



# Navigating the Diagnostic Maze: Unraveling the Non-invasive Evaluation of Bladder Outlet Obstruction in Men—a Comprehensive Systematic Review

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## Abstract

**Purpose of Review** Bladder outlet obstruction (BOO) encompasses the diagnosis of obstructive urinary flow accompanied by increased detrusor pressure. It can contribute to renal function deterioration, recurrent urinary tract infections, and potentially acute urine retention. While the diagnosis of BOO plays a critical role in clinical management and decision-making, a consensus on the precise evaluation remains elusive. This study aimed to comprehensively review non-invasive methods for diagnosing BOO, primarily in cases related to benign prostatic hyperplasia.

**Recent Findings** A systematic literature review was conducted on PubMed from January 2016 to November 2022, focusing on non-invasive tests and lower urinary tract symptoms (LUTS) or bladder outlet obstruction (BOO) in men. A total of 2520 results were included, resulting in 1620 unique findings after removing duplicates. From these, 263 abstracts were thoroughly evaluated, leading to a detailed review of 80 full-text articles and their references. The review identified numerous cutting-edge technologies, primarily ultrasound-based, such as intravesical prostatic protrusion (IPP), bladder wall thickness (BWT), and detrusor wall thickness (DWT), among others. These advancements demonstrate promising sensitivity and specificity, positioning them as valuable tools for evaluating patients with BOO.

**Summary** Achieving an accurate diagnosis and implementing effective management strategies for BOO patients can lead to improved patient care, optimized resource allocation for those in need, and significant reductions in unnecessary expenditures. In the near future, a plethora of additional tools will become available, poised to enhance our diagnostic and prognostic approaches for patients with BOO.

**Keywords** Lower urinary tract symptoms · Benign prostatic hyperplasia · Urodynamics · Ultrasonography · Urinary bladder neck obstruction · Transurethral resection of prostate

## Introduction

Lower urinary tract symptoms (LUTS) refer to a group of symptoms related to the urinary system that occur in the lower part of the urinary tract, which includes the bladder,

urethra, and prostate. The prevalence of LUTS is estimated to affect a quarter of men in their 6th decade [1] and up to 70% of men in their 9th decade [2], although the prevalence of LUTS can vary widely depending on the specific symptoms considered and the definition of LUTS used in a particular study [3].

The symptoms are classically divided into voiding symptoms and storage symptoms depending on the abnormality in the urinary cycle phase, though overlap between them is common [4•]. Voiding symptoms include slow-stream, hesitancy, intermittency, and straining, while storage symptoms include urgency, frequency, nocturia, and urge incontinence. These symptoms have a great impact on quality of life, associated with various health conditions [5, 6] and bear substantial economic burden [7].

Bladder outlet obstruction (BOO) refers to the diagnosis of obstruction and is defined as “reduced urine flow rate

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with a simultaneously increased detrusor pressure” [4•]. BOO may be a factor that can result in the deterioration of renal function [8•], recurrent urinary tract infections (UTI), and acute urine retention (AUR) [9], and these can be life-threatening [10].

While BOO can result in bladder dysfunction [11–13], the exact mechanism, the relation to symptoms, and the clinical course are unclear. While the diagnosis of BOO has a pivotal role in clinical management and decision-making [14, 15•], there is no consensus on the exact evaluation required.

In this review, we will focus on the non-invasive methods to diagnose BOO, concentrating on benign prostatic hyperplasia [16]. We will review the currently studied alternatives to the commonly used invasive tests. Urodynamic study (UDS) with the pressure-flow study (PFS) component is currently the gold standard for diagnosing BOO, and specifically differentiating voiding symptoms resulting from BOO or from detrusor underactivity (DU) [4•, 17••].

However, UDS is invasive, expensive, and bothersome [18, 19•] and bears several risks, namely infection [20, 21] and hematuria [22]. Moreover, UDS has several diagnostic drawbacks including suboptimal specificity [23, 24] and sensitivity [25, 26, 27•, 28] and inter-rater variability [29, 30], among others [17••, 31••, 32••]. These disadvantages led to a growing need to establish valid and reliable non-invasive tools to diagnose BOO.

Another invasive alternative is urethrocystoscopy, which can point out structural or anatomical BOO-related bladder wall trabeculations and diverticula [33, 34]. However, the correlation between urethrocystoscopy finding and symptoms is suboptimal and BOO maybe present in 15% of patients with normal cystoscopy finding, and therefore is

not recommended to replace UDS in the evaluation of BOO, though it has a place if it may change management prior to minimal invasive BPH interventions [17••].

