The Relationship Between Pressure Flow Studies and Ultrasound-Estimated Bladder Wall Mass

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The basic evaluation of suspected voiding dysfunction involves fundamental objective tools such as the pressure-flow study. Although accurate, the several drawbacks to this invasive study of bladder outlet obstruction (BOO) are discussed and evaluated. Other non-invasive and/or minimally invasive ways of diagnosing BOO continue to be the subject of investigation. The ultrasound-estimated bladder wall thickness and bladder wall mass indices are 2 parameters that may be useful for screening and diagnosing BOO. Preliminary results are presented from the prospective clinical trial comparing the diagnosing capabilities and results obtained with pressure-flow studies (the historic gold standard for BOO diagnosing) with that of ultrasound-estimated bladder weight.

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Key words: Bladder • Ultrasound • Pressure-flow study • Bladder outlet obstruction • Bladder wall thickness • Bladder wall mass

Bladder outlet obstruction (BOO) is a common urologic diagnosis, and is reported to be the most common urologic problem faced by elderly male patients.[1] The condition has many and varied etiologies and is frequently associated with an enlarged prostate gland. This unpleasant condition can lead to lower urinary tract symptoms, upper and lower urinary tract dysfunction, infections, bladder stones, and decreased quality of life. In animal models, BOO is known to cause bladder hypertrophy and increased bladder weight,[2,3] and in humans it can lead to detrusor hyperplasia or hypertrophy, collagen

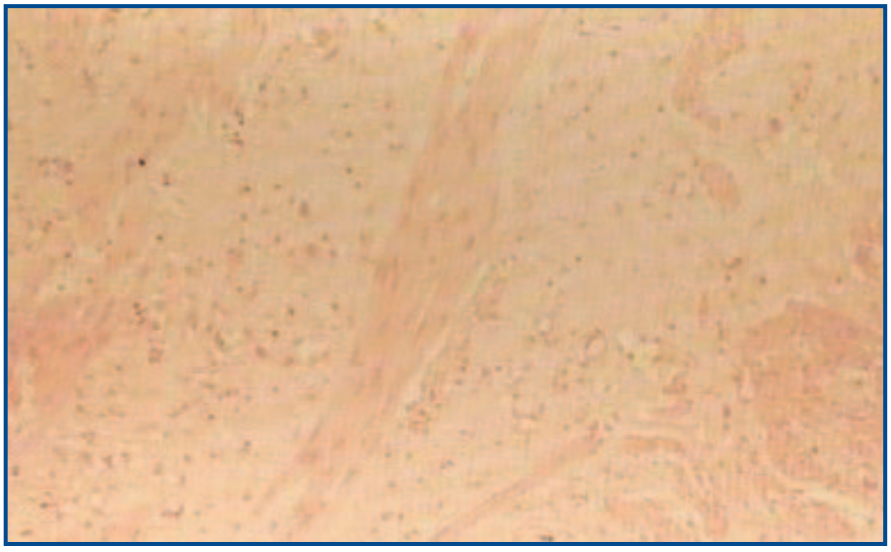

Figure 1. *Detrusor smooth muscle bundles infiltrated by collagen. This specimen demonstrates scarce smooth muscle cells with a significant increase in collagen. This increase in extracellular matrix limits the compliance of the bladder and contributes to an increase in bladder wall thickness. Courtesy of McConnell JD: Bladder responses to obstruction. In: Kirby R, McConnell JD, Fitzpatrick JM, Roehrborn CG, Boyle P, eds.* Textbook of Benign Prostatic Hyperplasia. *Oxford, England: Isis Medical Media Ltd; 1996:105.*

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deposition, and detrusor instability in 50% to 70% of men with benign prostatic hyperplasia.[1]

Diagnosing Bladder Outlet Obstruction

The putative role played by bladder wall thickness (BWT) and bladder wall mass (BWM) in diagnosing bladder outlet obstruction (BOO) is being evaluated by experts in voiding dysfunction. Several studies have already correlated increased thickness and weight of the bladder with BOO.[3-6] Traditionally, the diagnosis of BOO was made with invasive urodynamic studies such as the pressure-flow study, which analyzes detrusor pressure and flow rate. Currently, however, research is determining if ultrasound-estimated BWT and BWM are useful noninvasive alternative tools for diagnosing BOO.

