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Storage-dominant lower urinary tract symptoms in the older male: Practical approach, guidelines recommendations and limitations of evidence

Sanjay Sinha [a,*], Anne P. Cameron [b], Vincent Tse [c,d], Jalesh Panicker [e]

[a] Department of Urology, Apollo Hospital, Hyderabad, India
[b] Department of Urology, University of Michigan, Ann Arbor, MI, USA
[c] Department of Urology, University of Sydney, Australia
[d] Macquarie University, Sydney, Australia
[e] Department of Uro-Neurology, The National Hospital for Neurology and Neurosurgery and UCL Queen Square Institute of Neurology, London, United Kingdom

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ABSTRACT

Purpose: Lower urinary tract symptoms (mLUTS) are common and bothersome in the older male with significant impact on the quality of life. There is a paucity of good evidence and guideline recommendations with regard to management decisions for men with a storage-dominant presentation. This review is based on a workshop on the subject at the International Continence Society (ICS) Annual Congress in Toronto, 2023 and follows the format of the workshop.

Materials and Methods: This review follows the structure of the workshop. Storage-dominant mLUTS is discussed is five sections: diagnosis and stratification of risk, urodynamics findings, evidence and guidelines recommendations, geriatric neuro-urological conditions in the elderly male, and recommendations for clinical practice.

Results: Careful clinical evaluation including history, examination, co-morbid conditions, co-prescriptions, use of standardized questionnaires, bladder diary, urine analysis, uroflow, postvoid residual urine, and void% can help formulate a treatment plan based on non-invasive evaluation. Behavioral therapies recommended for overactive bladder are appropriate. Drug therapy includes judicious use of alpha-adrenergic blockers, antimuscarinics, beta-3 adrenergic agonists, and other standard mLUTS medication. Men who are refractory to conservative options might often benefit from invasive urodynamics before escalation of therapy. There is a striking dearth of evidence with regard to the management of storage dominant mLUTS. Consequently, guidelines recommendations are often inadequate for individual patients encountered in clinical practice. Geriatric neuro-urological conditions are common in the elderly male and can confound diagnosis and management. Urologists have a particular responsibility to suspect neuro-urological conditions that first present with mLUTS.

Conclusions: The management of mLUTS requires detailed clinical assessment with judicious use of investigations. The underlying philosophy of management is alleviating the patient's symptoms using the minimum number of medicines. Invasive urodynamics are useful before escalation to invasive therapies for refractory storage-dominant mLUTS. There is an urgent need to direct research to answer questions that are fundamental to the management of mLUTS.

Contents

* Corresponding author.
E-mail addresses: drsanjaysinha@hotmail.com (S. Sinha), annepell@med.umich.edu (A.P. Cameron), vwmtse@gmail.com (V. Tse), j.panicker@ucl.ac.uk (J. Panicker).

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1. Introduction

Lower urinary tract symptoms (LUTS) are common and bothersome in the older male affecting at least a quarter of the population [1]. Most men find storage symptoms more bothersome than voiding symptoms and there can be a significant impact on the quality of life [2]. Management decisions are affected by the complex interaction between voiding and storage symptoms and the impact that treating one component of LUTS has on the other. There is a paucity of good evidence and guideline recommendations with regard to management decisions. From a historical extreme of regarding all LUTS in older men as 'prostatism' in the past, there now seems to be a lack of adequate recognition with regard to the role of treating voiding abnormalities on the resolution of storage symptoms.

This review is based on a workshop on the subject at the International Continence Society (ICS) Annual Congress in Toronto, 2023 and follows the format of the workshop.

2. Diagnosis and stratification of risk in the older male with storage LUTS

When confronting the older male patient with urgency, frequency, nocturia or urgency incontinence it is important to balance the risk and benefits of both investigations as well as treatments. This is different than in younger men given this population's higher risk of medical comorbidities as well as their potential frailty making management decisions higher risk. The most basic and risk-free assessment includes a detailed medical and urologic history, physical exam, and symptom scores such as the LURN SI 10 or ICIQ-mLUTS [3]. Unique to the older male as part of medical history one should focus on their cognitive status, functional status, comorbidities such as diabetes and other progressive neurological conditions such as Parkinson's. Screening for prostate cancer should follow guidelines recommendations based on risk-stratification. Physical examination includes a genitourinary examination, abbreviated neurological assessment and determination of frailty by a test such as the 'timed get up and go' test [4].