## Literature Review

### Methodology

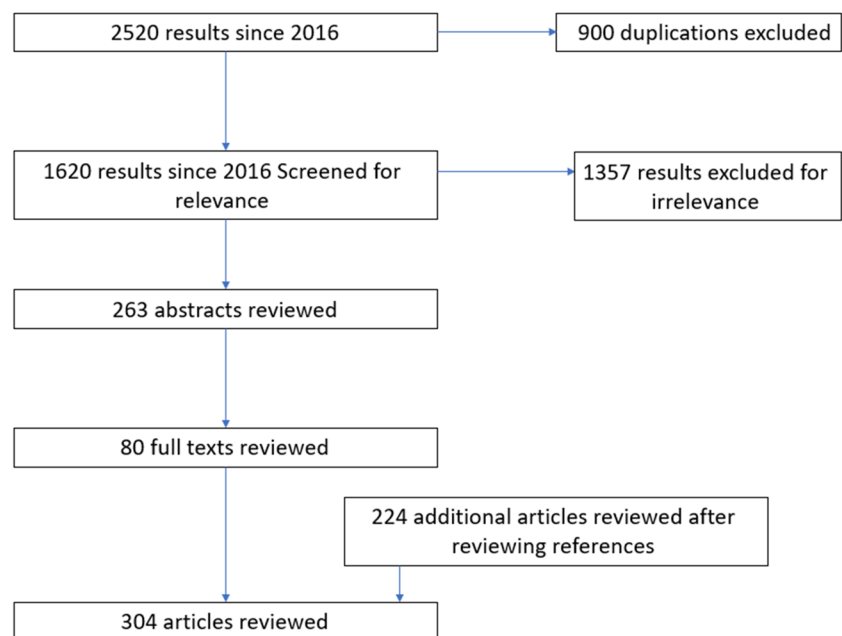
A systematic literature review was conducted on PubMed between January 2016 and November 2022, using a set of specific terms related to non-invasive tests and phrases relevant to LUTS or BOO in men, as outlined in the supplementary materials. Searches were conducted for general terms as well as for specific tests or test groups, few key manuscripts that were essential for specific topics, and manuscripts referred by the key studies yielding a total of 2520 results. After removing duplicates, 1620 unique results were obtained, of which 263 abstracts were reviewed. A total of 80 full-text articles were thoroughly reviewed, including the relevant references, as depicted in Fig. 1.

Following that, we reviewed the current American Urological Association (AUA) and European Association of Urology (EAU) guidelines and commented accordingly on each test, if it was available.

### Aim of the Study

The primary aim of this review is to provide a comprehensive analysis of the current literature pertaining to non-invasive methodologies for assessing BOO. In doing so, we will

**Fig. 1** Flow diagram of the evidence acquisition in this systematic review on non-invasive methods to diagnose bladder outlet obstruction



scrutinize the efficacy and benefits of various techniques and methods that have been employed for this purpose. Moreover, we will undertake a thorough evaluation of the diagnostic and prognostic value of these modalities, taking into consideration the varying conditions and scenarios that may influence their utility.

## Value of diagnostic steps in the evaluation of voiding LUTS- systematic review

### Medical History

The objective of a medical history assessment is to identify possible causes and relevant comorbidities, which includes an evaluation of symptoms; sexual history; past medical history and procedures; history of trauma to the perineum, genitalia, or spine; neurological comorbidities; medication usage; and psychological and emotional factors. Severity of BOO-related symptoms among other LUTS can be assessed using the International Prostate Symptom Score (IPSS) questionnaire, which is commonly used in these settings. The severity of LUTS may be simplified to three grade scales as mild (< 7), moderate [8•, 9–14, 15•, 16, 17••, 18, 19•], or severe ( $\geq 20$ ) LUTS, based on the total IPSS score. Additional question assesses the impact of symptoms on quality of life (QOL) which is pivotal in assessing patient's level of bother. The IPSS score is useful for initial assessment and also for monitoring LUTS during follow-up. Several studies have found that symptom severity is not well-correlated with or is not an independent indicator of obstruction [25, 26, 27•, 28, 35•, 36], but may indicate the prognosis and the response for some treatments [9, 37–40]. Systematic reviews (SR) [41•] have also demonstrated poor correlations between IPSS scores and BOO grades. Although some new nomograms [42•, 43•] have shown that IPSS can contribute to models of BOO-prediction, they are not yet widely used.

The latest guidelines recommend incorporating the use of a reliable questionnaire that is valid for LUTS estimation and follow-up, and in our view, it is worthwhile to use IPSS in daily practice.

