ABSTRACT. Bladder wall hypertrophy due to bladder outlet obstruction (BOO) is seen in animals and humans. Ultrasound detrusor wall thickness (DWT) measurement is a new non-invasive technique to visualize bladder hypertrophy and diagnose BOO in men. DWT increases with increasing BOO grade. Measurements should be performed with a 7.5 MHz ultrasound array at the anterior bladder wall of a bladder filled with at least 250 ml. The diagnostic accuracy of DWT measurements to detect BOO is higher than the accuracy of the maximum urinary flow rate of free uroflowmetry, post-void residual urine, or prostate volume. Therefore, DWT measurements are recommended to detect BOO.

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BACKGROUND

Basic knowledge about changes of the human bladder as a result of bladder outlet obstruction (BOO) was obtained from experimental animals in which a suture was placed around the catheterized urethra and an increase of urethral resistance occurred after catheter removal. Changes of the obstructed bladder are time dependent and can be divided into three distinct stages which are characterized by typical morphological, functional, and biochemical alterations (1):

Initial stadium: a progressive increase of bladder weight due to thickening of the bladder wall can be found within two weeks after induction of BOO. Compared to sham operated animals, the bladder weight increases 3-5fold in rats and 5-6fold in rabbits (2).

Compensation stadium: the bladder weight remains stable, detrusor strength is unchanged or even increased, and bladder emptying is complete. Microscopic investigations of the bladder
wall of these animals show a hypertrophy of smooth muscle cells, hyperplasia of fibroblasts, and deposition of collagen fibers between bundles of the detrusor (3).

Decompensation stadium: three weeks to six months after induction of BOO (rabbits) a further increase of bladder weight occurs, detrusor strength decreases, post-void residual urine progressively increases, urinary retention occurs, and the animal dies in renal insufficiency. Microscopic studies of the bladder wall in this stadium show that the space between smooth muscle cells becomes wider due to additional deposition of collagen and elastic fibers. Urodynamic studies reveal reduced bladder compliance (4). The more pronounced the deposition of the connective tissue becomes the more the bladder compliance decreases.

In comparison with experimental animals, BOO due to benign prostatic hyperplasia (BPH) in men develops slowly during years or even decades and a strict distinction between three stages is not possible (1). Compensation mechanisms could therefore be more effective than after a sudden induction of BOO. Nevertheless, similar morphological, functional, and biochemical changes of the bladder wall have been observed in men with BOO. In analogy with animals, hypertrophy of smooth muscle cells, hyperplasia of fibroblasts, and infiltration of collagen and elastic fibers between muscle cells develop (5, 6). Bladder weight in men with BOO increases 2-4 fold as a result of bladder wall hypertrophy (7, 8). Urodynamic studies in men with BOO confirmed a decreasing bladder compliance with increasing BOO grade (9). Low-compliance of the bladder seems to be responsible for upper urinary tract dilatation and renal insufficiency in men with BOO (10).

All data indicate that thickening of the detrusor occurs as a result of BOO similar to the heart in which the muscular wall thickens due to a valve stenosis or arterial hypertension (11). Consequently, it is hypothesized that the thickness of the detrusor wall reflects the workload of the bladder and provides information about the degree of BOO. Thickening of the detrusor wall seems to be a compensation mechanism of the bladder to maintain voiding in the presence of BOO.

TECHNICAL REQUIREMENTS

The choice of the correct ultrasound probe is essential for exact measurements. The depth of penetration of the ultrasound waves and the resolution of the ultrasound image is frequency dependent: the higher the ultrasound frequency the better the resolution but, however, the lower the penetration of the ultrasound waves in the tissue (12). Ultrasound waves with a frequency of 3.5 MHz penetrate deeper into the tissue than a 7.5 MHz probe but give less resolution and image quality at the anterior bladder wall. The distance between a suprapubically-positioned ultrasound probe and the anterior bladder wall is dependent on the thickness of the subcutaneous fatty tissue and rectus abdominis muscle as well as the state of bladder filling (13). The distance between the ultrasound probe and the anterior bladder wall of a full bladder is even in obese patients ≤8 cm which is sufficient to image the anterior bladder wall with a 7.5 MHz ultrasound probe with good quality. The resolution given by the ultrasound frequency is <0.13 mm with a 7.5 MHz array and ~0.3 mm with a 3.5 MHz array (13). Therefore, a 7.5 MHz ultrasound probe shows the ideal characteristics for DWT measurements at the anterior bladder wall (7). 7.5 MHz ultrasound arrays are usually used for scrotal imaging and, therefore, widely available in urology offices.

