Male LUTS diagnostics: Where are we in 2018?

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Abstract
The pathophysiology of male lower urinary tract symptoms (LUTS) includes numerous different clinical conditions and organs such as prostate, bladder, urethra and nervous system. A paradigm shift of modern urological practice against male LUTS lies on the fact that instead of focusing into each individual component of the system, we now face lower urinary tract as a single functioning unit simplifying evaluation and targeting only its clinical manifestations that have impact to the patient. In this mini review recent advancements in the diagnosis of male LUTS are presented.

Introduction
Clinical management of only few diseases in urological practice underwent such a dramatic change during the last 20 years, as the one observed in the treatment of male lower urinary tract symptoms (LUTS). Benign prostatic enlargement (BPE) due to benign prostatic hyperplasia (BPH) which is the normal consequence of aging on male prostate, was traditionally considered the main underlying mechanism of lower urinary tract dysfunction resulting on male LUTS. Urodynamic evidence against this “prostatocentric” understanding of LUTS revealed that only 50% of male patients with LUTS are indeed clearly obstructed by an infravesical aetiology, while clinical data documented that nearly 30% of patients with LUTS and BPH undergoing elective deobstructing surgery will report poor outcomes in their symptoms [1, 2].

Current understanding of the pathophysiology behind male LUTS has implicated a wide spectrum of clinical conditions including bladder dysfunction, prostatic and urethral bladder outlet obstruction (BOO), sphincter dyssynergia as well as non lower urinary track contributing factors such as metabolic syndrome, drug side effects and lifestyle habits.

Key words
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Someone would expect that as our knowledge on the pathophysiology of male LUTS has included numerous different clinical conditions and organs its clinical investigation would have become even more complicated. Still, the paradigm shift of modern urological management of male LUTS was that instead of focusing into each individual component of the system, we now face lower urinary track as a single functioning unit simplifying evaluation and targeting only its clinical manifestations that have impact to the patient. The two cornerstones of LUTS assessment are the investigation of differential diagnosis to ensure the safety of the underlying clinical condition and the evaluation of patient’s clinical profile to define the risk for progression or complications as well as the impact of specific symptoms on patient’s quality of life (QoL) (Figure 1).

Enabling patient safety: Differential diagnosis
As several clinical conditions associated with LUTS might pose some risk for the patient, initial assessment should aim to ensure the safety of the underlying clinical condition. EAU guidelines have stressed the necessary investigation pathway to exclude abdominal malignancies such as bladder and prostate cancer, urinary tract infections, neurological diseases and chronic urinary retention [3]. Apart from clinical history and physical examination, screening tools for the initial assessment include prostate specific antigen testing, urinalysis, urinary track ultrasonography with post void residual urine volume measurement and digital rectal examination. Once safety of the underlying condition has been ascertained, assessment can focus on patient’s clinical profile to evaluate the risk for clinical progression and future complications and access the impact of specific symptoms to patient’s quality of life (QoL).

Building patient’s clinical profile
Prostate volume, PSA levels, post void residual urine, Qmax and age at baseline are all factors that have been strongly associated with the risk for clinical progression and occurrence of future BOO related complications such as acute urinary retention or need for surgery [4]. Given that LUTS is a progressive condition as patient grows older, assessing the risk for clinical deterioration in all patients is of paramount clinical importance for the proper management of LUTS.

Figure 1. Proposed algorithm for initial evaluation of LUTS by European Association of Urology guidelines
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The rationale behind addressing the effect of LUTS on QoL and not bladder or prostatic dysfunction per se lies on the fact that up to 70% of healthy volunteers undergoing urodynamic investigation demonstrate pathologic findings such as asymptomatic obstruction or bladder instability [5]. These conditions are not a disease and should not be treated as long as they do not cause complications and do not affect patients QoL.

Apart from medical history, several well validated tools are available to quantify the level of bother caused by LUTS and define patient’s predominant complain. International prostate symptom score (IPSS) and American Urological Association Symptom Score (AUASS) are by far the most well documented questioners employed in clinical studies. Still, both tools have significant limitations including their complexity especially when filled by elder and not well educated patients. Visual Prostate Symptom Score presents an emerging validated alternative to these questioners which combines simplicity to a comparable with IPSS clinical validation [6] (Figure 2). Another limitation of IPSS and AUASS is that the main treatment target of modern practice, which is the effect of LUTS on patient’s QoL, is only evaluated by a single question in each questioner. Additional tools such as the Benign Prostatic Hyperplasia Impact Index (BII) have been developed and validated to capture more effectively the symptom specific impacts in QoL [7]. In addition, in patients with nocturia or storage predominant symptoms, clinical evaluation using specially designed tools such as Overactive Bladder Symptom Score (OABSS) and Nocturia QOL questionnaire (NQOL) can reinforce clinical evaluation and assist monitoring of employed treatment [8]. Moreover, accumulating evidence has shown a strong relationship in epidemiology, physiology and pathophysiology of both male LUTS and erectile dysfunction (ED) [9]. Both IPSS and AUASS do not assess sexual function and given the potential impact of LUTS treatment on sexuality (retrograde ejaculation by a-blockers and surgery, loss of libido by 5a-reductase inhibitors) the employment of a validated tool such as the International Index of Erectile Function (IIEF-5) Questionnaire is strongly advised to guide clinical management. Finally, detailed lifestyle factors such as fluid intake and caffeine use have been associated with LUTS and as such a detailed lifestyle history should not be omitted as diet modifications can have a significant impact in LUTS [10].

