



## Review Article

# Current consensus and controversy on the diagnosis of male lower urinary tract symptoms/benign prostatic hyperplasia

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### ABSTRACT

Traditionally, male lower urinary tract symptoms (LUTS) have been considered a synonym for benign prostate hyperplasia (BPH) because most male LUTS develops in aging men. Medical treatment should be the first-line treatment for BPH and surgical intervention should be performed when there are complications or LUTS refractory to medical treatment. Recent investigations have revealed that bladder dysfunction and bladder outlet dysfunction contribute equally to male LUTS. In the diagnosis of LUTS suggestive of BPH (LUTS/BPH), the following questions should be considered: Is there an obstruction? Are the LUTS caused by an enlarged prostate? What are the appropriate tools to diagnose an obstructive BPH? Should patients with LUTS be treated before bladder outlet obstruction is confirmed? This article discusses the current consensus and controversies in the diagnosis of LUTS/BPH.

**KEYWORDS:** *Lower urinary tract symptoms, Medical treatment, Overactive bladder, Quality of life, Surgery*

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## BENIGN PROSTATE HYPERPLASIA – CURRENT CONCEPT OF LOWER URINARY TRACT SYMPTOMS/BENIGN PROSTATE HYPERPLASIA

Lower urinary tract symptoms (LUTS) are highly prevalent in men and the incidence increases with age [1]. LUTS is usually considered a synonym for benign prostatic hyperplasia (BPH). However, only 25% to 50% of men with BPH have LUTS, and urodynamically-proven bladder outlet obstruction (BOO) is only seen in 50% of men with LUTS [2]. Clinically, the diagnosis of BPH and BOO is usually made based on a total prostate volume (TPV) >40 mL, and a maximum flow rate (Qmax) <10 mL/s, in combination with a high International Prostate Symptom Score (IPSS) [3]. Many clinical studies have demonstrated that LUTS have poor diagnostic specificity for BOO and the symptoms of some patients with LUTS/BPH do not improve after transurethral resection of the prostate (TURP) [4]. Although an enlarged prostate might not indicate the presence of BOO, the mean TPV of patients with

BOO is significantly greater than that of patients without BOO [5]. In addition, patients with LUTS/BPH and a Qmax of <10 mL/s have a greater improvement in the Qmax after TURP compared with those with a Qmax >10 mL/s. Patients without urodynamic evidence of BOO may have a poor surgical outcome after TURP [6]. In one study, patients with persistent LUTS after TURP were found to have a small TPV at the time of surgery, suggesting that a non-BPH etiology might account for their LUTS [7]. Therefore, diagnosis of clinical BPH should be undertaken carefully, especially when an invasive procedure such as TURP is going to be performed. The differential diagnosis for non-BPH lower urinary tract dysfunction (LUTD) is important in the management of LUTS/BPH.

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## **DIFFERENTIAL DIAGNOSIS OF LOWER URINARY TRACT SYMPTOMS BASED ON THE INTERNATIONAL PROSTATE SYMPTOM SCORE VOIDING TO STORAGE RATIO**

The focus on LUTS has recently shifted from the prostate to the bladder [8]. Several investigations suggest that not all male LUTS are associated with prostate pathology or BOO and bladder dysfunction plays a role in the pathogenesis. However, it is difficult to distinguish the causes of male LUTS based on clinical symptoms, and a subset of patients receiving treatment for prostatic conditions may have residual overactive bladder (OAB) symptoms [7,9,10]. Although urodynamic pressure flow study is helpful in the differential diagnosis, the equipment is not available in every clinic.

The pathophysiology of male LUTS could be bladder dysfunction, (including hypersensitive bladder, detrusor overactivity [DO], detrusor hyperactivity and inadequate contractility [DHIC]), BOO (including bladder neck dysfunction [BND], prostatic obstruction, urethral stricture, poor relaxation of the urethral sphincter), or a combination of these etiologies. It has been estimated that only 48%–53% of men with LUTS have urodynamically-proven BOO due to BPH or other bladder outlet dysfunctions [2]. In addition, approximately 50%–75% of patients with BOO have OAB symptoms [11,12], and 46 to 66% of patients with BPO on urodynamics have DO [13,14].