The assessment of males presenting with LUTS requires a comprehensive physical examination that constitutes an essential component of the diagnostic process. This evaluation usually involves an examination of the suprapubic region to detect significant urinary retention or the existence of a palpable bladder. Additionally, a thorough assessment of the external genitalia and perineum is necessary to identify any indications of urethral stricture, fibrosis, or cutaneous findings suggestive of various pathologies. These pathologies may include lichen sclerosis, sexually transmitted infections, or neoplastic changes, all of which may manifest as BOO if resulted in urethral stricture.

Furthermore, digital rectal examination (DRE) should be routinely performed to assess rectal tone and detect any suspicious nodules in the prostate gland that may indicate

prostate cancer (PCa) while excluding acute prostatitis. Although lacking in accuracy [44–48] in determining the prostate size and the cause of BOO, DRE may provide a crude estimation of prostate volume [49, 50•] and raise suspicions for significant pathology requiring further workup. Notably, the EAU and the AUA both recommend a physical examination for the evaluation of men BOO. However, the EAU guidelines additionally suggest a DRE as part of the physical examination, whereas the AUA guidelines do not explicitly include it in their recommendations [17••, 32••].

### Uroflowmetry (UF)

Uroflowmetry is a test that is non-invasive and straightforward in its application, assessing the rate and volume of urine flow during urination. The occurrence of BOO may result in a slow urine flow, which is evidenced by a lower maximal flow rate (Q<sub>max</sub>). While some researches have suggested that a high Q<sub>max</sub> threshold of 15 mL/sec with 99% sensitivity and a negative predictive value (NPV) of 97% be used to rule out BOO [51], others have suggested a cutoff of 10 mL/sec [52, 53•, 54••]. Q<sub>max</sub> has been widely incorporated as a component of UDS nomograms, such as the bladder outlet obstruction index (BOOI) and the bladder contractility index (BCI) [55, 56]. However, the use of Q<sub>max</sub> to predict BOO is limited due to the variability of the studies' results [42•, 43•, 52, 53•, 57, 58•].

A lower Q<sub>max</sub> has been shown to be associated with higher IPSS [59, 60], onset of new LUTS [61], AUR [9], and a higher success rate in obstruction-relieving surgeries, mainly Holmium laser enucleation of the prostate (HoLEP) [62•] and transurethral resection of the prostate (TURP) [40]. Additionally, several studies have found that lower Q<sub>max</sub> is correlated with a higher need for surgical intervention [39, 63•], while others have contradicted this association [64]. It should be noted that low Q<sub>max</sub> is not specific to BOO, as DU or poor relaxation of the urinary sphincter may also impede urine flow [65•, 66].

Of note, several studies utilize the graph form of the UF to differentiate BOO from DU. As such, some shapes of the uroflowmetry graph may suggest DU rather than BOO [67, 68]. Some models utilize different parameters of UF to accurately calculate the probability of BOO [69, 70]. A novel method of standardization of volume-corrected Q<sub>max</sub> has been investigated as a better predictor of surgery outcome [71].

Given its non-invasive nature, simplicity, and acceptable NPV, UF has a role in the initial evaluation and disease monitoring, particularly in repeated exams over a long follow-up period. The guidelines of the EAU recommend uroflowmetry in the initial assessment, and the AUA keeps it as an optional test. However, both associations strongly recommend it prior to surgical intervention [17••, 32••].

## Post-voiding Residual (PVR)

Post void residual (PVR) volume denotes the quantity of urine that remains in the bladder subsequent to voiding. Ordinarily, after micturition, the bladder is expected to be voided completely or contain a negligible residual volume of urine. Chronic urinary retention, as measured by physical examination, or ultrasound (US) using a cutoff of 300 mL in two 6-months-apart measurement is a suggestion by consensus by the AUA guidelines [72•].

The correlation of PVR and the cutoffs used changed very widely from being non-predictive, while others showed predictive value and accuracy of 0.8 [51, 53•, 73, 74].

Elevated PVR (ePVR) in the presence of BOO may have an important role in predicting the coming clinical course. Several investigators reported a higher rate of disease progression to medication or surgical intervention with a higher PVR [39, 63•, 75•]. Additionally, studies found that PVR is associated with complications of BOO, like recurrent UTI [76], progression of symptoms [77], AUR [63•, 77–79], bladder calculi, and renal failure [79]; however, the robustness of the evidence should be better before determining the causality of these factors to BOO complications.

AUA guidelines summarize that PVR does not seem to be a strong predictor of complication in the absence of other high-risk features [32••]. However, EAU guidelines recommend measuring PVR as part of the initial assessment, and the AUA supports including it as an optional test, with more emphasis on following the PVR trend over time, and as a recommended test prior to surgical intervention [17••, 32••].

