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Invited Review

Where can urodynamic testing help assess male lower urinary tract symptoms?

Cenk Gürbüz[1], Marcus J. Drake[2]

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ABSTRACT

Urodynamic studies assess the function of the bladder and bladder outlet. They are often useful in the assessment and diagnosis of patients presenting with lower urinary tract symptoms (LUTS). The evidence regarding the value and risks of invasive urodynamics remains insufficient. However, men with LUTS who are assessed by invasive urodynamics are more likely to have their management changed and less likely to undergo surgery. This review discusses the role of urodynamic diagnosis and application in the diagnosis and treatment of male LUTS.

Keywords: Benign prostate hyperplasia; lower urinary tract symptoms; prostate; urodynamic study.

Introduction

Lower urinary tract symptoms (LUTS) comprise storage symptoms, voiding symptoms, and post-voiding symptoms.[1] LUTS are prevalent and bothersome in men of all ages.[2,3] Determination of the underlying mechanism is important in choosing the optimal management.[4] Invasive urodynamic tests (filling cystometry (CMG) and pressure-flow studies (PFSs) are used to investigate men with LUTS to determine a definitive objective explanation. The Committee of the International Consultation on Incontinence (ICS) advised that the investigation should be performed before surgical intervention.[5] However, urologists have been undecided on whether urodynamic studies (UDSs) bring essential information, or whether a sufficient assessment can be achieved by clinical evaluation alone.

This review discusses the recent research on the role of urodynamic diagnosis and application in the diagnosis and treatment of male LUTS. Several tests, including non-invasive free flow-rate testing, penile cuff test, external condom catheter, and doppler ultrasound and near-infrared spectroscopy, can be described as urodynamic tests. Attempts to find non-invasive alternatives have not yet revealed an adequate approach. Therefore, invasive urodynamics remains the key indicative test in the care pathway for male LUTS.[6]

Urodynamic testing

The term "urodynamics" was defined as the assessment of the function and dysfunction of the urinary tract by any appropriate method.[7,8] UDS allows the direct assessment of LUT function by the measurement of relevant physiological parameters during filling CMG and PFS. It is performed in an assessment pathway that also can include symptom score, bladder diary assessment, uroflowmetry, and post-void residual (PVR) urine evaluation, as defined by the International Continence Society (ICS).[9] It is always driven by the LUTS reported by the patient, specifically whether any particular symptom remains bothersome despite conservative or medication therapy.

Invasive urodynamics involves the placement of intravesical and rectal catheters (Figure 1). Bladder pressure (P_{ves}) is normally recorded via a fine, fluid-filled catheter passed into the bladder via the urethra with the distal end connected to an external pressure transducer. The continuous subtraction of the pressures in the rectal line (P_{abd}) from those in the vesical line gives the "detrusor pressure" (P_{det}) and

ORCID IDs of the authors:
C.G. 0000-0003-0341-1326

[1]Department of Urology Medistate Hospital, Beykoz University, İstanbul, Turkey
[2]Bristol Urological Institute and Bristol Medical School, University of Bristol, Southmead Hospital, Bristol, UK

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Corresponding Author:
Cenk Gürbüz
E-mail:
gurbuzcenk@yahoo.com

Available online at
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estimate of bladder contraction. The bladder is filled at a steady rate with body temperature isotonic saline (filling CMG) until the patient reports a strong desire to void or experiences severe urgency or incontinence (Figures 1 and 2). Uroflowmetry is performed while still recording pressures (PFS) following "permission to void" (Figures 1 and 3).

Rationale of testing and interpretation of findings

The measurements are performed with the aim of answering the following two questions:

1. Can the bladder be filled to normal capacity without leakage or significant pressure increase due to either an overactive detrusor or low compliance in the storage phase?
2. Can the patient empty his bladder completely, with a normal flow rate and voiding pressure, without straining in the voiding phase?