A bladder diary is invaluable and provides information on functional bladder capacity and nocturnal polyuria as well as guidance for patients on better fluid consumption patterns to improve lower urinary tract symptoms. Urinalysis can help exclude microscopic hematuria or glucosuria due to uncontrolled diabetes mellitus or use of SLG2 inhibitors. It is important to exclude microscopic hematuria due to an underlying urothelial neoplasm that can present with storage LUTS. Identification of glucosuria can help identify the cause of storage symptoms in patients with uncontrolled diabetes mellitus.

Non-invasive tests such as postvoid residual (PVR) and uroflowmetry give valuable information and might offer clues to abnormal voiding accompanying or underlying the storage-dominant presentation. It would be reasonable to start with an alpha-adrenergic blocker in men with an abnormal flow or elevated PVR. Poor void% might preclude use of antimuscarinics. These tests have limitations and can be confounded by technical issues such as delay in measuring PVR or a bladder that is under- or over-filled.

Urodynamics provide excellent information regarding bladder capacity, the presence of detrusor overactivity as well as any bladder outflow obstruction but is not without risk of infection, urethral trauma from catheterization as well as time, discomfort, and cost. Hence, when deciding on the need for urodynamics one needs to weigh the risk of a missed diagnosis as well as the risk of the planned treatment since if the planned intervention is not dependent on accurate diagnoses then urodynamics do not yield actionable information. Behavioral therapy, noninvasive treatments such as physical therapy and pharmacotherapy with anti-muscarinic or beta-3 agonists are all low-risk interventions and none require urodynamics to safely implement provided PVR is reasonable. It should be possible to avoid invasive testing in most men with frequency, urgency, and nocturia after documenting a reasonable flow and low PVR. In men with storage-dominant LUTS but significant evidence of voiding dysfunction, invasive urodynamics might help decide whether relief of bladder outflow obstruction is indicated to resolve symptoms or enable invasive therapies for storage LUTS *(vide infra)*.

3. Urodynamics findings

Urodynamic evaluation usually implies a failure of medical management and the threshold of a decision for invasive therapy. It is important to ensure a high-quality urodynamic study with a well-defined question, tailored test, and attention to detail, while minimizing the risk of infection.[5,6] The feasibility and utility of urodynamics in older males has been examined earlier [7]. There is significant potential for harm from inappropriate treatment, especially in older individuals. There is also potential harm from a poor-quality study that results in erroneous or no conclusions. Quality control is increasingly recognized as a problem even at academic centers [8].

In older men with storage dominant LUTS, typical findings during filling cystometry include early sensations resulting in reduced capacity, detrusor overactivity with or without urinary incontinence which might be terminal, and reduced compliance. The entire spectrum of voiding pressure flow findings can be seen and these might prove decisive. Pressure flow study can show normal voiding, various grades of bladder outflow obstruction, and the entire spectrum of detrusor voiding contraction from a strong to very weak detrusor (Fig. 1A, 1B, 1C; Fig. 2; and Fig. 3). Ordinarily, one would not expect an acontractile detrusor in men who void spontaneously and have no neurological conditions. Hence, the absence of a voiding contraction in this setting must be viewed with suspicion. Most such men turn out to have situational inability to void, or a technical inability to record a valid voiding phase due to severe storage abnormalities precluding bladder filling. Severe urgency can also result in a failure of sphincter relaxation. Such situations must be recognized during the test and should instigate repeat cycles of testing with appropriate measures as outlined elsewhere [5].

Current standards include a new nomogram for men undergoing pressure flow studies, use of the term 'Detrusor contraction index (ICS-DCI)' rather than 'bladder contractility index (BCI)' a new category of severe obstruction (severe obstruction, BOOI $\geq$80), a new term 'intermediate obstruction' (in place of 'equivocal obstruction') for BOOI 20–40, and a new category of very weak detrusor (ICS-DCI <50). The reader is referred to the recent ICS-SUFU standardization documents for a more detailed reading [9].