## Laboratory Workup

**Prostate-Specific Antigen (PSA) Test** Prostate-specific antigen (PSA) is a protein that is synthesized by the epithelial cells of the prostate gland. While it is primarily used as a biomarker for PCa screening and monitoring, elevated levels of PSA can also indicate other prostate-related conditions, such as prostatitis, benign prostatic hyperplasia (BPH) [80, 81], and UTI [82].

Several studies have demonstrated that PSA levels are well-correlated with prostate volume (PV). For instance, Roehrborn et al. [83] showed that in BPH trials involving 4448 patients, the area under the curve (AUC) for PSA levels (adjusted for age) was 0.76–0.78, with a specificity and sensitivity of 70% for prostate volumes of 30, 40, and 50 mL cutoff. Another study [84] confirmed that PSA levels can predict PV with an accuracy of  $\pm 20\%$  for over 90% of patients. Furthermore, PSA has been found to be a predictor for male LUTS [85]. It has also been shown to correlate with the natural progression of BPH, including

future prostate growth [86], worsening symptoms [87], progression to the need for escalating therapy [39], risk of AUR [88, 89], and BPH-related surgery [88]. However, these findings were challenged by Kim et al. [64], who found no correlation between PSA levels and the need for BPH-related surgery among 679 patients.

Higher PSA levels ( $> 1.4$  ng/mL) have also been shown to predict response to 5-alpha-reductase inhibitors (5-ARIs) [90], and this has been incorporated as one of the factors to consider when deciding whether or not to initiate 5-ARI therapy in men with LUTS, according to the AUA guidelines [32••]. While PSA is not recommended as part of the assessment of BOO, it can aid in differential diagnosis and treatment decision-making. However, the use of PSA testing as a part of shared decision-making with the patient remains controversial, as it has been extensively debated in the context of early detection of prostate cancer [91–93].

**Renal Function** The presence of BOO may result in the retrograde flow of urine into the kidneys, culminating in the development of obstructive uropathy and potentially leading to the insidious onset of renal failure [8•, 94, 95]. In addition to the initial measure of bladder decompression via catheterization, alleviation of the obstruction through interventions such as TURP has been proposed as a means to potentially restore or stabilize kidney function, as evidenced by findings from Lee [96]. While some dispute the strength of this correlation [97], the cost-effectiveness and accessibility of kidney function testing warrant its inclusion as an initial diagnostic step, which may also serve to exclude alternative etiologies. Although renal failure is a belated consequence of BOO and may not manifest in the initial assessment, both the AUA and EAU recommend its use as a baseline test and as a means of monitoring progression over time [17••, 32••].

**Urinalysis (UA)** Despite its widespread use as a screening tool for medically important conditions (MIC), a recent study [98•] evaluating the efficacy of urinalysis (UA) for diagnosing these conditions among data obtained from three studies comprising 2894 men found that it was only effective in detecting UTI and diabetes mellitus (DM). However, for these conditions, more sophisticated diagnostic methods, such as urine culture for suspected UTI and glucose blood testing for DM, are available. Moreover, its utility to diagnose UTI was questioned by Khasriya et al. [99]. Despite the limited utility of UA, its low cost, availability, and non-invasive nature have led to its adoption as a routine diagnostic test, which has garnered strong endorsement from leading associations [17••, 32••] and is widely accepted in clinical practice [100].

## Prostate Volume (PV)

Prostate volume (PV) is a term that pertains to the size of the prostate gland, which may become enlarged and cause BOO. The conventional methods for PV measurement include transrectal ultrasound (TRUS) and trans-abdominal ultrasound (TAUS), while cystoscopy or cross-sectional imaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI) are less commonly employed for that purpose [17••, 101]. Of the available methods, TRUS and MRI are deemed the most accurate for PV measurement [41•, 102–104].

Despite some debate concerning the correlation between PV and BOO, several studies have indicated moderate association between the two, with larger prostates being linked to an increased likelihood of BOO and its associated symptoms as well as obstructive urodynamic findings [27•, 43•, 75•, 105•]. However, although the applicability of PV to predict may raise an AUC of between 0.6 and 0.7 according to many studies [51, 106–108], the cutoff changes widely and so do the PPV and NPV [41•, 58•]. Additionally, there is low to no association between PV and validated symptoms questionnaire [109, 110•, 111, 112]. A recent meta-analysis involving 2767 men demonstrated that a threshold of 40-mL size prostate had an AUC of 0.68, although sensitivity and specificity were limited (0.54 and 0.76, respectively) [54••]. Furthermore, larger PV was associated with a threefold risk for progression to AUR [9], a heightened (OR = 2.48) risk for disease progression [113•], with better response to 5-ARI [114, 115•, 116], and to TURP [40] but not for response to alpha-blockers [117, 118, 119•, 120].

