Recent advances in the diagnosis of bladder outlet obstruction in men

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Abstract

Background: Bladder outlet obstruction (BOO) represents a common cause of lower urinary tract symptoms in men, frequently resulting from benign prostatic hyperplasia. Key symptoms include both obstructive and irritative urinary tract symptoms, such as dysuria, increased frequency and urgency of urination, and recurrent urinary tract infections. BOO can also cause upper urinary tract dilation (hydronephrosis), damage structure, and impair function of the bladder. **Objective:** Early diagnosis of BOO is essential to the protection of kidney and bladder functions. The gold standard for diagnosing BOO is urodynamic studies (UDS), which measure detrusor pressure and urinary flow. However, UDS is an invasive test and is associated with risks for urinary tract infections, bothersome urinary symptoms, and hematuria. Given the invasiveness and discomfort associated with UDS, non-invasive diagnostic methods have been developed. Nevertheless, the main limitation of these techniques is the variability in threshold values, highlighting the need for further standardization of measurement protocols. This article reviews the current diagnostic approaches for BOO in men and explores their clinical utility. **Conclusion:** Various non-invasive diagnostic methods are promising; yet, UDS remains the primary diagnostic approach.

Keywords: Benign prostatic hyperplasia, Bladder outlet obstruction, Diagnosis

1. INTRODUCTION

Bladder outlet obstruction (BOO) is a prevalent cause of lower urinary tract symptoms (LUTS), significantly impacting the quality of life in men [1]. The International Continence Society (ICS) defines BOO as a condition characterized by increased detrusor pressure and decreased urine flow rate resulting from obstructive factors during the voiding phase [2]. Among older men, LUTS related to BOO is most frequently associated with benign prostatic hyperplasia (BPH), although other common factors involving primary bladder neck obstruction (PBNO), urethral strictures, and posterior urethral valves [3]. Based on current human studies, bladder function and urodynamic changes due to BOO can be described in three distinct stages: hypertrophy, a compensatory phase characterized by increased detrusor contractility during voiding, and a decompensatory phase marked by detrusor underactivity. Although urodynamic studies (UDS) remain the gold standard, their invasiveness limits their routine use in all patients. Non-invasive diagnostic methods include measurement of urine flow rate, post-void residual (PVR), and use of ultrasound to assess prostate volume (Pvol), bladder wall thickness (BWT), and intravesical prostatic protrusion (IPP) [4]. The typical presentation of BOO includes dysuria, increased urinary frequency and urgency, and recurrent urinary tract infections. Early diagnosis and treatment are crucial to avoiding irreversible kidney and bladder damage. Available treatment modalities encompass pharmacotherapy and surgical intervention. This article provides a comprehensive review of BOO diagnosis in men, examining current research findings on BOO and their clinical value.

2. ETIOLOGY AND PATHOPHYSIOLOGICAL MECHANISMS

The principal etiologies of lower urinary tract obstructive symptoms in men include both anatomical factors (BPH,

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urethral strictures, and posterior urethral valves) and functional factors (PBNO, detrusor-sphincter dyssynergia, dysfunctional voiding, and neurogenic disorders) [5]. The most prevalent cause of BOO leading to LUTS in men is benign prostate enlargement secondary to BPH [6]. Animal studies have demonstrated that BOO causes an initial inflammatory reaction and ischemia in the detrusor, ultimately resulting in smooth muscle hypertrophy [7,8]. As obstruction progresses, bladder weight and BWT increase to stabilize and compensate for the heightened urethral resistance [9]. In the detrusor muscle, hypertrophy alters the expression of myosin heavy chain isoforms and other muscle proteins [10,11], causing increased collagen production and the replacement of smooth muscle fibers with collagen, a process that may eventually cause bladder function decompensation [12]. Reduced detrusor blood flow related to BOO has been strongly correlated with the level of bladder decompensation. The cyclical ischemia/reperfusion of the detrusor muscle generates reactive free radicals, activating specific phospholipases and proteases that are responsible for cellular and subcellular membrane damage, progressively impairing bladder function [9].