4. Clinical practice guidelines and evidence

The European Association of Urology (EAU) Guidelines recommends use of an antimuscarinic (strong recommendation) or beta-3 adrenergic agonist (weak recommendation) in men with moderate to severe storage symptoms [10]. The guidelines also suggest that men with storage

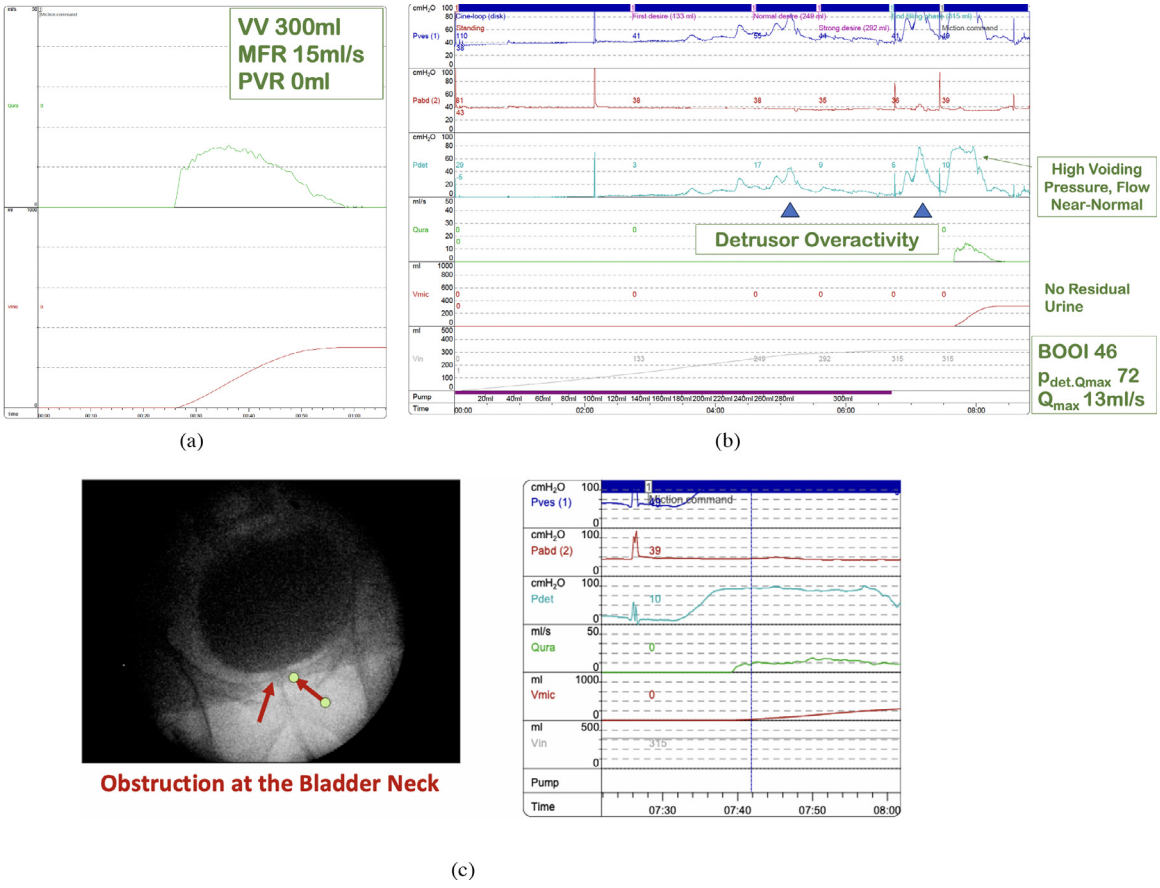

Fig. 1. 47yM with markedly bothersome urinary frequency and urgency for 2 years refractory to lifestyle changes as well as a combination of mirabegron 50 mg with solifenacin 5 mg. Postvoid residual was urine 35 ml (prevoid 315 ml); maximum flow rate 15 ml/s (1 A). Video-urodynamics before the planned botulinum toxin injection revealed high-flow primary bladder neck obstruction (1B and 1C). Counseling included discussion regarding uncertainties and possible need for further therapies. The patient underwent bladder neck incision with satisfactory resolution of symptoms. *(Courtesy SS)*.