It is imperative to acknowledge, however, that the correlation between PV and BOO is influenced by various factors, including age, hormonal changes, and other medical conditions [121–123].

According to the latest guidelines from the EAU, while imaging prior to medication is suggested as a supportive measure, prostate imaging prior to intervention is strongly recommended by the EAU and considered by the AUA [17••, 32••]. This recommendation is aimed at facilitating the selection of an appropriate intervention [32••], as well as aiding in the preparation of the operative room and staff from a technical standpoint.

## Intravesical Prostatic Protrusion (IPP)

Intravesical prostatic protrusion (IPP) is a metric used to evaluate the proximity between the median lobe of the prostate and the bladder neck along the midsagittal plane. This assessment is generally conducted using a suprapubically positioned US scanner, and it is classified into three grades

based on the extent of protrusion: grade I (0–4.9 mm), grade II (5–10 mm), and grade III (> 10 mm) [17••]. In contrast to PV, which measures the size of the prostate, IPP assesses the configuration of the prostate and the presence of the median lobe, which can result in obstruction even in small prostates through a ball-valve mechanism [32••, 124].

The accuracy of IPP in detecting BOO has been demonstrated, even in patients with normal flow (hence  $Q_{max} \geq 12$ ) [125•], displaying a remarkably high (100%) NPV to rule out BOO while using grade II as a cutoff, and a reasonable specificity (76.6%) for grade III [125•]. Several studies have investigated the correlation between IPP and the BOO index measured in UDS, with correlation coefficients ranging from 0.21 to 0.67 [107, 108, 126–128]—higher than PV. The AUC of predicting BOO with an IPP > 10 mm ranges between 0.71 and 0.885 [106, 107, 129]. Other investigators have used varying cutoffs, ranging from 5 to 12 mm, with AUC values ranging from 0.76 to 0.905 [105•, 108, 130, 131]. While a SR of 1013 cases revealed a pooled PPV of 73.8% and NPV of 69.3% [58•], other SRs reported AUC ranging from 0.7 to 0.86 [41•, 132•, 133], and the most big and recent meta-analysis including 2136 cases found AUC of 0.83 [54••]. Whether IPP correlates with symptom severity is a subject to controversy and the results of studies that examined this question vary widely from good to no correlation [27•, 120, 128, 134–137].

Moreover, IPP had shown to be predictive of BOO outcome. Numerous studies have indicated that higher grades of IPP are correlated with negative outcomes of conservative management, including watchful waiting, alpha-blockers [32••, 119•, 120, 130, 138, 139•, 140, 141], 5ARI [142•], and oral combination therapy [142•, 143].

IPP has exhibited the potential to serve as a prognostic indicator for an elevated probability of advancing to TURP [143], along with a heightened susceptibility to AUR [126], failure to void following AUR [132•, 144, 145], and overall higher probability of disease progression [113•, 146]. Additionally, it is supported by empirical evidence that an elevated IPP parameter is positively associated with superior post-operative outcomes subsequent to surgical interventions targeted at relieving BOO, including HoLEP when contrasted with matched cohorts possessing a smaller IPP parameter [62•] and TURP [147•].

Despite the promising potential of IPP in both diagnosis and prognosis, the optimal cutoff has yet to be determined. Presently, the EAU does not incorporate IPP into its evaluations due to insufficient evidence regarding its reliability and possible learning curves [17••]. The AUA advises considering abdominal ultrasonography before surgical intervention or reevaluating patients in the event of treatment failure; however, there is no explicit requirement of including IPP in the prostate imaging in the initial evaluation of BOO [32••].



## Bladder Wall Thickness (BWT) and Detrusor Wall Thickness (DWT)

Bladder wall thickness (BWT) and detrusor wall thickness (DWT) are two measurements used to evaluate the health of the bladder wall, commonly obtained through trans-abdominal ultrasound. BWT and DWT can be thickened pathologically due to prolonged BOO, or thinned in atonic bladder [148]. While BWT measures the entire bladder wall, DWT refers specifically to the thickness of the muscular layer [17••]. Several studies [36, 130, 149, 150] have examined the predictive value of BWT and have shown an area under the curve (AUC) of 0.67–0.94 when using different cutoffs of 3.2/3.7/5 mm, with specificity to diagnose BOO exceeding 90% according to most studies. However, the contribution of BWT in predicting BOO in multivariate analysis, particularly when QMAX is added, is currently debated [36, 149, 151]. Nevertheless, high BWT has shown a poor response to alpha-blocker treatment [130, 152] and TURP surgery [147•].