Filling is ideally started with an empty bladder. Normally, detrusor pressure should remain near zero during the entire filling cycle until voluntary voiding is initiated. Involuntary bladder contractions can occur with filling and are seen as an increase in P_{ves} in the absence of an increase in P_{abd}. This phenomenon is known as detrusor overactivity (DO) (Figure 2). DO may be accompanied by a feeling of urgency or even loss of urine (DO incontinence). A steady increase in pressure with filling indicates impaired compliance, which is quantified by the relationship between change in bladder volume and detrusor pressure (ΔVolume/ΔP_{det}); a value of <20 ml/cm H_2O implies a poorly accommodating bladder.[10]

The most important values from the PFS are the maximum flow rate (Q_{max}) and the P_{det} at that moment (also termed as $P_{det}Q_{max}$) (Figure 3). High pressure associated with a slow flow rate implies bladder outflow obstruction (BOO); if slow flow is associated with low pressure, it signifies detrusor underactivity (DUA). The BOO index (BOOI) gives a quantitative assessment of BOO and is calculated as $P_{det}Q_{max}-2Q_{max}$. If the BOOI is >40, the patient has BOO; if <20, no obstruction exists; values between 20 and 40 are described as equivocal.[11] The bladder contractility index (BCI) is another parameter calculated as $P_{det}Q_{max}-5Q$.[12] A BCI of >100 is normal, and <100 indicates DUA.

Clinical applications of UDS for male LUTS

The PFS measures the relationship between detrusor pressure and flow rate during voiding. While a low flow rate alone may be more likely to be associated with BOO, it is not always the case. Hence, the principal purpose of the PFS is to differentiate BOO from DUA. Similarly, patients with relatively normal flow rate sometimes emerge to have rather elevated detrusor pressures suggestive of obstruction, a diagnosis that can only be made during pressure-flow analysis.[13,14] The importance of recognizing BOO and/or DUA is in deciding treatment, specifically whether to recommend BOO-relieving surgery, such as transurethral resection of the prostate (TURP). DUA is found in 9%-48% of men