The natural history of BOO spans both an early and a late phase. At the outset of obstruction, the detrusor contracts against increased outlet resistance leading to a compensatory upregulation in muscle mass (muscle hypertrophy) and collagen deposition (Figure 1). This early phase involves bladder wall thickening and weight increase. Over time and depending on obstruction severity, the detrusor muscle may lose some or all contractility. The fate of compliance is variable and has not been fully understood; some bladders may develop into poorly compliant bladders, some maintain normal compliance, and others may become large capacity "floppy" bladders (Figure 2). The clinical challenge for physicians is to identify patients with BOO before they enter these widely variable (and sometimes irreversible) alterations in contractility and/or compliance.

Diagnosing BOO Dynamically

The gold standard method for diagnosing BOO, dynamically, is the pressure-flow study (PFS) (Figure 3). Researchers are investigating alternatives to this technique because of its several downsides, including the fact that the study is invasive, psychologically stressful for some patients, messy, time consuming, and requires the constant presence of a trained professional (a urodynamicist) in order to perform and interpret the study meaningfully. Moreover, the patient may not even be able to urinate with a catheter in the bladder, and there is neither a consensus

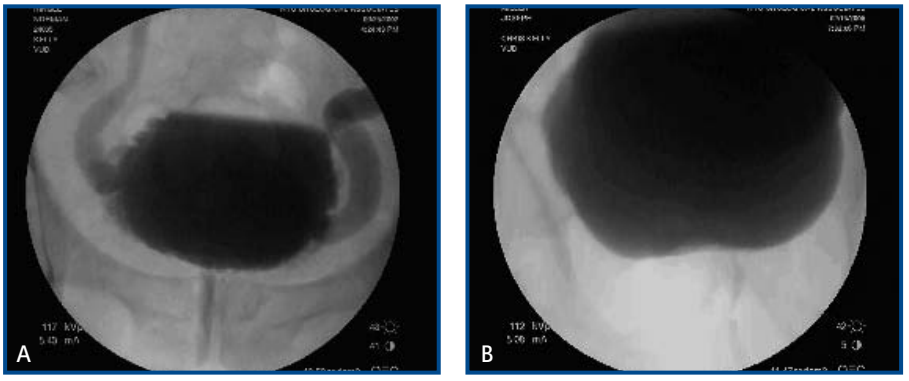

Figure 2. *Fluoroscopic images of bladders with outlet obstruction. The first image (A) reveals a poorly compliant, small capacity bladder with outlet obstruction. Note the irregular bladder contour and the bilateral vesicoureteral reflux that occurred because of dangerously high storage pressures. Image B shows a large capacity (greater than 700 mL), poorly sensate, hypocontractile bladder that resulted from longstanding bladder outlet obstruction.*