Detrusor wall thickness (DWT) has emerged as a potentially more precise indicator of BOO compared to BWT. This distinction is attributed to the pivotal role of ultrastructural changes in muscle and connective tissue within the pathophysiology of BOO [153, 154]. Multiple investigations have yielded encouraging results, reporting DWT to have an area under the curve (AUC) ranging from 0.78 to 0.88 [51, 106, 108, 155, 156], accompanied by a notable degree of specificity. In a recent meta-analysis encompassing 1003 patients, DWT demonstrated an AUC of 0.87, exhibiting a sensitivity of 71% and a specificity of 89%. Furthermore, when adopting the widely utilized cutoff of 2 mm, the AUC increased to 0.9, with a sensitivity of 79% and a specificity of 89% [54••].

However, despite the potential importance of BWT and DWT in the pathological pathway of BOO, their usefulness is currently limited due to the lack of standardization of measurements, thresholds, and the operator-dependency of their assessment. Consequently, leading guidelines do not include these measurements in BOO evaluations [17••, 32••]. Therefore, further studies are needed to investigate their clinical utility and establish standardized protocols for their assessment.

## Upper Urinary Tract Imaging

Upper tract imaging pertains to the utilization of diagnostic imaging techniques in assessing the upper urinary tract, encompassing the kidneys and ureters, in situations where BOO is suspected. This obstruction may bring about an accumulation of pressure within the bladder, leading to hydronephrosis and consequential renal damage [95]. Common imaging modalities employed for upper tract

imaging comprise TAUS [17••], whereas CT and MRI are seldom conducted for BOO diagnosis, but rather to rule out other medical conditions. Nonetheless, in the absence of accompanying indications such as urinary retention or indications of renal failure, hydronephrosis is infrequently observable during the initial presentation of BOO [157–159]. Nevertheless, the EAU advocates for the use of upper tract imaging, while the AUA does not include it in the evaluation of index patients with BOO [17••, 32••]. It is important to note that in a patient with chronic urinary retention, the AUA recommends the utilization of upper tract imaging for diagnosis and monitoring of the disease state [160].

## The Utility of Other US Measurements to Diagnose BOO

**Ultrasound Estimated Bladder Weight (UEBW)** Ultrasound estimated bladder weight (UEBW) is a technique that employs trans-abdominal ultrasound to estimate the weight of the bladder, leveraging the physiologic principle of BWT by multiplying the volume of the bladder wall by the specific gravity of bladder tissue [161, 162]. Unlike BWT, which assesses a specific part of the bladder, UEBW provides a comprehensive assessment of the entire bladder and therefore may add an advantage.

Several studies have endeavored to investigate the diagnostic and prognostic value of UEBW. While various investigations have posited the potential of UEBW to forecast BOO with an AUC ranging from 0.6 to 0.85 [130, 161, 163], the limited quantity of research and participants, coupled with diverse cutoff values, and conflicting findings, precludes a conclusive determination regarding its clinical applicability [41•, 58•, 164].

UEBW has been modestly positively correlated with the IPSS ( $r=0.28$ ), and after prostatectomy, it significantly decreases [162, 165]. Furthermore, UEBW is an identified predictor of alpha-blocker treatment's inefficacy in a 157-participant study [130]. Additional studies [166, 167] have investigated the potential of UEBW in predicting AUR, with one study [166] reporting that individuals with a heavier bladder had a 13.4-fold increased risk of AUR. Nonetheless, these preliminary findings are yet to achieve standardization, and the predictive power of UEBW remains unclear.

Presently, the EAU and the AUA guidelines do not recommend UEBW's inclusion in the initial approach or follow-up of BOO patients [17••, 32••].

**Measurements of the Prostate Zone: Volume or Index of the Transitional Zone** The measurement of the transitional zone volume (TZV) is indicative of the quantity of prostate tissue present in the area surrounding the urethra. As BPH is known to result in an increase in the size of the transitional zone, the measurement of TZV and its proportion relative