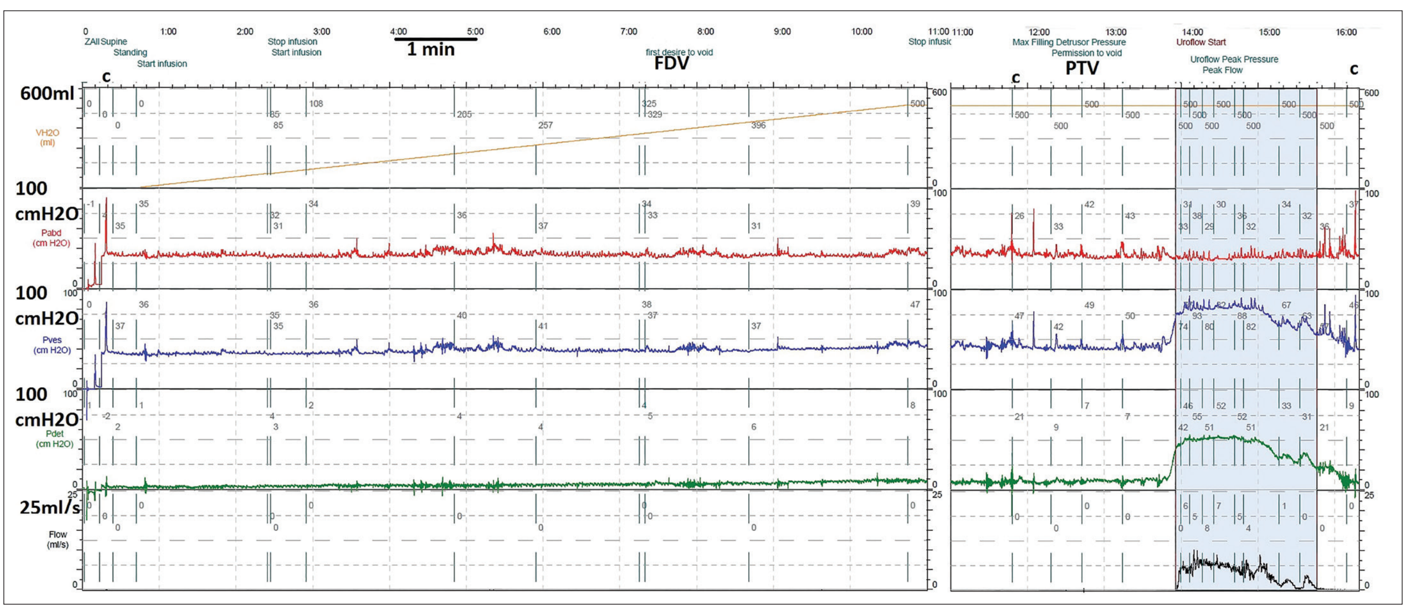

Figure 1. An example of a full urodynamic trace, plotting volume instilled (orange), P_{abd} (red), P_{ves} (blue), P_{det} (green), and flow (black). The filling cystometry is before PTV, and the pressure-flow study is after PTV. Coughs are denoted by the letter c, and FDV is also annotated. The detrusor is stable (no change in P_{det} during filling), and the bladder shows a clear contraction for voiding (increase in P_{det} for voiding), though flow is rather slow (8 mL/s) and prolonged (more than a minute). $P_{det}Q_{max}$ was 51, so the bladder outlet obstruction index was 35 (i.e.,., equivocal), and the bladder contractility index was 91 (underactive)
PTV: permission to void; FDV: first desire to void