Notably, some young male patients without BPH exhibit lower urinary tract obstructive symptoms, characterized by incomplete relaxation of the bladder neck sphincter during the voiding phase, resulting in urinary flow obstruction [13]. Turner-Warwick *et al*. [14] believed that normal bladder neck opening is typically governed by the coordination between the detrusor and trigonal muscles, and therefore, the uncoordinated or incomplete opening of the bladder neck may be attributed to inherent muscle dysfunction during bladder neck development. This dysfunction may be due to three causes: (i) hypertrophy of the muscular layer surrounding the bladder neck, which can cause a physical obstruction to the urethra; (ii) reduced elasticity and narrowed lumen of the bladder outlet due to excessive fibrous tissue accumulation, leading to bladder contracture; and (iii) chronic inflammation, particularly noted in pediatric cases [15]. In contrast to fibrotic bladder neck strictures, Bates *et al*. [16] proposed that, in some cases, bladder neck obstruction is functional, arising from bladder neck tightening during detrusor contraction rather than fibrous tissue proliferation. Previous research also suggested that the progression of BOO and its contribution to bladder neck dysfunction could be ascribed to an increase in protein gene product 9.5 and neuropeptide Y-immunoreactive nerves, which are integral components of the sympathetic contractile system that regulate bladder neck function [17]. In addition, as the bladder fills, both intravesical and intraluminal urethral pressures rise. During volitional voiding, the initial decrease in urethral pressure is attributable to the relaxation of the external sphincter and pelvic floor muscles. Voiding only takes place when proximal urethral pressure equals or exceeds intravesical pressure. Yalla *et al*. [18] observed that proximal urethral pressure increased during the initial voiding phase, a finding with important implications for understanding the underlying causes of bladder neck dysfunction.

3. DIAGNOSIS

3. 1. UDS

The ICS defines BOO as an obstruction that occurs during bladder emptying, characterized by increased detrusor pressure and decreased urine flow rate, as measured by pressure-flow studies (PFS). UDS undeniably remains the definitive diagnostic tool for identifying BOO in male patients [2]. In addition, video-urodynamic studies (VUDSs) combine UDS with synchronous imaging of the lower urinary tract to evaluate both anatomical and functional aspects during urination. The maximal flow rate (Q_{max}) [19] and various flow-rate nomograms have gained popularity among urologists, being increasingly accepted by clinicians [20]. However, this test is associated with relatively high false-negative and false-positive rates [21,22]. To enhance diagnostic precision and better assess the degree of BOO, PFS data are analyzed, often using the Abrams and Griffiths nanogram [23]. This nomogram [24] provides a straightforward method for categorizing data, differentiating between obstructed, unobstructed, or uncertain cases of bladder neck obstruction by graphing Q_{max} against detrusor pressure during micturition. In the cases where patients fall within an "uncertainty zone," further assessment is conducted using the mean slope of the pressure-flow chart and minimum detrusor pressure to confirm obstruction. The Abrams-Griffiths nomogram includes the bladder outlet obstruction index (BOOI), represented by Equation I:

$$BOOI = P_{det}Q_{max} - 2Q_{max} \quad (I)$$

where $P_{det}Q_{max}$ represents detrusor pressure at maximum urine flow rate. The ICS nomogram [25] categorizes men based on their BOOI scores as follows: Obstructed, if BOOI > 40, equivocal, if BOOI is between 20 and 40, and unobstructed, if BOOI < 20. However, BOOI has limitations. Since it uses only two parameters, it may produce inaccurate results in the cases where the detrusor muscle is weak or damaged, potentially leading to clinical misjudgment. Nitti *et al*. [26] categorized primary bladder obstruction into three types: Typical high-pressure low flow, normal pressure low flow with bladder neck stenosis, and delayed bladder neck opening, all caused by bladder neck dysfunction. Fluoroscopic imaging of the bladder outlet during voiding was utilized to assess whether the bladder neck opened or remained closed, and to identify any localized narrowing. External sphincter activity was evaluated by combining electromyography and fluoroscopy during voiding. Norlen and Blaivas [27] described findings in men with proximal urethral obstruction, including high detrusor pressure, complete relaxation of the external urethral sphincter during detrusor contraction, decreased urine flow rate, and radiological evidence of bladder neck obstruction with no distal obstruction. Nitti [28] emphasized that primary PBNO diagnosis relies heavily on VUDS, characterized by high detrusor pressure and decreased urinary flow, accompanied by imaging evidence of bladder neck obstruction while ruling out distal urethral obstruction. However, consensus remains lacking regarding the definitions of "high detrusor pressure" and "decreased urinary flow" in PBNO. In general, it is widely accepted that the maximum urinary flow rate is below 15 mL/s, and detrusor pressure ranges from 20 to 70 cmH_2O at maximum urinary flow in male patients.

3. 2. Magnetic resonance imaging (MRI) and magnetic resonance voiding cystourethrography (MR-VCU)

Recently, Di Girolamo *et al*. [5] evaluated PBNO in men using MRI and MR-VCU to investigate anatomical aspects of the bladder neck and urethral cavity. MRI allows for assessment of the muscular composition of the urethral lumen and bladder neck muscles. MR-VCU is a diagnostic method that provides real-time visualization of the urethral lumen during urination after injection of a suitable concentration of contrast agent into the bladder [29]. In this study, 21 patients were evaluated, and four subgroups of PBNO patients were identified: 52% exhibited hypertrophy of the posterior lip of the bladder sphincter, 20% showed asymmetry in the lateral portion of the bladder sphincter, 14% had a cyst at the bladder neck, and 14% displayed a normal appearance in this region. Comparison with a control group of five healthy volunteers revealed statistically significant differences between the control group and the first two PBNO subgroups, with a diagnostic accuracy of 87%.

3. 3. Pvol and height

Watanabe and Miyagawa [30] investigated the utility of Pvol and the ratio of prostate height to width (H: W) from the maximum horizontal section, as measured by transabdominal ultrasound, in assessing the severity of benign prostate obstruction. These parameters were compared with PFS results in 51 patients, excluding cases of bladder neck contracture and urethral stricture confirmed through urethroscopy. The PFS recordings were digitized to facilitate the calculation of the urethral resistance parameter and linear passive urethral resistance relation (lin-PURR). In this classification, classes 0 and 1 indicate normal flow, class 2 signifies ambiguous obstruction, and classes 3 and above are indicative of varying degrees of BOO, based on UDS results [31]. The study showed a significant positive correlation between Pvol and the degree of prostate obstruction. Adopting an ultrasonographic threshold of Pvol > 30 mL and an H: W ratio exceeding 0.8 as preliminary criteria for identifying patients with obstruction, all 10 selected cases had lin-PURR values above 3. When lin-PURR = 3 was classified as obstructed, the sensitivity was 42%, and the specificity was 100%. Transabdominal ultrasound is thus a useful screening modality for assessing the extent of benign prostatic obstruction by measuring Pvol and the H:W ratio. However, it is imperative to acknowledge the limited efficacy of transabdominal ultrasonography (TAUS) in detecting a small prostate with elevated urethral resistance [32]. Furthermore, its effectiveness is limited in assessing BOO due to detrusor sphincter dyssynergia, bladder neck disease, and similar conditions.