to the entire prostate gland (referred to as the transitional zone index (TZI)) may serve as a surrogate marker for BOO [168]. Two large-scale studies found transition zone indices to be good independent predictors in multivariate analysis and included them in a BOO predicting nomogram [36, 43•]. Certain studies have demonstrated that TZV was associated with higher IPSS [169, 170], while others did not [171, 172]. Moreover, TZV can predict acute AUR, with an AUC of 0.74 [78], and likewise, a higher TZI (AUC of 0.775–0.860) showed similar results [78, 89]. Additionally, Qian et al. examined 1038 patients and discovered that disease progression was associated with TZV > 15 mL and TZI > 0.5, with odds ratios of 1.68 and 1.89, respectively [113•]. Other studies have shown that TZI is a predictor of a more favorable response to 5-ARI add-on therapy, with an AUC of 0.71 [116, 173•] and medical combination therapy [174], and that TZI correlated with better response to TURP [40, 175]. Despite these promising preliminary findings, further research is needed before TZV and TZI can be recommended for routine use. The EAU and AUA have yet to incorporate these indices into their BOO index for patient workup [17••, 32••].

**Measurement of Resistive Index in the Capsular Arteries** The resistive index (RI) is a measurement of resistance within the prostate capsular arteries. It is calculated by assessing the changes in blood velocity measured through TRUS, specifically peak systolic velocity minus end diastolic velocity divided by peak systolic velocity. Studies have shown that high RI values are associated with BPH and are believed to be due to prostate enlargement, which can compress the capsular arteries against the capsule, thereby increasing resistance.

For instance, several studies have reported RI values predicting BOO with varying thresholds, sensitivities, and specificities, with AUC values ranging from 0.785 to 0.82 [57, 105•, 176], and accuracy of 83.8–86% [177, 178]. Furthermore, RI values have also been found to correlate with the BOOI in multivariate analysis [105•, 179]. However, different investigators reported conflicting results regarding RI correlation with IPSS [180, 181].

Interventions aimed at relieving BOO, such as TURP, have been shown to decrease RI values [163]. In addition, higher baseline RI values have been associated with better outcomes of transurethral resection of the prostate after 12 months, with an AUC of 0.845 and a PPV of 85.1% [40], and a predictor of AUR, with AUC of 0.867 [78].

However, RI has limitations as every cause of endothelial dysfunction may impair vascular compliance and increase RI, such as atherosclerosis and DM [182].

Moreover, it should be noted that the RI is operator dependent and lacks a universally accepted reference point, thereby limiting its applicability across different settings. In

light of this, additional research is required to determine the efficacy of RI as a straightforward prognostic tool for both clinical outcomes and BOO, and the AUA and the EAU currently do not recommend the use of RI [17••, 32••].

**Urethral Measurements: Prostatic Urethral Angle (PUA)** Several measurements related to the urethra and its positioning in relation to the urinary bladder were meticulously scrutinized. Of particular interest was the acute angle of the prostatic urethra, as it has been postulated to elicit resistance and impede urine flow. Researchers have delved into the role of the prostatic urethral angle (PUA) in BOO, and it was observed that higher PUA was associated with more pronounced symptoms as assessed by the IPSS [136, 137, 183, 184•], with lower Qmax [136], and with BOOI as determined by urodynamic studies, even when IPP was controlled [183]. Higher PUA was also correlated with poor improvement after alpha-blocker treatment with an AUC of 0.65 [184•]. While the PUA measurement is relatively easy to employ, circumvents a learning curve, and enables seamless comparison between operators, its utility is yet to be fully established in BOO. It is plausible that with further investigation, the PUA measurement may become more widely utilized and prove valuable in predicting BOO. In addition, various other ultrasonographic measurements are currently under scrutiny, and more compelling evidence is likely to surface in the foreseeable future.

### Near-Infrared Spectroscopy (NIRS)

In the realm of urology, a cutting-edge method for monitoring tissue oxygenation and hemodynamics is near-infrared spectroscopy (NIRS). By detecting changes in the concentrations of oxyhemoglobin (O<sub>2</sub>Hb) and deoxyhemoglobin (HHb), NIRS can provide a non-invasive optical approach to observe these indicators [185]. In light of this, Macnab and colleagues postulated that during voiding, the thickened detrusor would consume oxygen and subsequently reduce its concentration, thereby enabling differentiation between BOO and DU [186]. Despite the potential of NIRS to estimate the presence of obstruction, there is still a scarcity of studies that employ NIRS as part of an algorithm. Some research groups reported highly encouraging results with a sensitivity of 86%, specificity of 88%, and 94% precision, with an AUC of 0.91 [185, 187, 188]. Conversely, other studies reported much lower values, with a sensitivity and specificity of 68.3% and 62.5%, respectively [189], and an AUC of 0.484 [190]. In a SR conducted by Malde and colleagues, the median sensitivity and specificity were determined to be 85.7% and 87.5%, respectively [58•]. It is important to note, however, that most of these studies are relatively small-scale and did not predict prognosis or treatment outcomes. Additionally, the utilization of NIRS in clinical practice is

impeded by the need for specialized equipment and personnel with extensive training, which could limit its routine application. As a result, leading urology associations do not recommend the routine use of NIRS in the evaluation of bladder dysfunction [17••, 32••].