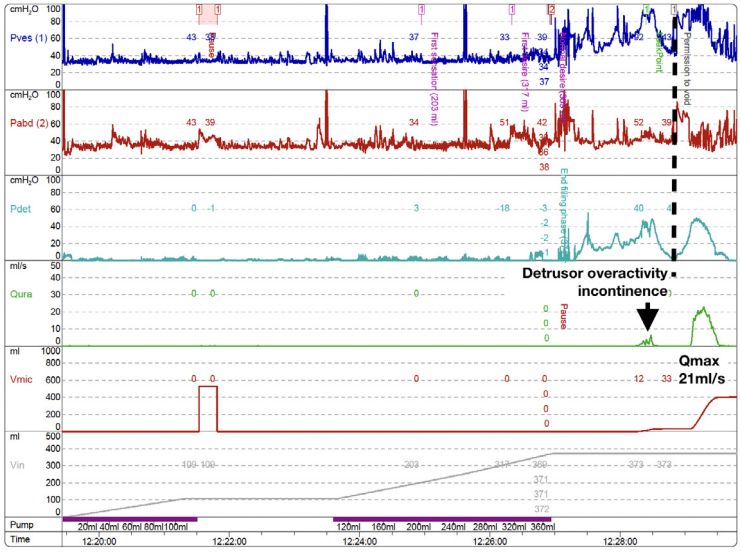

Fig. 2. 67yM with refractory urgency incontinence despite conservative measures and combined overactive bladder medication. His prostate was 30 g, residual urine was 40 ml (prevoid 290 ml) and maximum flow rate was 18 ml/s with a normal pattern. Urodynamics showed detrusor overactivity with incontinence with normal voiding phase. His $p_{\mathrm{det.Qmax}}$ was 43 cm H20 and Q_{max} was 21 ml/s. He underwent Onabotulinum toxin A 100 Units injection with resolution of symptoms. *(Courtesy SS)*.

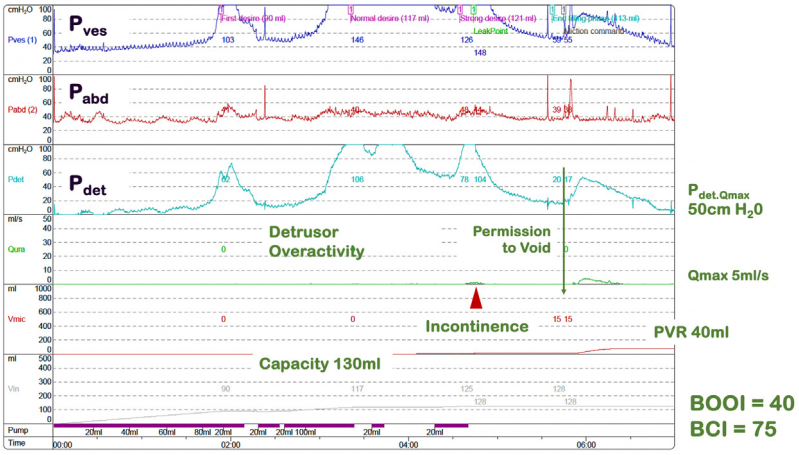

Fig. 3. 70yM with refractory urgency incontinence despite conservative treatment and combined overactive bladder medication. His prostate was 42 g, residual urine was 30 ml (prevoid 130 ml) and maximum flow rate was 8 ml/s. Urodynamics showed high-pressure detrusor overactivity incontinence and bladder outlet obstruction with an underactive detrusor voiding contraction (BOOI 40, DCI 75). He underwent TURP but had persistent storage symptoms (although better). Re-challenge with combined mirabegron 50 mg and solifenacin 5 mg proved to be effective and he is comfortable on long-term medication. *(Courtesy SS)*.

LUTS who fail to benefit adequately with either an antimuscarinic or an alpha-adrenergic blocker alone should be offered a combination of the two [10]. However, for beta-3 adrenergic agonists, the recommendation is to use an alpha blocker first and to add the beta-3 adrenergic agonist only in case of an unsatisfactory response [10]. The American Association of Urology (AUA) Guidelines has similar recommendations and mentions the advisability of initiating treatment with an alpha-adrenergic blocker alone to minimize the possibility of adverse events related to combination therapy [11].