3. 4. IPP

Recent studies have indicated that assessing IPP through TAUS holds potential for diagnosing BOO. In one study, 200 men aged ≥50 years with LUTS [33] were evaluated after ruling out tumors and neurogenic bladder conditions. TAUS was used to assess prostate protrusion into the bladder neck, with IPP graded on a 3-point scale based on protrusion extent: grade I (<5 mm), grade II (5 – 10 mm), and grade III (>10 mm). IPP was measured by determining the vertical distance between the tip of the protrusion and the circumference of the bladder at the base of the prostate gland. Among the 120 patients diagnosed with BOO (BOOI > 40), 95 were classified as grade III. In contrast, among the 75 patients without BOO (BOOI < 40), only six exhibited grade III IPP. The study demonstrated a strong correlation between IPP and BOO, with a positive predictive value (PPV) of 94% and a negative predictive value (NPV) of 79%. An IPP of 8 mm was identified as the optimal threshold for predicting BOO [34], offering the highest sensitivity and specificity on the receiver operating characteristic curve. With an area under the curve of 0.885, the sensitivity was 80%, specificity was 80%, PPV was 73.7%, and NPV was 85.1%. These findings suggest that IPP assessed through TAUS is a reliable and accurate predictor of BOO [35]. However, alternative perspectives exist regarding the predictive capability of IPP for BOO. Kadihasanoglu *et al*. [36] conducted a study on 240 male patients over 50 years with LUTS, comparing groups with and without IPP. While IPP grade consistently correlated with Pvol and PVR, other findings contrasted with previous studies. Although a significant proportion of grade III IPP patients exhibited obstruction, IPP did not correlate with obstructed urine flow, and no statistically significant correlations were observed between IPP grade and Q_{max}. A systematic review further analyzed five studies using a 10-mm IPP threshold to define BOO and found only moderate sensitivity (67.8%) [37]. This study reinforced the argument by Chia *et al*. [33] that symptoms alone may not necessarily indicate obstruction, as urinary flow rate and PVR primarily reflect the functional status of the lower urinary tract rather than anatomical obstruction. BOO is a dynamic condition affected by both bladder function and physical obstruction from the prostate. Therefore, incorporating an anatomical evaluation, such as IPP grading, can improve the assessment of significant BOO and help correlate findings.

3. 5. Prostatic urethral length

To investigate the correlation between prostatic anatomical factors and PFS, Yaris and Oztekin [38] conducted a study involving 41 patients. These patients underwent PFS and transrectal ultrasound assessment to measure the prostatic indentation, prostatic urethral length, and bladder-prostatic urethral angle. Significant correlations were observed between the BOOI and both prostatic indentation ($r = 0.479, p = 0.002$) and prostatic urethral length ($r = 0.386, p = 0.013$). However, no association was found between the bladder-prostatic urethral angle and BOOI. The study suggests that prostatic indentation and prostatic urethral length correlate with the severity of BOO. Additional research involving larger sample sizes is warranted to confirm these findings and enhance the accuracy of these measurements.

3.6. Detrusor wall thickness (DWT)/BWT

A noninvasive approach proposed by Belal and Abrams [39] introduces the potential for diagnosing BOO through transabdominal ultrasound measurement of BWT. The rationale for utilizing BWT as a diagnostic parameter is based on the association between increased prostate obstruction and detrusor hypertrophy, which results in elevated BWT [39]. Inui *et al*. [40] used a computer-assisted color image analysis to quantify the proportion of smooth muscles relative to connective tissue. Their findings suggested that abnormal connective tissue deposition might contribute to advanced bladder hypertrophy due to intravesical obstruction. In a study by ElSaied *et al*. [41], transabdominal ultrasound was employed to evaluate 50 patients by measuring detrusor wall thickness (DWT) with a 7.5 MHz probe during episodes of strong urge to urinate. These results were compared with the findings of PFS analysis, which was conducted following the ICS standard nomogram. BOOI was calculated using Equation I.

On the basis of PFS analysis, patients were categorized into an obstruction group (BOOI≥40 cmH_2O) and a non-obstruction group. Among the 23 patients diagnosed with BOO, 21 had a DWT of ≥2 mm. The sensitivity, specificity, and PPV for this DWT threshold were 88.0%, 92.6%, and 90.5%, respectively. Oelke *et al*. [42] also explored DWT as a diagnostic tool for BOO, observing a strong positive correlation between increased DWT and BOO severity. The mean DWT in patients with BOO was 2.4 mm, and a DWT threshold of 2 mm yielded a high PPV of 95.5%. DWT measurement is thus a clinically practical approach for evaluating patients with LUTS suspected of BOO [43]. However, further research with larger patient cohorts is necessary to establish a definitive threshold for DWT [41].