The practice guidelines of the both the European Association of Urology and the American Urological Association (AUA) recommend that evaluating symptom severity with a symptom score is an important part of the assessment of male LUTS [15,16]. The IPSS and American Urological Association Symptom Index (AUA-SI) have been widely used for decades in many languages to evaluate the severity of LUTS/BPH, and have been applied to other conditions causing LUTS for comparison of treatment outcomes. Measuring the IPSS-storage (IPSS-S) and IPS-voiding (IPSS-V) subscores separately and using the IPSS-V/S ratio can help differentiate bladder- and urethra-related conditions [17]. We have previously constructed an IPSS voiding to storage (IPSS-V/S) ratio for differential diagnosis of bladder and bladder outlet dysfunction. An IPSS-V/S <1.0 was noted in 80% of patients with bladder-related LUTS and an IPSS-V/S >1.0 was seen in 76% of patients with BPH-BOO and non-BPH voiding dysfunction.

Alpha-blockers and 5-alpha-reductase inhibitors (5ARIs) are effective in the treatment of men with BOO due to BPH or non-BPH voiding dysfunction. These agents

may not be effective treatment for storage symptoms [9]. Antimuscarinic or anticholinergic agents are the first-line treatment for patients with OAB [18]. According to the initial differential diagnosis and medication given, 75% of patients with bladder-related conditions (IPSS-V/S <1) and 80% of those with urethral-related conditions (IPSS-V/S >1) reported improved outcomes after medical treatment with antimuscarinic agents and alpha-blockers, respectively [19]. Further urological investigations can be reserved for those with failed initial treatment based on the IPSS-V/S ratio.

Alpha-blockers have been considered the first choice for men with voiding or storage LUTS. Antimuscarinic agents usually are not prescribed as the first-line medication because acute urinary retention is possible. Combined therapy with an alpha-blocker and antimuscarinic agent may be the choice for male patients with storage LUTS [20]. Recent study revealed that combined treatment with tolterodine ER plus tamsulosin resulted in significantly greater improvement in LUTS than placebo or either active medication alone [21]. However, it is not reasonable or cost effective for doctors to prescribe both medications for men with storage LUTS alone. If we can use the IPSS-V/S ratio as a screening tool to prescribe first-line medication, most patients will improve. Those who do not respond should have further urological investigation.

## **DIAGNOSIS OF MALE LOWER URINARY TRACT SYMPTOMS/BENIGN PROSTATE HYPERPLASIA AND TREATMENT ALGORITHM**

BPH is highly prevalent in older men. However, it has been estimated that only 25%–50% of men with BPH have LUTS, and only 50% of men with LUTS have urodynamically-proven BOO due to BPH or another bladder outlet dysfunction [2]. Previous studies have shown weak correlations of LUTS with prostate size, uroflow measures and pressure flow study data [22-25]. Nevertheless, the AUA-SI was found effective in predicting BPH progression to surgery [26]. The symptom score is better for quantifying symptoms for the evaluation of BPH treatment than for diagnosis of BPH [27].

Although BPH is one of the most common diseases in elderly men, not all LUTS are caused by BPH. BPH with BOO was only found in one third of a cohort of patients with both storage and voiding LUTS [28]. In fact, LUTS can be the clinical presentation of OAB or BOO in both men and women, and in the elderly and children. Using a LUTS symptom score such as the IPSS or AUA-SI as a diagnostic tool for BOO or BPH could

be inappropriate and lead to an incorrect therapeutic strategy.

The prostatic specific antigen (PSA) level is indicated in all men with LUTS and an enlarged prostate or abnormal digital rectal examination (DRE) finding. Men with high PSA levels have a higher risk of future growth of the prostate, symptom and flow rate deterioration, acute urinary retention and BPH-related surgery [29-31]. PSA levels increase with age [32], and approximately 25% of men with BPH have a PSA level of >4 ng/mL [33]. Uroflowmetry for Qmax and the post-void residual (PVR) should be measured concomitantly. However, uroflow study has poor diagnostic specificity for BOO [34,35]. Bladder sonography is indicated to measure the PVR and investigate bladder stones, bladder wall thickness, and intravesical prostate protrusion. Patients with an estimated bladder mass weight greater than 35 g on sonography were 13.4% times more likely to develop acute urinary retention than patients with a lower bladder weight [36]. A significant correlation between bladder wall trabeculation and the grade of BOO has been reported [37,38].