The current EAU Guidelines algorithm does not discuss the possible benefits of treating voiding dysfunction in men who present with storage-dominant LUTS. The algorithm also fails to consider the possibility that a man with voiding dysfunction might present with storage-dominant LUTS. The indications for urodynamics in storage-dominant mLUTS are hidden within the standard indications. Patients who are unable to provide ≥150 ml volume at uroflow, those with a large residual urine, those with suspected neuro-urological conditions, and situations where patient or clinicians seek more information are all more likely in storage-dominant presentations [10].

There is evidence to show that alpha-adrenergic blockers improve storage symptoms in addition to their beneficial impact on voiding, although these benefits are more modest and inferior to that seen with standard medication used for overactive bladder [12,13]. Hence, in men with a component of voiding symptoms, or in those with investigative findings consistent with abnormal voiding, it is reasonable to initiate an alpha-adrenergic blocker as suggested by the AUA Guidelines [11]. Studies have shown that men with inadequate response to an alpha adrenergic blocker often respond when an overactive bladder medication is added [14]. However, this does not imply that men with marked bother due to storage-dominant symptoms should be denied concomitant overactive bladder medication. As will be noted vide infra, overactive bladder medication is safe in men with LUTS. One must be mindful of the potential increase in adverse events with the use of combined therapy as well as the associated economic burden [10].

Overactive bladder medication is generally safe in men. Antimuscarinics rarely cause retention when used in combination with alpha blocker [15]. In fact, no increase in the rate of retention was noted in men with urodynamic obstruction or underactivity given an antimuscarinic alone [16,17]. However, these studies all had specific inclusion criteria that patients in clinical practice might not always fulfill. Guidelines recommend against the use of an antimuscarinic in men with postvoid residual urine >150 ml [10]. Similarly, the use of mirabegron in men is generally noted to be safe. Our understanding of the mechanism of action of these drugs suggests that they might have a lower propensity to impact voiding. A systematic review did show a small statistically significant increase in residual urine when mirabegron was added to an alpha-adrenergic blocker, although one might argue that the 12 ml increase observed was not clinically significant [18]. Mirabegron has been shown to be safe in men with bladder outlet obstruction [19].

Studies show that men undergoing prostate surgery experience an improvement in storage symptoms. This improvement is noted in about two-thirds of men and seems to be sustained at two years [20]. This suggests that it might be appropriate to discuss the potential role for surgery in men with storage-dominant LUTS who have abnormal voiding. Surgery might have the potential to lead to a long-term resolution of storage symptoms. An association between obstruction and storage dysfunction lends further credence to this hypothesis although long-term data is lacking. Attempts have been made to predict the resolution of storage symptoms following prostate surgery. Older men or those with more severe storage symptoms are less likely to experience resolution of storage symptoms. On urodynamics, unequivocal obstruction and normal detrusor contractility favor resolution while early or high-pressure detrusor overactivity during filling, terminal detrusor overactivity, or low bladder capacity, are less likely to improve [21–26].

Guidelines widely recommend the use of botulinum toxin or sacral neuromodulation in men with refractory storage symptoms but the evidence base is rather tenuous. Men constitute less than 10% of subjects in trials related to refractory overactive bladder. There are very few large cohort studies either. There are specific concerns regarding the retention rate in men following botulinum toxin injection. In a study of 120 men who received botulinum toxin, retention rate was noted to be 28.6%, 7.5% and 4.2%, in men who had not undergone prostate surgery, in those with prior transurethral resection of the prostate, and in those with prior radical prostatectomy, respectively [27,28]. Following prostate surgery the retention rates were similar to that noted historically in women. Older men might not have the physical or cognitive skills required to perform clean intermittent catheterizations [29].

With regard to sacral neuromodulation, again, the data is very sparse. There are no urodynamic parameters that predict success, complications or failure in percutaneous tibial nerve stimulation nor with sacral neuromodulation [30]. Men offered sacral neuromodulation do not convert from the test stimulation step to final implantation as often as women do. However age does not seem to result in poorer outcomes [31]. However, in general, untreated anatomical obstruction is considered a contraindication. Hence, it might be reasonable to

consider evaluating and treating any element of obstruction in men prior to sacral neuromodulation.

