall and dome in all patients, lateral walls or trigone in 18 patients) and an average DWT was determined for each examination. The DWT for our patients ranged from 0.7 mm to 7 mm with a mean (±SD) of 2.39 (±1.64) mm. Table 2 describes the finding of bladder outlet obstruction (BOO) based on the results of different non-invasive tests.

According to the results of urodynamic evaluation and pressure flow studies, 23 patients were diagnosed with bladder outlet obstruction while 27 patients were non-obstructed. Table 3 describes the main urodynamic parameters while Table 4 compares the performance of the various non-invasive tests to pressure flow study (as reference) in diagnosing BOO. DWT had the highest accuracy (88.0%), the highest specificity (92.6%) and the highest positive predictive value (90.5%) among the non-invasive tests, while maximum flow rate (Q-max) was the most sensitive (100.0% sensitivity).

Table 1 Patients' initial evaluation data and test results.

	Mean (SD)	Range
IPSS	13.4 (4.2)	4–22
PSA (ng/dL)	2.79 (0.89)	0.7–3.9
S. creatinine (mg/dL)	1.47 (0.43)	0.9–2.7
Prostate volume (g)	39.9 (18.5)	13–90
PVR (ml)	83.2 (60.1)	10–250
DWT (mm)	2.39 (1.64)	0.7–7
Q-max (ml/s)	9.0 (5.6)	3–28
Q-ave (ml/s)	4.8 (3.0)	1.5–14

Table 2 Suggestion of bladder outlet obstruction (BOO) based on non-invasive tests.

Index test	Normal/abnormal (BOO)	Patients with normal result (%)	Patients with abnormal result (%)
Prostate volume (g)	≤25/>25	11 (22)	39 (78)
PVR (ml)	≤50/>50	18 (36)	32 (64)
DWT (mm)	<2/≥2	29 (58)	21 (42)
Q-max (ml/s)	≥10/<10	10 (20)	40 (80)
Q-ave (ml/s)	≥7/<7	15 (30)	35 (70)

Discussion

Despite a consensus on pressure flow studies being the most reliable tool to establish BOO [2], the generalized use of PFS to diagnose BOO in men presenting with LUTS has been limited by factors such as invasiveness, cost, availability and potential morbidity [4]. Numerous "less-invasive" approaches have, therefore, been investigated as alternatives to PFS. These have included symptoms, PSA, PVR, ultrasound derived measurements (prostate volume, intravesical prostatic protrusion, bladder wall thickness, bladder weight), uroflowmetry, and Doppler urodynamics. Among noninvasive methods reviewed by Belal and Abrams in 2006, ultrasound derived measures such as bladder wall thickness were considered promising tools [5]. In the current study, we compared Detrusor Wall Thickness (DWT) to other commonly used non-invasive tests and to PFS in the establishment of BOO diagnosis.

The rationale behind the use of DWT as a surrogate to BOO comes from the numerous studies describing detrusor hypertrophy as a consistent consequence of bladder outlet obstruction in animal models and in humans [6–9]. Mirone et al. describe in a comprehensive review how BOO causes morphologic and functional changes in bladder epithelial and smooth muscle cells through modifications in gene expression and protein synthesis, ultimately leading to LUTS [10]. In addition, some animal models of obstruction have shown increased detrusor hypertrophy, which decreases after obstruction is relieved [11]. Determination of DWT seems therefore, at least in theory, more closely linked to BOO than other commonly used parameters such as prostate volume or PVR. Clinical studies exploring DWT as a tool to diagnose BOO include the study by Oelke et al. noting a statistically significant increase in DWT coinciding with increasing degree of obstruction on PFS, with a mean DWT of 1.33, 1.62, 2.4 and greater than 3 mm in unobstructed, equivocal, obstructed and severely obstructed patients, respectively [12]. In a comparable study by Kessler et al. reporting on 102 men with LUTS, median DWT was 1.7, 1.8 and 2.7 mm in the unobstructed, equivocal and obstructed groups, respectively [13]. Our results are consistent with the above mentioned reports, with 19 (90.5%) of 21 patients having a DWT 2 mm or thicker being classified as obstructed by PFS. Another recent study by Franco and associates in Italy was performed with 100 patients having bladder prostatic obstruction. They compared the ultrasound findings to the urodynamic parameters and found a highly significant correlation for DWT and BOOI (Spearman's $p = 0.57$, $p = 0.001$) and between DWT and Schaefer obstruction class (Spearman's $p = 0.432$, $p = 0.02$) [14]. In a recent systematic literature review, Bright and colleagues they concluded that although a consistent trend between BWT/DWT and BOO can be appreciated, no definitive reference ranges have been established. They also suggested that it is likely that confounding differences among tests, for example measurements at different filling volumes, are to blame [15].

In practice, however, the usefulness of DWT is hampered by a number of factors. The first factor is the influence of bladder filling on DWT (namely the stretch of bladder wall with increasing bladder volume resulting in a decrease in measured DWT). In a study by Oelke et al., DWT decreased at increasing bladder volumes up to 250 ml but remained largely stable beyond that point till capacity. The mean DWT for asymptomatic men in this study was 1.4 mm at 250 ml bladder volume [16]. In another study by Kuo, the decrease in DWT with increasing bladder volume was rapid up to 250 ml; beyond that point (from 250 ml to capacity) a continued but much slower decrease in DWT was observed [17]. To overcome this effect of filling on DWT, some authors have measured DWT or bladder

Table 3 Performance of non-invasive tests compared to PFS in diagnosing BOO.