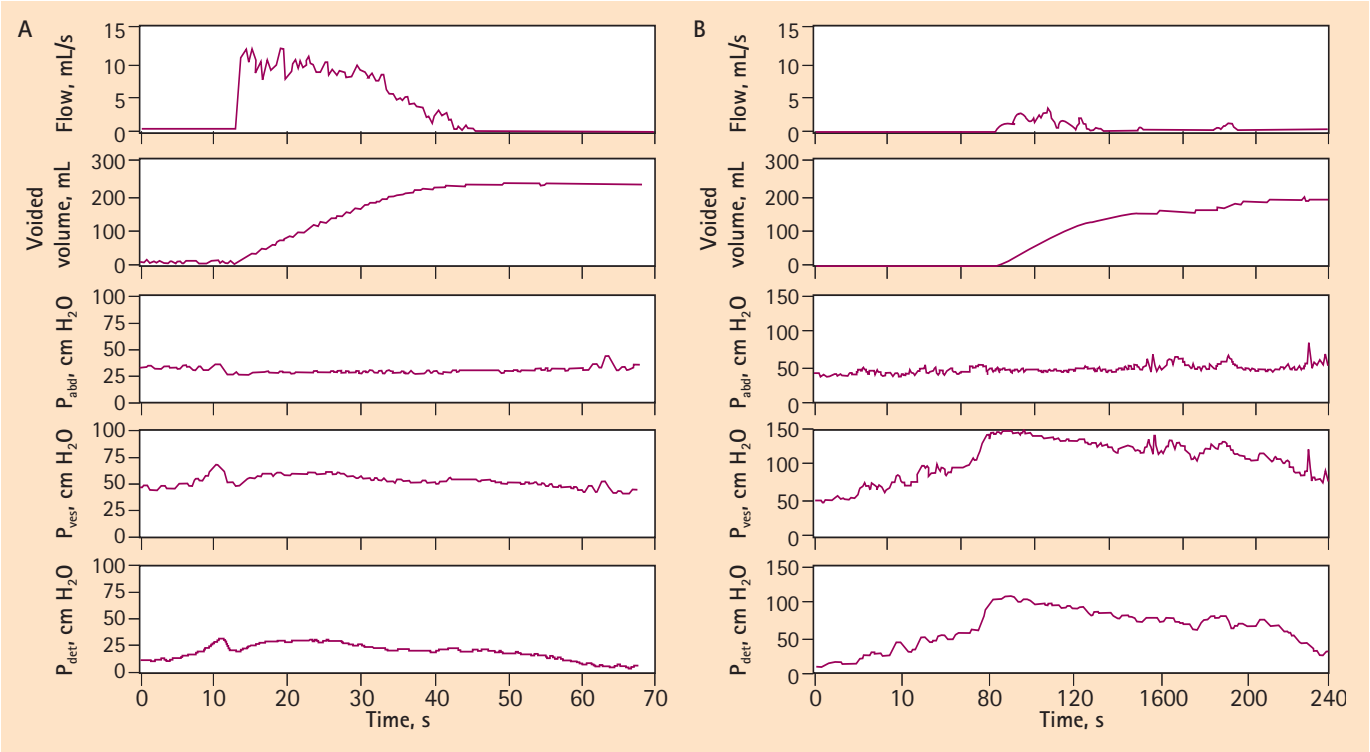

Figure 3. *The pressure-flow study is widely accepted as the "gold standard" for assessing bladder contractility and outlet resistance. Simultaneous intravesical pressure, intrarectal pressure, and urinary flow rate are measured during voiding. These figures show pressure and flow tracings from a non-obstructed control (A) and from a severely obstructed patient (B). P_{abd}, abdominal pressure; P_{det}, detrusor pressure; P_{ves}, vesical pressure. Courtesy of Yalla SV and Sullivan MP in: Kelly CE, Zimmern PE: Clinical evaluation of lower urinary tract symptoms due to benign prostatic hyperplasia. In: Bruskewitz RC, ed.* Atlas of the Prostate. *2nd ed. Philadelphia, PA: Current Medicine; 2003:16-17.*

about nor nomograms for a standardized way to measure obstruction in certain patients. Although not widely used, the urethral pressure-profilometry (UPP) is another technique for diagnosing BOO, but it shares the same above-described disadvantages. Fluoroscopy has been described as a useful adjunct to the PFS, but unfortunately it has the quadruple threat of being invasive, costly, time consuming, and radioactive.