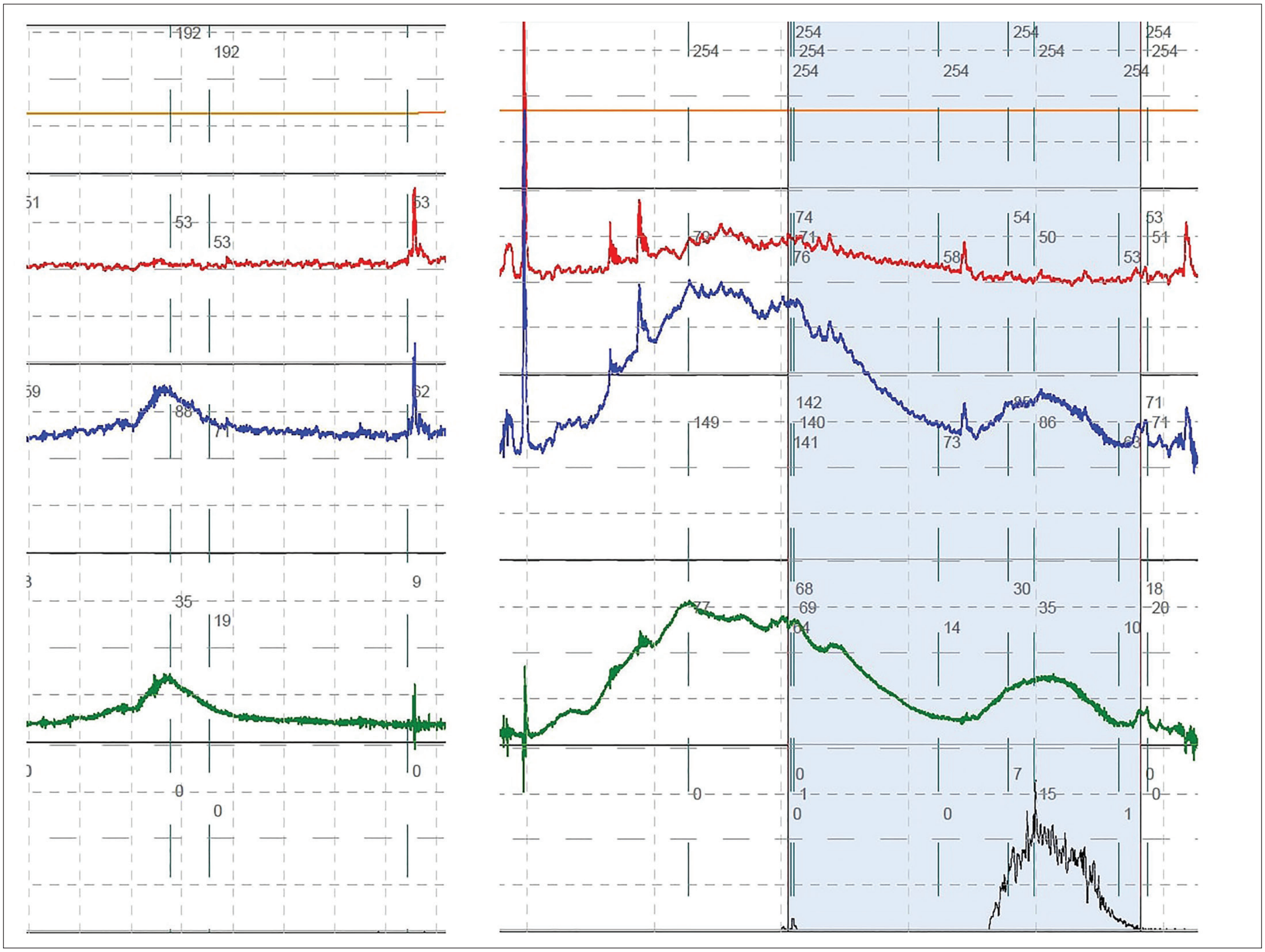

Figure 2. Detrusor overactivity during filling cystometry. On the left, a bladder contraction (increase in pressure in P_{det}, caused by an increase in P_{ves}) is seen. On the right, a high amplitude DO contraction is seen, initially without leakage. At this point, the patient is preventing leakage by contracting his pelvic floor (which can be seen because the rectal catheter crosses the pelvic floor, and so there is an increase in the pressure plotted in the red line). After a while, the pelvic floor gets tired, so incontinence occurs. This is not voiding, as permission to void has not been given
DO: detrusor overactivity

undergoing urodynamic evaluation for non-neurogenic LUTS.[15] If BOO is truly present, successful surgery should improve voiding, but not if DUA is a significant factor.[16,17]

Lower urinary tract symptoms may reflect many potential underlying pathophysiological mechanisms. Young men with LUTS have a different prevalence of underlying etiologies than older men. Approximately one-third of men >55 years with LUTS had benign prostatic obstruction, but younger men were more likely to have poor relaxation of the urethral sphincter.[18]

The ICS defines overactive bladder (OAB) syndrome as urgency, with or without urgency incontinence, usually with increased daytime frequency and nocturia. This symptom-based definition is distinct from DO, which is the urodynamic observation of bladder contractions during filling, which may be spontaneous or provoked. The correspondence of OAB symptoms and urodynamic DO is fairly reasonable in men-more so than in women.[19] However, the symptoms of OAB can be mistakenly attributed to benign prostatic enlargement (BPE). The logic behind this is unclear. Since obstruction impedes urine flow, detrusor contraction is not influenced during storage. Since it has not translated into observations relevant to therapy choice or prediction of outcome, the role of UDS in the initial evaluation of men with OAB is unclear. Nonetheless, many physicians perform UDS after the failure of conservative medical management.

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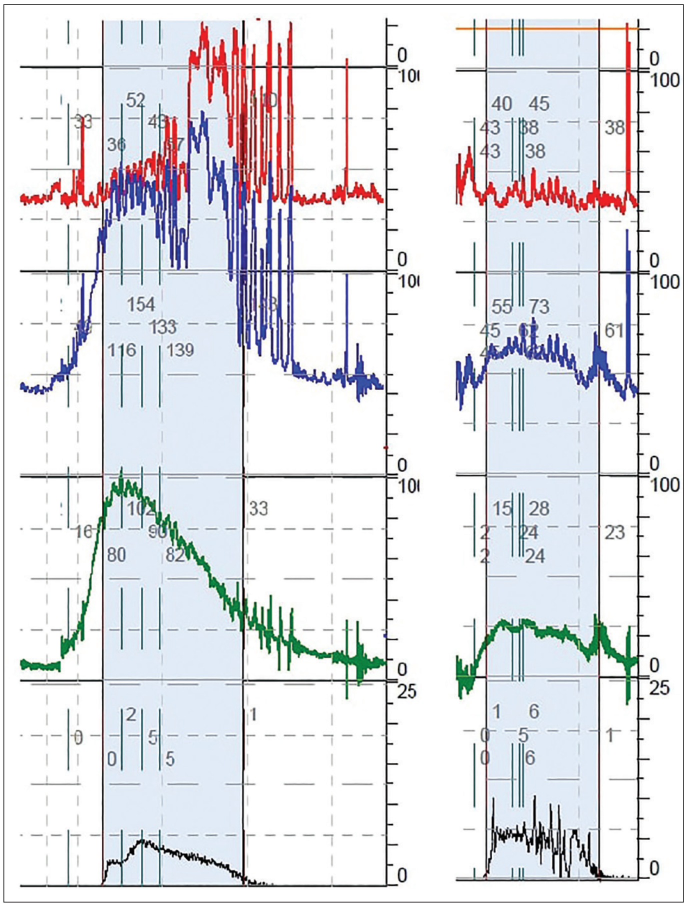