### Non-invasive UDS: Penile Cuff Test

The penile cuff test (PCT) aims to achieve the maximum detrusor pressure without requiring catheter insertion. This is accomplished by inflating a cuff around the penis to interrupt the flow, equalizing the internal pressure of the cuff with the isovolumetric pressure of the detrusor [191]. The PCT is a simple, painless, and rapid test [19•] with low inter-observer variability [192], making it an attractive alternative to UDS.

Earlier efforts to diagnose BOO using the PCT had modest results with a PPV of 68% and a NPV of 78% although the addition of the criterion of  $Q_{max} < 10$  mL/sec improved its accuracy [193]. Subsequent studies have found high sensitivity (NPV = 88–100%), making the PCT a good test for ruling out patients without BOO [19•, 194, 195]. Moreover, a recent meta-analysis involving 806 patients found an AUC of 0.88, a sensitivity of 87%, and a specificity of 78% [54••].

One significant drawback of the PCT is the inability to distinguish between abdominal pressure and detrusor pressure, which is a pivotal factor in UDS in differentiating DU from BOO [196]. In conclusion, the current evidence may support the use of the PCT as an adjunct tool and provide important insights into BOO. However, the evidence is still preliminary for utilizing the PCT as a full substitute for UDS, and leading associations have yet to include it in their assessment recommendations [17••, 32••].

### Nomogram Models in Predicting BOO

To seek an alternative to urodynamic testing, one approach is to utilize nomogram models incorporating known and novel risk factors correlated with BOO. A plethora of researchers have proposed diverse models for prognosticating varied outcomes of BOO and predicting treatment outcome.

For the purpose of predicting BOO, Lee et al. (2019) employed a sizeable cohort of 750 medication-refractory individuals to develop a nomogram predicated on age, IPSS,  $Q_{max}$ , prostate volume, and TZI, achieving an AUC of 0.88 for BOO, as well as an AUC of 0.81 on a distinct validation set [43•].

Ganpule (2021) constructed a nomogram predicated on IPSS, PSA,  $Q_{max}$ , PV, and IPP, designed to predict the necessity for surgical intervention. The model demonstrated a sensitivity of 88.24%, specificity of 97.33%, and accuracy of 95.65% [197•].

Furthermore, Tian et al. (2022) developed the PROSTATE nomogram, based on a sample of 356 individuals,

using age, IPSS, IPP, BWT, peripheral zone thickness, and transitional zone thickness as predictors, with a PPV of 90.6% and NPV of 43.7% for predicting the efficacy of TURP. The trained model exhibited an AUC of 0.86 [147•].

However, a notable drawback of these studies lies in the absence of standardization, particularly concerning the test population, such as individuals with optimal urinary flow, treatment-resistant symptoms, and varying age demographics, among other factors. Moreover, these nomogram models lack external validation studies involving divergent population groups, impeding the generalization of results to all BOO patients. Currently, these models were not implemented by the AUA and EAU guidelines committees [17••, 32••].

### Future Directions

The pressing challenge facing physicians today is the need for a precise diagnostic tool that is non-invasive, user-friendly, and effective in identifying obstruction of the urinary bladder outlet. Various avenues for the future are being explored, such as blood or urine markers, wearable technologies, and even in the realms of genetics or genomics. While in other areas of medicine, including urology, these research endeavors are well-established and advanced, no single test has yet been identified to bridge this gap. As BOO is a multifactorial disease that relies on clinical diagnosis, along with the incorporation of diverse metrics, the challenge falls to the clinical judgment of the treating physician.

We anticipate that in the near future, a range of diverse technologies and tests will emerge that will provide a suitable response to the current deficiency in the field.

### Conclusions

Bladder outlet obstruction (BOO) represents a frequently encountered phenomenon, exhibiting a wide array of manifestations that span from asymptomatic occurrences to potentially life-threatening comorbidities. Attaining precise diagnosis and implementing effective management strategies for patients afflicted by BOO can yield enhanced standards of patient care, optimized allocation of resources for those in need, and substantial reductions in superfluous expenditures. Within this study, we undertook an extensive examination of the available literature concerning non-invasive diagnostic modalities for BOO, thereby offering treating physicians a valuable instrument to inform their medical decision-making process.

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## Declarations

**Competing interests** The authors declare no competing interests.

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