A high rate of intravesical prostatic protrusion (IPP) has been associated with a higher risk of treatment resistance, acute urinary retention, and the need for prostatic surgery in patients receiving dutasteride treatment for symptomatic BPH. Dutasteride might not be effective for IPP reduction [39,40]. Recently, a greater prostatic urethral angulation was found to associate with a lower Qmax [41]. Similarly, patients with a higher bladder neck elevation angle ( $\geq 35^\circ$ ) had a higher BOO index and more obstructed voiding patterns than those with a lower bladder neck elevation angle [42]. Urethral closure pressure had a significant positive linear correlation with the Abrams–Griffiths number and had a strong association with BOO. Micturition urethral pressure profilometry was able to localize the site of obstruction in patients with BOO [43]. Therefore, urethrocystoscopy and urodynamic study can be considered in cases of invasive treatment, recurrent incontinence and specific situations [44]. These clinical investigations can help in the diagnosis of male LUTS/BPH.

### **URODYNAMIC STUDY – DO MEN WITH LOWER URINARY TRACT SYMPTOMS NEED URODYNAMIC STUDY BEFORE SURGICAL INTERVENTION?**

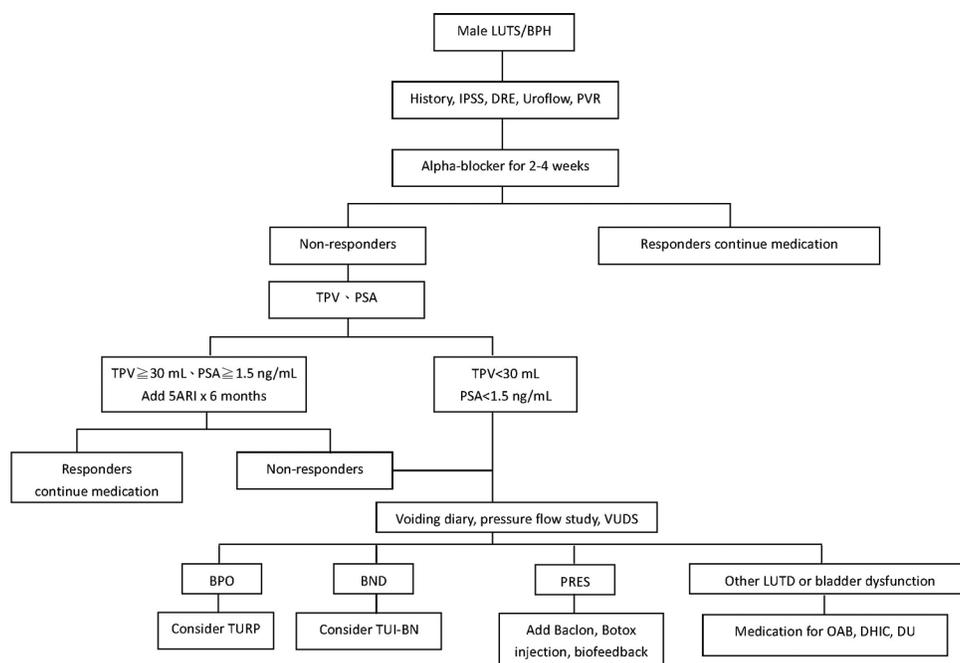
The diagnostic rationale of urodynamic study in association with the currently changing management paradigm of LUTD has been debated for long time. Surgical intervention to relieve BOO and LUTS based

on urodynamic diagnosis resulted in improvement in the flow rate after TURP [45]. Preoperative urodynamic diagnosis of DO was associated with significantly more storage LUTS requiring antimuscarinic treatment after prostate surgery than that seen in patients without DO [46]. In patients with OAB symptoms and failed empirical treatment, urodynamic study can provide definite information that can identify associated pathologies and/or alter the treatment course [47]. In patients with detrusor underactivity (DU), diminished bladder sensation to volume increase was noted in nonobstructive, nonneurogenic symptomatic patients [48]. A retrospective study of urodynamic studies in men with OAB symptoms revealed that most of these patients also had voiding symptoms and 43% of them had BOO [49].

Urodynamic studies are useful in the evaluation of LUTD in patients with BOO and DU, especially when invasive treatments are being considered [50]. A systemic review of the diagnostic value of office-based tests for BOO in men with LUTS revealed that individual symptoms and questionnaires for diagnosing BOO are not significantly associated with each other. An IPSS score cutoff of 20 or greater increased the likelihood of BOO [51]. Invasive urodynamic study did change decision making in the management of male LUTS/BPH. However, men who received urodynamic study were less likely to undergo surgery as treatment for voiding LUTS [52].