3. 7. Ultrasound-estimated bladder weight (UEBW)

Current research suggests that BOO results in bladder hypertrophy, accompanied by compensatory changes in the bladder and detrusor muscles, ultimately increasing both BWT and bladder weight [44]. A study involving 193 men over 50 with LUTS categorized patients into obstructive and non-obstructive groups based on the BOOI [45]. Bladder weight was measured using a three-dimensional ultrasound system, and the findings revealed a positive correlation between corrected bladder weight and BOOI. A significant increase in corrected bladder weight was observed as the obstruction deteriorated. A threshold value of 28 g/m^2 for diagnosing obstruction yielded a sensitivity of 61%, specificity of 59.8%, PPV of 33.8%, and NPV of 82.6%. However, bladder weight alone is inadequate for accurately predicting BOO due to its limited correlation strength and diagnostic accuracy.

3. 8. Doppler ultrasound

Saito *et al*. [46] proposed that reduced blood flow to the detrusor muscle contributes to detrusor dysfunction resulting from BOO, a hypothesis supported by experimental studies in male rats. Belenky *et al*. [47] investigated the clinical value of detrusor blood flow measurement through Doppler ultrasonography for diagnosing BOO. Twenty-nine patients with LUTS were enrolled, with BOO diagnosed through UDS (BOOI > 40 as the criterion). Doppler ultrasound was performed on both full and empty bladders to measure arterial blood flow in three different bladder regions, and the detrusor resistance index (RI) was calculated using Equation II:

$$RI = (V_{MAX} - V_{MIN})/V_{MAX} \quad (II)$$

A logistic regression analysis-based formula was devised to predict BOO, with a PPV of 95% and an NPV of 57%. Zhang *et al*. [48] further assessed the correlation between the RI of prostate capsular arteries and BOO severity in men diagnosed with BPH. Using simple regression analysis, they observed that the RI of the prostate capsular artery was significantly higher in patients with BOO compared to those without BOO. With a threshold RI of 0.69, the sensitivity for diagnosing BOO was 78.0%, specificity was 86.4%, PPV was 92.85%, and NPV was 62.5%. These results suggest that Doppler ultrasound can provide significant clinical information for BOO diagnosis. However, further studies are needed to confirm the reliability of RI measurements, as current research has its limitations.

3. 9. Near-infrared spectroscopy (NIRS)

NIRS is an increasingly utilized non-invasive technique for monitoring oxygenation and hemodynamics in various organs, primarily for cerebral and skeletal muscle assessments. Recently, there has been mounting interest in exploring the application of NIRS in urology [49]. In a previous study, a specific algorithm and a software package were employed to observe variations in chromophore concentration in the bladder detrusor [50]. A dedicated algorithm also analyzed Q_{max} and PVR, allowing for the categorization of patients into obstruction and non-obstruction groups. Simultaneously, 55 patients underwent UDS and were classified as either obstructed (28 patients) or non-obstructed (27 patients) based on the UDS results, with NIRS data matched accordingly. In the study, NIRS accurately identified 24 patients in the obstruction group with a sensitivity of 85.71%, while correctly classifying 24 patients in the non-obstruction group with a specificity of 88.89%. MATLAB software was utilized to develop a CART-model algorithm for evaluating the variations in chromophore concentration during the complete voiding cycle [51]. The analysis, based on 64 NIRS datasets compared with UDS data, demonstrated exceptional performance, with a sensitivity of 100%, specificity of 87.50%, and precision of 93.75%. In another study by Zhang *et al*. [52], 94 male patients with LUTS due to BPH were assessed, using uroflow rate and PVR as indicators. NIRS results were compared with PFS, demonstrating higher diagnostic accuracy and offering a promising noninvasive approach for diagnosing BOO in men. Further investigations are warranted to ascertain the potential of NIRS as a reliable non-invasive screening method for BOO.