A digital ultrasound machine helps to capture the relevant area and allows enlargement of the ultrasound picture. We used in all our studies a digital ultrasound machine (SONODIAGNOST360, Philips) that allowed enlargement of the ultrasound picture by a factor 9.8. More advanced ultrasound machines even allow a magnification by a factor
30. Additional enlargement of the ultrasound picture is provided by the screen of the ultrasound machine; the picture of a seven centimeter ultrasound probe is imaged on a 50 cm screen. Enlargement of the ultrasound picture helps to place measurement markers correctly and measure detrusor wall thickness (DWT) precisely.

MEASUREMENT OF DETRUSOR WALL THICKNESS

Ultrasound studies in human bladders demonstrated that all parts of the bladder (anterior, posterior and lateral walls as well as the trigone and dome) have the same thickness in one individual (7, 14). Therefore, the anterior bladder wall is a reliable location to obtain information about detrusor wall thickness (DWT). For measurements of DWT at the anterior bladder wall the ultrasound array is positioned suprapubically in either horizontal or vertical position. With a low magnification factor of the ultrasound picture, the anatomy of the anterior abdominal wall and anterior bladder wall can be visualized (Fig. 1). The anterior layer of the rectus sheath, transversalis fascia, adventitia and mucosa (together with submucosal tissue) appear hyperechogenic (white) (7). The detrusor and urine in the bladder lumen appears hypoechochogenic (black). The subcutaneous fatty tissue, the rectus abdominis muscles, and the retropubic space have a mixed hypo-hyperechogenic texture. After identification of the anatomical structures, the digital ultrasound image is enlarged maximally (9.8fold) and the three layers of the bladder wall can be identified (Fig. 2). The hypoechochogenic area between the hyperechochogenic adventitia and mucosa represents the detrusor (7). DWT can be measured with the integrated measurement system of the ultrasound device. Intraobserver variability of ultrasound measurements is ≤5% and interobserver variability between 4-12% (15, 16).

Some investigators measured bladder wall thickness instead of detrusor wall thickness (15, 17). This technique has the disadvantage that the measurement marker might not be placed correctly at the outer site of the adventitia because the tissue of the retropubic space appears hyperechogenic as well. Furthermore, the thickness of the mucosa or adventitia might be affected by other diseases (infection or tumor). In contrast to this, the inner...
and outer border of the detrusor during DWT measurement can always be identified easily. Because only the detrusor adapts to the increased workload in patients with BOO, it was proposed to sonographically measure DWT instead of the entire bladder wall in order to receive more detailed information about the bladder muscle and the state of muscle decompensation (18).

Identification of the anatomical structures and ultrasound measurements of DWT are usually quick and easy. However, the investigator has to be aware of some potential pitfalls during DWT measurements:
- Measurements should not be performed in the midline of the anterior bladder wall because remnants of the urachus or the median umbilical ligament could be mistaken for detrusor wall enlargement (Fig. 3) (19);
- Sometimes it appears difficult to place the measurement markers at the correct outer position of the bladder wall because the hyperechogenic transversalis fascia and the hyperechogenic bladder wall adventitia can be changed by mistake. Wrong placement of the markers would indicate BOO. Both structures run in an almost parallel direction. If the investigator is in doubt of the correct anatomical structure it is helpful to follow the hyperechogenic lines to the lateral direction. The transversalis fascia extends horizontally whereas the lateral bladder wall bends in the dorsal direction (Fig. 4);
- Imaging of the bladder wall in a tangential direction could be mistaken for enlargement of the detrusor and indicate BOO. Therefore, the bladder wall should be imaged in an orthograde manner to measure the true thickness (Fig. 5). Orthograde imaging can be confirmed if the inner and outer hyperechogenic lines of the bladder wall (mucosa and adventitia) appear as thin and sharp lines. In contrast, blurred hyperechogenic lines indicate tangential imaging.

With little experience in bladder wall imaging and knowledge about potential pitfalls ultrasound DWT measurements in one patient can be performed within 1-2 minutes. Reliable results are achieved after approximately 10-15 investigations (learning curve, unpublished data).