Pressure flow study provides valuable information on detrusor function and bladder outlet dysfunction. However, urodynamic study also can result in morbidity, such as urinary tract infection in 4%–6% of patients and dysuria in 75% of men with BOO and 55% of men without BOO [53]. Although pressure flow study can establish the diagnosis of BOO, the symptomatic outcome of treatment for BPH did not differ among different degrees of BOO [54]. Videourodynamic study (VUDS) provides a more accurate diagnosis of benign prostatic obstruction (BPO) and other bladder and urethral dysfunctions responsible for LUTS [55]. In patients with both storage and voiding LUTS, the incidence of DO and DHIC increases with age, whereas the incidence of poor relaxation of the urethral sphincter is seen more often in younger patients [56].

A diagnostic algorithm for LUTS/BPH may aid in determining the therapeutic strategy [57]. In the initial assessment, the history, IPSS, DRE, uroflowmetry and PVR provide information for the diagnosis of BPO and non-BPO. Short-term alpha-blockers can be used for patients with LUTS/BPH for 2–4 weeks [58]. If patients do not respond to initial treatment, measurement of



**Figure 1:** The diagnostic and treatment algorithm for male LUTS/BPH (LUTS = Lower urinary tract symptoms; BPH = Benign prostatic hyperplasia; IPSS = International Prostate Symptom Score; DRE = Digital rectal examination; PVR = Postvoid residual; TPV = Total prostate volume; PSA = Prostatic specific antigen; VUDS = Videourodynamic study; BPO = Benign prostatic obstruction; BND = Bladder neck dysfunction; PRES = Poor relaxation of the external sphincter; LUTD = Lower urinary tract dysfunction; OAB = Overactive bladder; DHIC = Detrusor hyperactivity and inadequate contractility; DU = Detrusor underactivity; TUI-BN = Transurethral incision of bladder neck; TURP = Transurethral resection of the prostate; 5ARI: 5-alpha-reductase inhibitor)

the TPV and PSA should be done and 5ARIs such as dutasteride or finasteride can be added in the presence of an enlarged prostate (TPV >30 mL) [59,60]. If patients do not respond to combination therapy for 6 months, a voiding diary (for nocturnal polyuria), pressure flow study (for DO or DU), or VUDS (to confirm the presence of BPO and BND or poor relaxation of the urethral sphincter) should be carried out to investigate diagnoses other than BPO. Cystoscopy may be an additional procedure to diagnose urethral stricture, bladder stones, or other urethral lesions. Surgical intervention for BPH should be considered only when a diagnosis of BPO has been clearly established [Figure 1].

### PRECISION MEDICINE FOR THE DIAGNOSIS OF MALE LOWER URINARY TRACT SYMPTOMS/ BENIGN PROSTATE HYPERPLASIA

Traditionally, male LUTS has been considered a synonym for BPH because most male LUTS develops in aging men. Recent investigations have revealed that bladder dysfunction and bladder outlet dysfunction contribute equally to male LUTS. BPH comprises only one-third of male LUTS. In patients with a TPV of less than 40 mL, diagnosis of bladder dysfunction such as hypersensitive bladder, DO, DHIC, or DU should be considered, whereas BND and poor urethral sphincter

relaxation should also be kept in mind in younger men. The IPSS V/S ratio can be used by general physicians for the first line diagnosis and medication can be prescribed without uroflowmetry or prostatic ultrasound examinations. Only patients who do not respond to initial treatment should be referred for further urological investigations.

### CONCLUSIONS

Male LUTS is a complicated symptom syndrome. It involves different disorders of the urinary bladder and the bladder outlet. Male LUTS should not be considered as merely one simple disease – BPH. Diagnosis and treatment of male LUTS is precision medicine. Urologists should take a detailed history, and perform a physical examination, laboratory investigations, symptom evaluation, transrectal sonography of the prostate and bladder, uroflowmetry, cystoscopy, or urodynamic study to make an accurate diagnosis. Life style modification and medical treatment should be used first, with surgical treatment reserved for patients with failed initial management.

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### Conflicts of interest

There are no conflicts of interest.

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