3. 10. Uroflowmetry

Uroflowmetry is a relatively straightforward approach for assessing BOO, although the choice of threshold value significantly impacts diagnostic accuracy. Reynard *et al*. [53] conducted a comprehensive analysis of the predictive capability of Q_{max} for BOO at various threshold values. The study, involving 1271 male patients from multiple age groups across 12 medical centers, aimed to elucidate the correlation between Q_{max} and BOO. The sensitivity, specificity, and PPV for BOO diagnosis were 47%, 70%, and 70%, respectively when the Q_{max} threshold value was 10 mL/s, and 82%, 38%, and 67%, and when the Q_{max} threshold value was 15 mL/s. The threshold values employed in urine flow rate in studies vary widely, and the observed ranges in sensitivity and specificity are often too broad to reach any definitive conclusions [54]. Lowering the Q_{max} threshold value enhanced sensitivity but diminished specificity, limiting the effectiveness of uroflowmetry in diagnosing BOO [37].

3. 11. Penile cuff test (PCT)

PCT has been developed as a less invasive alternative for BOO assessment [55]. The penile cuff automatically inflates at the initiation of urination, maintaining inflation until the flow stops, and then deflates to restore the initial state. This test measures the pressure required to halt urine flow, providing an estimate of bladder isovolumetric pressure [56]. Multiple inflation-deflation cycles may be performed within a single urination to obtain multiple bladder isovolumetric pressure readings. In a study by Bianchi *et al*. [57], 48 patients scheduled for transurethral resection of the prostate were divided into obstruction (31 patients) and non-obstruction groups (17 patients) based on PCT results. Comparison with PFS data revealed that out of the 31 patients classified as obstructed by PCT, 21 were confirmed as obstructed by PFS, while all 17 patients in the non-obstruction group were also verified to be non-obstructed by PFS. PCT achieved a sensitivity of 100%, specificity of 63%, PPV of 68%, and NPV of 100%. Another study by Borrini *et al*. [58] investigated PCT's diagnostic utility and patient tolerance, reporting a PPV of 82% and an NPV of 88%. Although PCT is generally well-tolerated, threshold values for diagnosing BOO vary across studies [59], making it challenging to establish a universally applicable standard.

3. 12. External condom catheter

The external condom catheter, similar to the PCT, is a noninvasive technique for measuring bladder isovolumetric pressure by obstructing urinary flow [60]. Pel and van Mastrigt [61] conducted a study involving 40 patients who received invasive UDS and were subsequently assigned into obstructive and non-obstructive groups. Bladder isovolumetric pressure was measured using the external condom catheter, with accurate results obtained in the non-obstructive group; however, in the obstructive group, the results were less reliable. When urine flow was interrupted, increased urethral pressure caused condom catheter to expand, often resulting in urine leakage. Therefore, achieving a proper fit between the penis and the condom catheter is imperative. In a subsequent study, Pel *et al*. [62] refined the test and expanded the sample size to 75 patients. After excluding cases with urine leakage, inability to urinate, or other complications, a total of 56 patients were successfully measured using the external condom catheter. With these refinements, the diagnostic accuracy rate reached 73%. However, limited research on this method and measurement failures due to various factors may hinder its clinical application.