Figure 3. Pressure-flow studies for two different men. On the left, the flow rate is slow, with a Q_{max} of only 5 mL/s. Detrusor pressure at the time of Q_{max} was 102 cm H_2O, so the BOOI was 92 (obstructed), and the BCI was 127 (normal contractility). On the right, the Q_{max} is also only 5, but the synchronous detrusor pressure was 24, so the BOOI was 14 (not obstructed), and the BCI was 49 (substantially underactive)
BOOI: bladder outlet obstruction index; BCI: bladder contractility index

Whether preoperative DO is a significant predictor of surgical outcomes in patients with male BOO remains unknown.[20] There are few available studies exploring the significance of preoperative DO in transurethral surgery, and some of them have controversial results.[21,22] Although men with urgency urinary incontinence ("OAB wet") usually have urodynamic DO incontinence, this is sometimes not the case.

Diagnostic value of urodynamic bladder outlet obstruction to select patients for prostate surgery

A meta-analysis performed by Kim et al.[23] in 2017 showed a significant association between urodynamic BOO and better improvements in all treatment outcome parameters. There were 19 articles that met the eligibility criteria, including a total of 2321 patients, but none of the studies employed a prospective design. The parameter to specify urodynamic BOO varied between studies, though, generally, the BOOI was defined as >40. The review reported that BOO positive patients have better surgical outcomes in all parameters (symptom score, quality of life, Q_{max}, and PVR) than BOO negative patients. BOO negative patients sometimes detected symptomatic improvement after surgery, whereas BOO positive patients detected less, and adverse effects compound the complexity of reporting LUTS improvement.

The Cochrane Database of Systematic Reviews searched for all randomized or quasi-randomized controlled trials on the management of voiding dysfunction in which men with symptoms were randomly assigned to invasive urodynamic testing in at least one arm of the study.[24] Only two trials met the inclusion criteria,[25,26] and analysis was only possible for 339 men in one trial. There was no difference in Q_{max} or International Prostate Symptom Score before and after surgery for LUTS in the two groups who underwent or did not undergo UDS. However, the test was influential for therapy choice.

The Urodynamics for Prostate Surgery Trial: Randomized Evaluation of Assessment Methods (UPSTREAM) study is a prospective randomized controlled trial of 820 men who have bothersome difficulty passing urine and who are considering having surgery for the symptoms.[27] Patients were randomized into two arms. The first underwent clinical evaluation and flow-rate testing, whereas the other additionally underwent urodynamic testing. The trial will determine whether urodynamics reduces surgery rates while achieving similar symptom outcome and will report in 2019. The first qualitative results have been published and revealed that the patients value the additional information that urodynamic testing brings.[28]

Implications of preoperative urodynamic DUA on prostate surgery

The effect of DUA on transurethral surgery outcomes was evaluated in 10 non-randomized studies of 1113 patients.[29] The parameter used to identify DUA was BCI <100. DUA was significantly associated with worse outcomes for symptoms and Q_{max}. However, since some improvement was sometimes seen, DUA is not an absolute contraindication for surgery, provided that the patient is fully counseled.

Implications of storage dysfunction for surgery to relieve BOO

Seki et al.[30] evaluated whether urodynamic findings have any predictive value regarding the outcome after TURP. A retrospective review was performed on 1397 men. A multivariate analysis suggested that the presence of DO was an independent determinant against symptom improvement. The statistical analysis revealed that patients with greater initial storage problems attained less improvement after prostatectomy. Persistent DO can be noted in approximately 30% and 50% of the patients after prostatectomy.[31,32] The emergence of de novo DO is unusual following prostatectomy, so any postoperative DO is likely to represent persistence of DO, as opposed to new onset.