Diagnosing BOO With Static Images

Although historically the gold standard test for BOO has always been a fluid dynamic study, urologists have also used static images or "snapshots" of the bladder to suggest or confirm the diagnosis of BOO. For example, cellules, trabeculations or diverticula – all seen on cystoscopy – are used to confirm BOO (Figure 4). Of course, using static images rather than fluid dynamics to diagnosis BOO may not be reliable because cellules, trabeculations, and diverticula all may persist after obstruction is relieved. As with cystoscopy, radiologic studies such as an intravenous pyelogram, computed tomography scans, or magnetic resonance imaging can reveal similar findings. The latter two radiological studies, along with ultrasonography, offer coronal bladder views that can even demonstrate bladder wall thickness. Ultimately, this BWT can be used to calculate the BWM. Recent evidence has demonstrated a positive correlation between both BWT and BWM with BOO, which will be discussed below.

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Interestingly, bladder ultrasound has a variety of uses in several medical settings including pediatrics, nursing homes, hospitals, and specialized practices (neurology, primary care, urology, and gynecology). Current uses for bladder ultrasound technology include a role in suprapubic aspiration, evaluation of prostate size, intravesical masses, debris, stones or diverticula in the bladder; evaluation of urethral jet phenomena in ureteral obstruction,

and the measurement of postvoid residual. The concept of a hand-held ultrasound device to measure BWT and BWM would be ideal if it measured BOO as accurately as PFS, required minimal patient participation, was noninvasive, reproducible, inexpensive, quick, and easy to use.

By ROC analysis, BWT measurement was found to be superior over uroflowmetry for the diagnosis of BOO.

Correlating BWT and BWM with BOO

There is scientific evidence correlating BOO with BWT and BWM. Hakenberg and colleagues[4] established a relationship between BWT and lower urinary tract symptoms (LUTS) and benign prostatic enlargement (BPE). After establishing that normal (ie, unobstructed) human BWT in males was approximately 3.0 mm ± 1.1 mm, the researchers found that men with documented LUTS and BPE had a significantly increased BWT compared with normal controls (P < .002). In another investigation, Manieri and associates[5] directly compared BWT with pressure-flow analysis. They studied 174 patients with LUTS who underwent pressure-flow analysis and ultrasound-determined BWT measurement. Results demonstrated a strong correlation between BOO and a BWT of > 5 mm at 150 mL. Thirty-seven per cent of those with BWT < 5mm were obstructed on pressure-flow analysis, whereas 87.5% of those with BWT > 5 mm were obstructed by pressure-flow analysis. The authors showed by ROC (receiver operating characteristics) analysis that BWT measurement was superior over uroflowmetry (a screening test for voiding dysfunction) for the diagnosis of BOO.

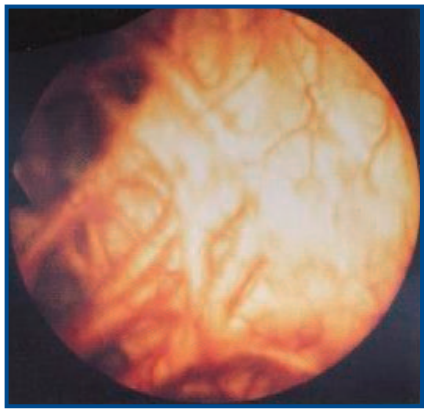

Figure 4. *Endoscopic image of an obstructed bladder. An increase in extracellular matrix (ie, collagen production) is responsible for the cellules and trabeculations seen in patients with bladder outlet obstruction. Courtesy of McConnell JD. The epidemiology and pathophysiology of benign prostatic hyperplasia. In: Bruskewitz RC, ed.* Atlas of the Prostate. *Philadelphia, PA: Current Medicine; 2003:10.*

Oelke and colleagues[6] also found a direct correlation between BWT and urodynamically diagnosed BOO (P < .001). The study included 70 men with LUTS and suspected BOO. Of these patients, 14 men had a mean BWT of 1.33 mm, 23 men with "equivocal" BOO had a mean BWT of 1.62 mm, and 33 obstructed men had a mean thickness of 2.4 mm.