Table 1. Diagnostic methods for BOO and their advantages and disadvantages

Category	Diagnostic methods	Advantages	Disadvantages
Definitive diagnostic tool	UDS/VUDS	The gold standard for diagnosing BOO by measuring the maximum flow rate during urination and its corresponding detrusor pressure.	(i) Invasiveness, cost, discomfort, time-consuming, risk of urethral trauma and urinary tract infection. (ii) The equation BOOI only uses two parameters, which may result in inaccurate results. (iii) VUDS will expose the patients to ionizing radiation.
MRI	MRI and MR-VCU	MRI allows the evaluation of the urethral lumen, peri-urethral structures, and muscular structures of the bladder neck without the use of ionizing radiation.	(i) High cost, time-consuming. (ii) Some patients may have difficulty urinating due to their position and environment.
Ultrasound (prostate)	(i) Prostate volume and height (ii) IPP (iii) Prostatic urethral length	Noninvasive, simple to perform, safe, low cost, suitable for monitoring treatment effectiveness.	(i) The results are easily influenced by subjective factors. (ii) Different studies have different thresholds, which limits the comparability of results and leads to significant differences in the sensitivity and specificity of each study.
Ultrasound (bladder)	(i) DWT/BWT (ii) UEBW (iii) BNA (iv) Doppler ultrasound (v) Radiofrequency ultrasound strain imaging		
Other noninvasive examination methods	NIRS	Noninvasive, safe.	(i) The research necessitates specific models and algorithms, entailing a complex modeling process. (ii) Optimization of algorithms is imperative to enhance sensitivity and specificity, while accurate foundational data support is essential.
	Uroflowmetry	Noninvasive, straightforward, safe, low cost.	The determination of the threshold value has a direct impact on the accuracy of the results.
	(i) Penile cuff test (ii) External condom catheter	Noninvasive, simple and easy to perform.	(i) Nervousness, anxiety, and other emotions may affect the accuracy of the results. (ii) The presence of urinary incontinence or urinary retention may lead to inaccurate measurements.
	Urine biomarkers	Noninvasive, promising.	(i) The accuracy of it may be influenced by various factors such as individual differences, the stage of the disease, and interference from other diseases. (ii) These biomarkers have not yet been widely used in clinical practice.

BNA: Bladder neck angle, BOO: Bladder outlet obstruction, BOOI: Bladder outlet obstruction index, BWT: Bladder wall thickness, DWT: Detrusor wall thickness, IPP: Intravesical prostate protrusion, MRI: Magnetic resonance imaging, MR-VCU: Magnetic resonance voiding cystourethrography, NIRS: Near-infrared spectroscopy, UDS: Urodynamic studies, UEBW: Ultrasound-estimated bladder weight, VUDS: Video-urodynamic studies.

3. 13. Bladder neck angle (BNA)

BNA refers to the angle subtended by the anterior and posterior walls of the bladder neck, typically resembling a funnel shape. Alterations in BNA can indicate structural changes in individuals with BPH. Li *et al*. [63] investigated the correlation between BNA, urinary flow rate, and LUTS. The study included 281 patients with LUTS who underwent transrectal ultrasonography. BNA showed significant variation in the severity of prostate symptoms. The mean BNA was 89.8° ± 16.3° for patients with Q_{max} <10 mL/s, 60.7° ± 10.4° for those with Q_{max} ranging 10 – 20 mL/s, and 57.8° ± 10.5° for patients with Q_{max} >20 mL/s. In addition, BNA was strongly correlated with both Q_{max} and the total international prostate symptom score ($r = 0.569$, $p < 0.001$ and $r = 0.718$, $p < 0.001$, respectively). These findings suggest that BNA is significantly associated with urinary flow rate and LUTS, potentially playing a crucial role in the pathogenesis of BPH. One potential drawback of the study is that BNA was measured while patients were at rest during transrectal ultrasound, whereas the bladder neck's shape and structure may vary during urination [64].

3. 14. Radiofrequency ultrasound strain imaging

Radiofrequency ultrasound is used to estimate deformation in biological tissues. This technique has been applied to quantify the deformation of the detrusor muscle during the voiding phase in both asymptomatic volunteers and symptomatic patients [65]. In asymptomatic volunteers, a slight reduction in axial strain was observed, followed by an increase at the start of the voiding cycle. Among symptomatic patients, a positive correlation was noted between axial strain and detrusor pressure. An increase in detrusor pressure indicates increased muscle activity, while a corresponding increase in axial strain reflects more intense bladder muscle response. As a result, radiofrequency ultrasound strain imaging may function as a non-invasive tool to distinguish individuals with BOO.