DETRUSOR WALL THICKNESS MEASUREMENTS IN HEALTHY VOLUNTEERS

It is important to know DWT values of healthy individuals, factors which influence
DWT, and requirements for DWT measurements. Values of healthy individuals are needed to judge measurements in patients with suspected BOO correctly.

Ultrasound studies in healthy neonates, children, and adults showed that the bladder wall becomes thinner with increasing bladder filling (13, 18, 20-22). However, there seems to be no direct relationship between bladder filling volume and DWT. The detrusor becomes thinner only until a bladder volume of 250 ml (Fig. 6). Thereafter, DWT remains almost stable until maximum bladder filling. No statistical differences were found

Figure 5 - Tangential (left measurement markers) and orthograde imaging (right measurement markers) of the anterior bladder wall in one patient. Blurred hyperechogenic lines indicate tangential imaging.

Figure 6 - Detrusor wall thickness in relation to different bladder filling volumes in healthy adult volunteers (one line represents the measurements of one volunteer). Detrusor wall thickness only decreases within the first 250 ml of bladder filling but, thereafter, remains constant until maximum bladder filling (reprinted with permission of Neurourol Urodyn 25: 308-317, 2006).
between a DWT measured at 250 ml and DWTs measured at 300-800 ml (13). These characteristics of the bladder wall are not well understood but were described in both children and adults (13, 21). DWT in relation to percent bladder filling can be used to compare the higher bladder volume of adults with children. These investigations demonstrated that the detrusor becomes thinner during the first 40-50% of bladder capacity but, thereafter, remains stable until maximum bladder capacity (Fig. 7) (13, 21, 22). DWT in both children and adults should therefore be determined at >50% of bladder capacity. A bladder volume of ≥250 ml indicates this state of bladder filling in adults. Insufficient bladder filling (<250 ml) might occur in patients with detrusor overactivity. In such cases, different reference values for DWT should be used. These can be estimated with the help of the DWT-bladder volume graphs (Fig. 6).

Ultrasound studies in healthy volunteers also demonstrated that DWT is dependent on the gender (13). With a bladder filling of ≥250 ml, men have a significantly thicker detrusor than women (1.4 vs 1.2 mm, p<0.001). This result might reflect the increased workload of the male detrusor due to the longer urethra which passes through the prostate. Hence, results obtained in men cannot be transferred to women. In healthy male volunteers, the normal DWT of a full bladder is between 1.2-1.6 mm (13). Ultrasound measurements in healthy children between 0 and 19 years of age revealed a DWT between 1.2 mm (14), 1.3 mm (23), 1.55 mm (24), and 1.38-1.63 mm (22).

One study group measured bladder wall thickness always with a bladder filling of 150 ml (15, 17). With this measurement technique, BPH-patients without BOO have a bladder wall thickness of about 2.9 mm which corresponds to the results of the DWT-bladder volume graph (Fig. 6), considering the additional width of the mucosa and adventitia. However, this technique has the disadvantage that men need catheterization to fill the bladder with 150 ml. In contrast, measurements at a full bladder (≥250 ml) do not require invasive catheterization and, therefore, are without morbidity.
DETRUSOR WALL THICKNESS MEASUREMENTS IN PATIENTS WITH BOO

Analyses of men with symptoms suggestive of BPH showed that a DWT of <2 mm indicates men without BOO the best (18, 26). DWT in unobstructed patients is 1.3 mm and patients with equivocal obstruction 1.62 mm (p=0.349, Fig. 8) (18). Therefore, symptomatic men without or equivocal obstruction do not have a different DWT compared to healthy adults. Men with urodynamically confirmed BOO have significantly thicker bladder/detrusor walls which can be imaged with ultrasound very well (Figures 8 and 9) (15, 16, 18). DWT shows a direct relationship with the obstruction grade; the higher the obstruction grade is the thicker the detrusor becomes (15). Detrusor wall thickening has been demonstrated in obstructed patients who were evaluated with the ICS- (15, 16), Schäfer- (15), or CHESS-classification (Fig. 8) (13, 26). The median value of DWT measurements at a full bladder in patients with BOO is between 2.4 mm (18) and 2.7 mm (16). However, there is a variance between measurements of men with different BOO-grades. A certain overlap between DWT measurements in men with or without BOO is responsible for the difficult definition of an accurate threshold value for BOO diagnosis. Thickening of the detrusor wall cannot be confirmed in up to 25% of urodynamically obstructed men. However, these men have a minor degree of BOO in pressure-flow analysis and it is doubtful if these men are really obstructed (18).