Ultrasound measurement of bladder wall mass has also been studied. Kojima and coworkers[7] reported results of the only study to compare ultrasound-estimated bladder width (UEBW) with BOO. These researchers studied 48 men with presumed BOO as measured by various methods; 15 men were unobstructed and 41 men were asymptomatic. The obstructed group had "heavier" bladders than the nonobstructed patients; in fact 94% of the obstructed patients had a UEBW greater than 35 g. The study would have been improved if BOO had been diagnosed in a uniform manner, such as with pressure-flow studies. In another study by Kojima and associates,[8] BWM was measured by ultrasound in 33 obstructed men before and after prostatectomy for BPE. Results indicated that the bladder weight of the obstructed group was nearly double that of controls. Interestingly, 3 months after a de-obstructive prostatectomy, the BWM of the obstructed group decreased significantly (against controls) from 52.9 g ± 22.6 g to 31.6 g ± 15.8 g (P < .05). This study also suggested that BWM greater than 80 g may signify irreversible pathological changes to the bladder detrusor muscle.

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The question of the accuracy of the ultrasound-estimated bladder mass was answered by Kojima and colleagues,[7] who compared the ultrasound-estimated BWM with varying infravesical volumes in 10 human cadavers, and compared these values with actual bladder weight of cadaveric bladders. They found a statistically significant correlation (P < .0001). The concern for reproducibility was addressed by Naya and associates[9] in their study of intraobserver and interobserver variance in BWM measurement. Only slight and non-significant differences were found between measurements within the 2 groups using Cochran's criterion test.

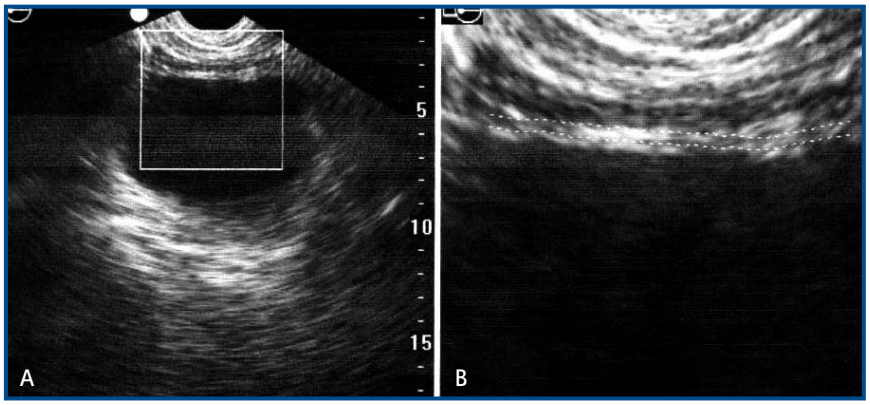

Figure 5. *Ultrasonographic image of the bladder (A) and close-up of the bladder wall (B). The BladderScan® BVM 6500 device (Diagnostic Ultrasound Corporation, Bothell, WA) accurately locates the bladder wall and analyzes the wall thickness.*

Other than being correlated with BOO, BWM may be a useful surrogate marker for bladder compliance. Examining 25 patients with neurogenic bladder, Kojima and associates[10] measured bladder compliance by cystometry and then correlated it with ultrasound-estimated BWM. A statistically significant ($P < .01$) inverse relationship between BWM and compliance was found. Eighty-six per cent of patients with bladder weights over 40 g had poor compliance whereas no patients with ultrasound-estimated bladder weights less than 40 g had poor compliance.[10] Sensitivity and specificity were reported to be 100% and 95%, respectively. The authors conclude that UEBW could be a new urodynamic parameter capable of evaluating functional as well as morphological changes of the bladder.[10]