Evaluation of the medical treatment of LUTS by UDS

Most recommendations designate UDS after the conclusion of conservative therapy, but if used at an earlier stage, the information does provide some insight into the mechanisms by which medications might bring clinical response. A systematic review and meta-analysis of studies evaluating alpha-adrenergic antagonists (alpha blockers) for urodynamic outcomes in patients with LUTS/BPE was performed by Fusco et al.[33] Alpha blockers improved the BOOI mainly by reducing $P_{det}Q_{max}$, particularly where BOO was present at baseline. A meta-regression analysis demonstrated a significant positive association between the percentage of patients with obstruction at baseline and the improvement in the BOOI after alpha blocker treatment. As a consequence, patients with obstruction can be regarded as the subpopulation that could benefit the most from alpha blocker therapy, as opposed to those merely with voiding LUTS. Nonetheless, PFS is not routinely performed in clinical practice to identify the subgroup of men with BOO among those presenting with voiding LUTS. This is simply because the easily reversible nature of drug therapy, and relatively low risk of adverse effect, makes the cost and adverse effects of UDS difficult to justify. Free uroflowmetry may be performed in the initial assessment of male LUTS according to the European Association of Urology guidelines. However, a threshold-free Q_{max} value of 15 ml/s has a positive predictive value of only 67% for BPO, meaning that approximately one-third of men treated with alpha blockers at this level do not really have obstruction.[34] Most studies evaluating alpha blocker therapy for LUTS/BPE consider free Q_{max} as the only urodynamic measure of treatment effect. However, treatment-induced improvements in this parameter are generally loosely related,[35] and the actual urodynamic response may be a relevant decrease in $P_{det}Q_{max}$.[33]

Of the male patients with LUTS, >50% have complaints of storage symptoms requiring anticholinergic therapy.[36] Initial combination treatment employing both alpha blockers and anticholinergics could improve response and ameliorate adverse events in male patients with voiding and OAB symptoms.[37-39] Only a few studies have used urodynamic measurements to monitor clinical changes with anticholinergic treatment in men with LUTS.[40,41] $P_{det}Q_{max}$ and Q_{max} were assessed by a combination of alpha blocker plus anticholinergic versus placebo and were found to be non-inferior to placebo. Hence, the clinical value of UDS on combination therapy choice is still doubtful.

Risks of invasive urodynamic tests

UDSs are generally well tolerated and perceived valuable by patients due to the additional insight brought into the symp-