Interesting results come from studies in which BOO was treated and bladder wall thickness was measured before and after therapy. Bladder wall thickness was significantly reduced already 1 week after transvesical prostatectomy and stable at about 56% of the original thickness after 6 weeks (17). Three months after α-blocker treatment, ultrasonically estimated bladder weight decreased significantly due to decrease of bladder wall thickness (27). Reduction of bladder hypertrophy correlates well with subjective and objective treatment success.

DIAGNOSTIC ACCURACY OF DWT MEASUREMENTS FOR BOO DETERMINATION

Bladder or detrusor wall thickness measurements for determination of BOO would only be useful in clinical practice if the diagnostic accuracy is higher than in other non-invasive tests. Four studies have evaluated the accuracy of DWT measurements compared to measurements of the maximum urinary flow rate ($Q_{\text{max}}$) of free uroflowmetry as well as the ultrasonically estimated post-void residual urine
and prostate volume. Despite different measurement techniques (150 ml bladder filling vs measurement at full bladder, 3.5 vs 7.5 MHz ultrasound array, retrospective vs prospective evaluation), threshold values, and BOO-classification systems, all studies confirmed that DWT measurements are more accurate for BOO-diagnosis (Fig. 10). The likelihood ratio to detect BOO with DWT measurements is between 5.8-21.3 (Table 1) which is clearly higher than with $Q_{\text{max}}$ (1.32-6.5), post-void residual urine (1.35), or prostate volume (0.72) (28). The area under the curve (AUC) of receiver-operating characteristic curves with ultrasound DWT measurements varies between 0.88-0.93 and, therefore, is higher than the AUC of $Q_{\text{max}}$ (0.78-0.82), post-void residual urine (0.64-0.72), or prostate volume (0.62-0.63) (15, 16, 18, 26).

**CONCLUSIONS**

Ultrasound measurements of DWT should be performed at the anterior bladder wall with a 7.5 MHz array and a bladder volume of ≥250 ml. DWT increases with increasing obstruction grade. The diagnostic accuracy of ultrasound DWT measurements is higher than the accuracy of uroflowmetry, post-void residual urine, or prostate volume. DWT measurements are quick, simple, cheap, non-invasive, and with-

Figure 9 - Ultrasound detrusor wall thickness measurements in four patients with symptoms suggestive of BPH. Patient A (DWT 1.5-1.6 mm) had no bladder outlet obstruction in pressure-flow analysis and patients B-D (DWT 2.4-4.1 mm) had different grades of obstruction (all images enlarged 9.8fold).
out morbidity. In a recently published meta-analysis of all available non-invasive, non-urodynamic tests for BOO evaluation, ultrasound measurements of DWT or bladder weight were the only promising methods with a good evidence base to support their use in entering clinical practice after further development (28). Future research should focus on the standardization of the measurement technique, definition of the threshold value to accurately distinguish between obstructed and unobstructed bladders as well as relationships between DWT and age, detrusor overactivity, compliance, or detrusor underactivity.

Table 1 - Diagnostic accuracy of ultrasound detrusor (bladder) wall thickness measurements to diagnose or to exclude bladder outlet obstruction in men with symptoms suggestive of BPH. Accuracy results are dependent on the chosen threshold value. A likelihood ratio above 5 indicates a good and a likelihood ratio above 10 indicates an excellent ability of the test to diagnose bladder outlet obstruction.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Threshold Patients</th>
<th>Positive value for BOO diagnosis</th>
<th>Negative predictive value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Likelihood ratio to detect BOO</th>
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<tr>
<td>Manieri et al. 1998 (15)</td>
<td>174</td>
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<td>88</td>
<td>63</td>
<td>54</td>
<td>92</td>
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<td>95</td>
<td>75</td>
<td>64</td>
<td>97</td>
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<td>100</td>
<td>100</td>
<td>15</td>
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<td></td>
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<td>85</td>
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<td>86</td>
<td>83</td>
<td>95</td>
</tr>
</tbody>
</table>

$^1$bladder wall thickness with 150 ml bladder filling volume.

$^2$detrusor wall thickness with ≥250 ml bladder filling volume (or >50% bladder capacity).
REFERENCES