### i. Assessing the impact of LUTS on QoL

#### Grossly, most patients with bothersome LUTS can be subdivided into patients suffering from storage predominant or voiding predominant dysfunction. IPSS voiding (V) to storage (S) subscore ratio (IPSS-V/S) has been proposed as a useful method for such a discrimination with IPSS-V/S < 1.0 indicating bladder related dysfunction and IPSS-V/S > 1.0 indicating a possible BOO etiology [11].

### ii. Addressing the storage/voiding elements of LUTS

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Storage symptoms are not only the most frequent symptoms in patients with LUTS (nearly 50% of LUTS patients demonstrate detrusor overactivity on urody-
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Dynamic study/UDS) but also the most bothersome clinical manifestation, affecting significantly QoL [7]. That’s why according to modern management of male LUTS, pharmacotherapy using drugs targeting the obstructing element of male LUTS (alpha blockers, 5a reductase inhibitors) should be added way after the exclusion of nocturnal polyuria and the assessment of irritative symptoms. A trial period with the use of a muscarinic receptor antagonist/beta-3 agonist can help elucidate LUTS pathology in patients with storage predominant symptoms. In patients suffering from voiding predominant LUTS, a recent systematic review proved that symptoms-only are inadequate to indicate BOO given that both increased outlet resistance and decreased detrusor muscle function have the same phenotype [12]. UDS remains the reference diagnostic standard to elucidate the real cause of voiding dysfunction yet its wide application is limited by its invasiveness. Several noninvasive diagnostic tools are available to substitute UDS including sonographic data suggestive of BOO (increased bladder wall thickness, bladder weight, intravesical prostatic protrusion, prostatic urethral angle and bladder wall trabeculation), penile cuff test, external condom method, urethral doppler and near infrared spectroscopy. A recent systematic review identified promising sensitivity and specificity in several of these tests rendering them a useful aid in decision making, yet they were all found less accurate that UDS [13]. Out of all non invasive tools, penile cuff test appears quite promising as its compact equipment and straightforward investigation setup are accompanied by a rapidly expanding high quality documentation [14]. Another very promising trend in LUTS diagnostics includes the combination of different non invasive tools into single diagnostic algorithms which increases the separate sensitivity and specificity of each individual test reducing the need for invasive diagnostics to only a minority of LUTS cases. An example of such algorithm has been recently proposed by Farag et al. While sonographic measurement of bladder wall thickness or Qmax have a relative small specificity in BOO diagnosis, combining these two together establish an acceptable diagnostic substitute to more invasive tests [15].

Novel test for the assessment of LUTS

i. Measurement of Detrusor Wall Tension

In contrast to our previous understanding on bladder biomechanics that employed two separate states of wall tension (relaxed during filling and contracted during active voiding or overactivity), modern data indicate that bladder wall exhibits an active preload tension during filling which has been described as dynamic elasticity as its being altered during passive filling and emptying. The latter may be defective in individuals with LUTS and further understanding of this mechanism could lead to future sub-typing of patients as well as potentially to new treatment options [16]. Several ultrasound based techniques have been described to measure actual detrusor wall tension including bladder vibrometry (which uses ultrasound excitation to measure bladder wall compliance), bladder elastography and 2D/3D ultrasound calculation of wall tension, stress, and strain [17-19]. Notably, wall tension, stress, and strain more closely reflect real-time sensation than bladder pressure alone [19].

ii. Bladder sensation tests

Current UDS technology is limited by the gross and subjective nature of self-reporting bladder sensation by the patient during the filling phase of the test. Magnetic Resonance Imaging during UDS has identified specific brain areas activated during micturition and been proposed as a promising tool for use in the future [20,21]. In addition, real time sensation-bladder capacity curves can be created by using touchscreen sensation meter tools aiming to create more objective data as verbal sensation thresholds have been proven inconsistent in OAB patients [22].

Conclusions

In conclusion, while the attributed pathophysiological mechanisms of male LUTS are growing, clinical assessment of the condition is more focused than ever before to the safety of the patient and to the effect of specific symptoms in patients QoL. LUTS diagnostic evaluation is treatment oriented and adopts diagnostic algorithms only when their outcome will alter decision making of patients. After all, LUTS should be faced as a normal consequence of aging and should be addressed to the level that affect patients safety or disrupts his way of living.

Conflicts of interest

The author declared no conflict of interest.
Περίληψη

Η παθοφυσιολογία των συμπτώματών του κατώτερου ουροποιητικού στους άνδρες περιλαμβάνει ποικίλες νόσους προερχόμενες από διαφορετικά όργανα όπως ο προστάτης, η ουροδόχος κύστη, η ουρήθρα και το νευρικό σύστημα. Παραδειγματική μετατροπή της σύγχρονης παθοφυσιολογικής πρακτικής έναντι των συμπτώματων αυτών αποτελεί το γεγονός ότι αντί να αναλύουμε τη λειτουργία καθενός από τα εμπλεκόμενα όργανα, αντιμετωπίζουμε την ούρηση ως ένα ενιαίο μηχανισμό, απλώνοντας την διερεύνηση και επικεντρώνοντας αυτή μόνο στα κλινικά συμπτώματα που επηρεάζουν την ποιότητα ζωής των ασθενών μας. Στην βιβλιογραφική αυτή ανασκόπηση οι σύγχρονες εξελίξεις στη διαγνωστική των συμπτώματων του κατώτερου ουροποιητικού στους άνδρες παρουσιάζονται.

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