Ongoing Prospective Clinical Trial

The BladderScan® BVM 6500 device by Diagnostic Ultrasound Corporation, Bothell, WA, is a hand-held 3-dimensional ultrasound device that derives bladder mass mathematically using measured bladder thickness and calculated bladder surface area (Figure 5). These parameters are measured by its 3.7 MHz single-element transducer steered mechanically to acquire a 120-degree cone of multiple, aligned B-mode images. It is accurate, fast, reliable, and easy to use. The device requires a bladder volume between 200 and 400 cc to make reliable measurements. Whether this hand-held device is comparable to PFS in diagnosing BOO is the subject of a prospective trial at New York University Medical Center and Sant' Andrea Hospital of "La Sapienza" University in Rome, Italy. Inclusion criteria will permit both men and women over age 18 years with LUTS for more than 6 months and suspected BOO by history, uroflow, and/or postvoid residual. Each patient will have a UEBW evaluation followed by a pressure-flow study. BOO will be defined by the International Continence Society nomogram and/or by fluoroscopic criteria. Figure 6 illustrates some preliminary findings from this prospective study that began accruing patients in Winter 2004.

Summary

The basic evaluation of suspected voiding dysfunction involves fundamental objective tools such as the pressure-flow study. Although accurate, there are several drawbacks to this invasive study as outlined above. Other noninvasive ways of diagnosing BOO are the subject of investigation. The ultrasound-estimated bladder wall

A statistically significant inverse relationship was found between BWM and compliance. The ultrasound-estimated bladder wall thickness and bladder wall mass indices are two parameters that may be useful in screening for and diagnosing bladder outlet obstruction.

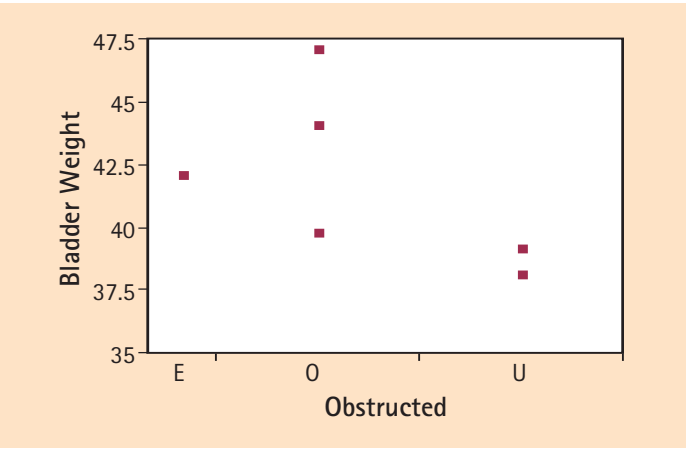

Figure 6. *One-way analysis of individual bladder weights and their respective pressure-flow analysis as determined by the International Continence Society nomogram. E, equivocal; O, obstructed; U, unobstructed.*

thickness and bladder wall mass indices are 2 parameters that may be useful in screening for and diagnosing bladder outlet obstruction. Devices such as the BladderScan BVM 6500 produced by Diagnostic Ultrasound Corporation may afford the urologist a minimally invasive way of making a diagnosis of BOO. ■

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Main Points

- Bladder outlet obstruction (BOO) increases bladder wall thickness and bladder weight.
- The gold standard for the diagnosis of BOO is invasive pressure-flow studies (PFS), which are uncomfortable, costly, messy, time consuming, and require an experienced urodynamicist during the entire study.
- To date, ultrasound-estimated bladder weight (UEBW) has not been rigorously compared with pressure-flow study analyses.
- UEBW measurements have only slight and non-significant differences in interobserver and intraobserver variances; degree of error was acceptable for clinical use using the Cochran criterion test.
- Preliminary comparison to PFS demonstrates that UEBW may correlate with BOO and may be useful as a diagnostic tool for BOO.
- The ultrasound-estimated bladder wall thickness and bladder wall mass indices are 2 parameters that may be useful in screening for and diagnosing BOO.