Test		PFS		PPV %	NPV %	Sens %	Spec %	Acc %	LR+	LR-
		BOO ($n = 23$)	No BOO ($n = 27$)							
Prostate vol.	BOO	20	19	51.3	72.7	87.0	29.6	56.0	1.25	0.44
	No Boo	3	8							
PVR	BOO	17	15	53.1	66.7	73.9	44.4	58.0	1.33	0.59
	No Boo	6	12							
DWT	BOO	19	2	90.5	86.2	82.7	92.6	88.0	11.2	0.19
	No Boo	4	25							
Q-max	BOO	23	17	57.5	100	100	37.0	66.0	1.59	0.0
	No Boo	0	10							
Q-ave	BOO	20	15	57.1	80.0	87.0	44.4	64.0	1.56	0.29
	No Boo	3	12							

Acc = accuracy; BOO = bladder outlet obstruction; DWT = detrusor wall thickness; LR + =likelihood ratio for a positive test; LR- = likelihood ratio for a negative test; NPV = negative predictive value; PFS = pressure-flow study; PPV = positive predictive value; PVR = post-void residual; Sens = sensitivity; Spec = specificity; Q-max = maximum flow rate; Q-ave = average flow rate.

wall thickness (BWT) at a fixed bladder volume (e.g. 150 ml in Manieri et al's report, 200 ml in Blatt et al.'s 200 ml in Franco et al.'s) [14,18,19], while others have suggested a bladder thickness index (to standardize BWT in relation to bladder volume by dividing 4 BWT measurements by the average of 2 internal bladder dimensions) or used a calculated bladder weight as a measure of detrusor hypertrophy [9,20]. In our study, we chose bladder capacity as a practical endpoint with the condition that bladder volume exceeds 250 ml at capacity. This obviously limits the generalization of our results in patients with significant detrusor instability who have a bladder capacity of less than 250 ml.

Other factors that may limit the reproducibility of DWT are technical and include operator dependence, the frequency of ultrasound probe used, the site of measurement and whether DWT or BWT is measured. Operator dependence is an issue in most ultrasound techniques, however studies have shown acceptable intraobserver variability (less than 5.1%) and interobserver variability (4–12.3%) when measuring BWT/DWT [13,18]. The ultrasound frequencies used in reported series range from 3.5 to 8 MHz [15]. While lower frequencies allow deeper penetration; higher frequencies produce a better resolution and higher image quality. In our study, we used a 7.5 MHz probe allowing clear identification and measurement of the detrusor layer. We took the average of multiple measurements done in various sections of the bladder and noted minimal differences between these sections. This was also seen in the study by Kojima et al. who noted no significant differences in bladder wall thickness between the various parts of the bladder [21]. In the study of Franco et al., they also used a 7.5 MHz probe with a minimum of 3 measurements of the anterior or lateral walls done and averaged [14]. Studies evaluating the effect of BOO on detrusor hypertrophy have measured either the bladder wall thickness (BWT) [9,12,22] or the DWT [12,13]. In our study, we used DWT which is believed to be a more accurate measure of detrusor hypertrophy since it excludes the mucosa, the thickness of which may be affected by other pathologies such as infection or tumor [15]. The use of 2 mm as cut off for normal vs. abnormal DWT was suggested by Oelke et al., while the use of a 2.5 mm cut off was suggested by Kessler et al., with both studies revealing comparable sensitivity and specificity and showing a close correlation of increased DWT with urodynamically established BOO [13,23], further studies may be needed to specify a cut off number.

When comparing DWT to other commonly performed "non-invasive" tests in the evaluation of BOO (IPSS, uroflowmetry, PVR and prostate size), the authors used the cut off values suggested by Koyanagi et al. for evaluation of men with LUTS [24] and also used by Oelke et al., who report that among 160 men with clinical BPH or LUTS, DWT was the most accurate test to determine BOO with a positive predictive value of 94%, specificity 95%, and an area under the curve of ROC analysis 0.93.The agreement between DWT and PFS was 89% compared to less than 70% for the other tests [23]. Similar findings were seen in our cohort, with DWT performing better than other tests and showing the highest accuracy (88.0%), the highest specificity (92.6%) and the highest positive predictive value (90.5%) when measured against the standard PFS. Additional advantages making DWT an attractive tool include the availability, relative ease, and absence of significant additional costs when adding DWT to a standard pelvic ultrasound study.

On multivariate analysis, Franco and associates found that intravesical prostatic protrusion and DWT were the only parameters associated with bladder prostatic obstruction ($p = 0.015$) and concluded that the association of intravesical prostatic protrusion and DWT produced the best diagnostic accuracy (87%) when the 2 tests were done consecutively [14]. In their review of non-invasive methods to diagnose BOO, Belal and Abrams recognize ultrasound measurements of bladder wall thickness and bladder weight as promising tools of diagnosing bladder outlet obstruction non-invasively, however they highlight the need to standardize the measurements and techniques used and the importance of large well designed studies before they can replace pressure flow studies as a standard for diagnosing BOO [5].

Conclusions

Detrusor wall thickness is a theoretically rational and clinically practical tool to evaluate patients with lower urinary tract symptoms suspected of having bladder outlet obstruction. Detrusor wall thickness measurement can be used alone or in combination with other tests to diagnose and quantify bladder outlet obstruction non-invasively, with an accuracy approaching that of the standard pressure flow studies. More studies with larger patient numbers are required to better identify the cut off values for DWT associated with BOO.

Competing interests

The authors have nothing to disclose.

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