3. 15. Urine biomarkers

Chronic bladder ischemia, along with repeated cycles of ischemia-reperfusion injury, leads to excessive oxidative stress, a key factor in the development of detrusor underactivity [66]. Detrusor underactivity may represent a decompensated phase of BOO, characterized by urothelial dysfunction, neuronal and smooth muscle cell degeneration, and associated histological and molecular alterations. Prostaglandin E2 (PGE2), released during detrusor contraction, plays a role in promoting this contraction [67]. Studies have shown that urinary PGE2 levels are significantly elevated in patients with BPH and overactive bladder (OAB) symptoms compared to those with BPH alone or healthy controls. These levels decrease as OAB symptoms improve following treatment [66]. Conversely, PGE2 levels in patients with detrusor underactivity are lower than in controls but increase significantly after bladder function is restored [68]. Neurotrophins, including nerve growth factor and brain-derived neurotrophic factor, have attracted considerable interest for their capacity to induce neuroplastic changes in the neuronal circuits that regulate bladder function [69]. Urinary levels of these neurotrophins increase in patients with BOO and OAB symptoms and decrease following effective medical treatment [70]. Cyclic ischemia-reperfusion injuries also contribute to the generation of reactive oxygen species, which are implicated in bladder dysfunction. In patients with BOO, urinary biomarkers of oxidative stress, including 8-OHdG, malondialdehyde, and F2-isoprostane, increased and subsequently decreased with recovery [71]. These urine biomarkers are potentially of clinical value for diagnosing and monitoring BOO.

4. CONCLUSION

UDS remain the gold standard for diagnosing BOO. Nonetheless, their invasive nature restricts their widespread application. Various pathological conditions lead to LUTS in men, impairing diagnostic accuracy. While voiding LUTS is commonly associated with benign prostatic obstruction in elderly men, these symptoms may also be of different origins [2]. Distinguishing PBNO from BPH can be clinically challenging, and misdiagnosis might result. Urethrocystoscopy serves as a diagnostic tool to exclude potential underlying causes of BOO, such as urethral strictures [13]. VUDS, which combine UDS with imaging, show promise but may increase the risk of radiation exposure.

A variety of non-invasive methods are available for assessing BOO, though a unified standard remains absent for most. Studies on urine flow rate thresholds reveal significant variability [54]. Lowering the Q_{max} threshold increases sensitivity but decreases specificity. In addition, studies that used prostate parameters for diagnosis yielded inconsistent threshold values and low diagnostic accuracy when a only a single parameter, such as DWT/BWT, IPP, Pvol, and H: W ratio, was tested. The external condom method shows promise but is restricted by factors that can lead to test failure [62]. Moreover, ultrasound examinations, depending on examiner's expertise and experience, may introduce potential observational errors. In addition, some non-invasive methods require specialized equipment, which limits their broader application. Research suggests that urine biomarkers could provide valuable information about various pathological bladder conditions relevant to BOO diagnosis and treatment. Biomarkers, such as PGE2, oxidative stress biomarkers, and neurotrophins, could help in assessing BOO severity, monitoring disease progression, and evaluating treatment efficacy [66,67]. However, conflicting findings in the literature indicated that the role of urine biomarkers in diagnosing bladder diseases remains controversial and warrants further investigation [72] (Table 1).

Noninvasive tests are limited primarily by variability in threshold values and differing reference standards. Another drawback lies in that invasive UDS is generally assumed necessary for a definitive BOO diagnosis in men [37]. Invasive UDS results can vary significantly between investigators, and retest results may differ from previous findings [73]. Despite these challenges, UDS remain the preferred standard in the absence of more accurate diagnostic alternatives.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Bing Li
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CONSENT FOR PUBLICATION

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