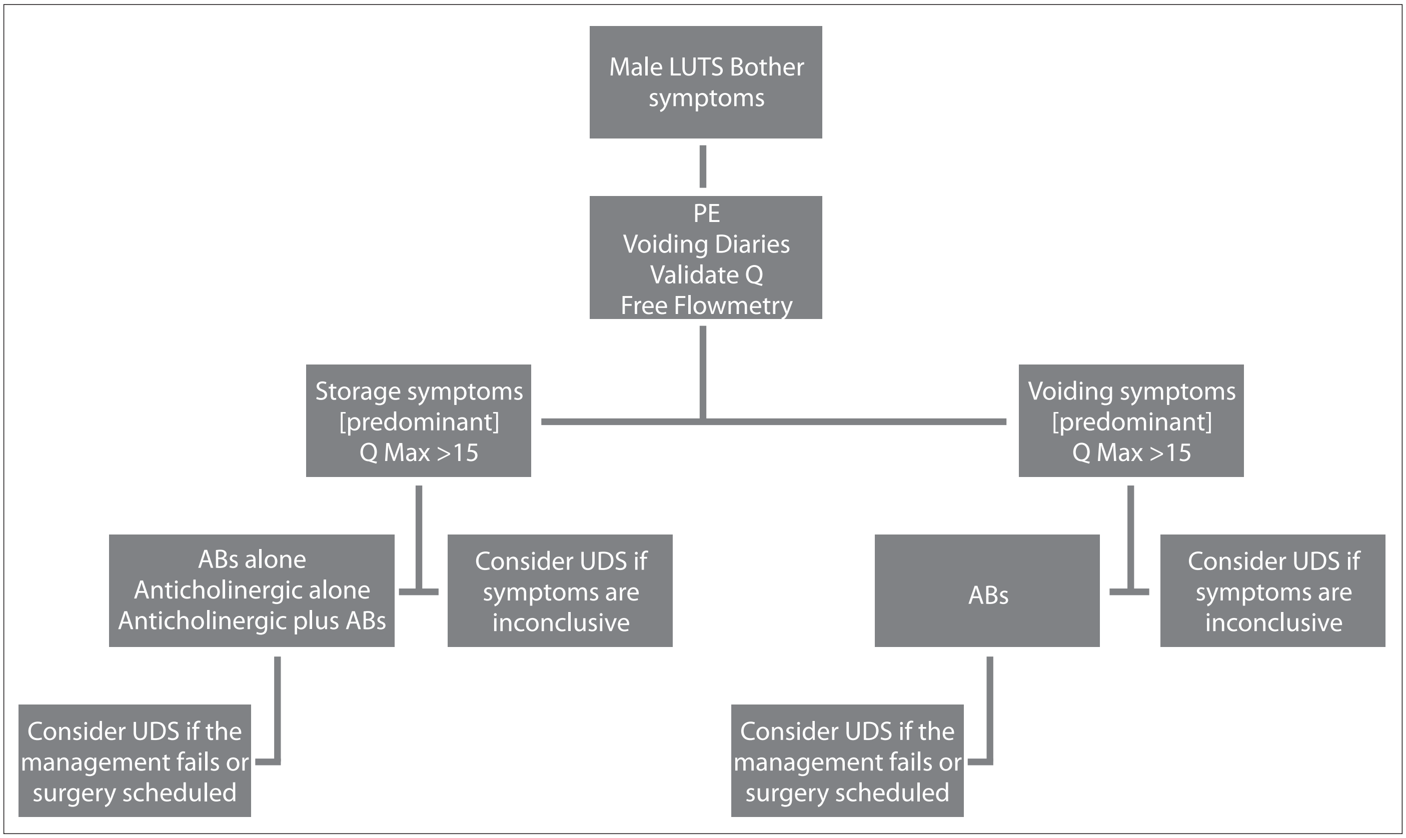

Figure 4. A flow diagram of the assessment of male LUTS
PE: physical examination; AB: alpha blocker; UDS: urodynamic study; Q: questionnaire; LUTS: lower urinary tract symptoms

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toms[28] However, men may find testing to be an uncomfortable or embarrassing experience. The main risks of urodynamic testing are those associated with the process of urethral catheterization, such as dysuria (painful urination) and urinary tract infection. The rate of bacteriuria reported after UDS ranges from 4% to 9%.[42,43]

Practical management of male LUTS

Diagnostic pathways and thresholds of testing to evaluate male LUTS generally include evaluations to exclude a serious underlying health factor, symptom score, bladder diary, urinalysis, and free flow-rate testing with PVR measurement. Additional tests may be performed individually. The flow diagram illustrates an approach to the diagnostic pathway for male LUTS and the potential contribution of UDS (Figure 4).

In conclusion, UDSs provide an objective evaluation of the patients presenting LUTS, often providing an uncertain relationship in predicting the underlying UDS findings. Distinguishing between voiding LUTS due to BOO and/or DUA is important, as this issue may influence management decisions specifically related to surgery for BOO. Low-level evidence suggests that making this distinction is important, as clinical outcomes may be affected.

Limited evidence in the literature suggests that UDS helps to predict which men with bothersome LUTS will benefit from surgery and medical treatments. Invasive urodynamics is generally well tolerated and leads to far fewer complications than avoidable surgery and very few serious long-lasting issues. Publication of the UPSTREAM trial data will help identify the best approach to the diagnostic pathway. Until then, we recommend an inclusive approach to using invasive urodynamics to complete the full assessment of those men who have failed conservative management of bothersome LUTS.

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