Overall other than pharmacotherapy the literature on the treatment of men with overactive bladder both young an old is lacking [20]

5. Special considerations in the Geriatric neuro-urology patient

5.1. Parkinson's disease

Lower urinary tract (LUT) symptoms occur commonly in Parkinson disease (PD), and a prevalence figure ranging between 38%–71% has been reported [32]. LUT dysfunction occur in early in the disease course and symptom severity has been shown to be related to the duration and extent of disease [33]. Studies have in fact demonstrated a relationship between symptoms and extent of dopamine depletion [34,35].

Patients most often report urinary storage symptoms, seen in more than 60% of PD patients, and these symptoms have a considerable impact on quality of life [36,37]. Nocturia (56.7%) is the most common symptom, followed by urinary urgency, and these are the commonest nonmotor symptoms in PD. Urodynamic studies most commonly demonstrate detrusor overactivity [36] and antimuscarinic agents should be used with caution in elderly patients with neurodegenerative disorders as patients may already be suffering from dry mouth and constipation, the commonest side effects reported when using these medications, arising due to their underlying neurological disorder. These drugs can also block central muscarinic M1 receptors and cause impairment of cognition and consciousness in susceptible individuals. This may be mitigated by using antimuscarinic agents which have greater selectivity for the M3 receptor rather than the M1 receptor, such as darifenacin, or that have restricted permeability across the blood–brain barrier because of physicochemical properties, such as trospium chloride [38]. Furthermore, antimuscarinic agents can interact with other medications used in Parkinson's disease, and awareness about drug interactions can help reduce the risk of developing adverse effects [39].

Patients with PD may have nocturnal polyuria (NP), characterized by excessive production of urine at night, which is a significant cause for nocturia [40,41]. Benign prostate enlargement may occur concomitantly in men, and proper patient selection involving neurological and urological input should be undertaken before proceeding with transurethral resection [42].

LUT symptoms in PD is often multifactorial and other comorbidities including vascular disease, cervical spondylosis, diabetes mellitus, congestive cardiac failure, ankle edema, and medications use such as diuretic can contribute to symptoms.

5.2. Multiple system atrophy

Not all patients presenting as parkinsonism have PD, and Multiple System Atrophy (MSA) presents with early and severe bladder symptoms that dominates the clinical picture. Autonomic dysfunction is a cardinal feature of MSA and LUT dysfunction often predates the occurrence of cardiovascular autonomic failure [43]. Patients experience LUTS during the disease course including daytime frequency, nighttime frequency, urinary urgency and urgency incontinence [44]; voiding dysfunction is significant in MSA, and the postvoid residual volume increases as the disease progresses [45]. However, in a cohort of patients urinary retention may be one of the first presentations, occurring prior to making the neurological diagnosis [46]. Some patients present with cerebellar signs predominantly and severe autonomic dysfunction (MSA-C), however motor dysfunction severity correlates poorly with LUT dysfunction [47]. Videourodynamic studies demonstrate detrusor overactivity, detrusor underactivity, detrusor–sphincter dyssynergia and an open bladder neck at the start of bladder filling [48,49], and anal sphincter electromyography demonstrates neurogenic changes [50].

5.3. Other disorders

Urinary incontinence commonly occurs in patients with dementia and is probably multifactorial. Behavioral and cognitive changes occurring in dementia can contribute to LUT symptoms (Table 1). Amongst different neurological disorders associated with dementia, incontinence has been observed to occur in more advanced stages of Alzheimer disease, whereas it may occur earlier on in the course of patients with dementia with Lewy bodies [51]. Incontinence is a dominating feature in normal pressure hydrocephalus which is resulting from detrusor overactivity. Drainage of cerebrospinal fluid has been shown to be associated with an improvement in urinary urgency and incontinence, as well as urodynamic findings [52].

LUT symptoms are commonly reported following stroke. Urinary incontinence 7 days following stroke has been shown to predict poor survival, disability and institutionalization. Urinary incontinence is most often associated with strokes occurring anteriorly. Urodynamic studies in incontinent patients most often demonstrates detrusor overactivity, and in patients with cortical lesions voiding is most often coordinated. Patients with hemorrhagic stroke are more likely to have detrusor underactivity in urodynamic studies [53]. Small vessel disease affecting the subcortical white matter has been shown to be associated with urgency incontinence [54].

5.4. When to suspect an undiagnosed neurological disorder

At times, LUT symptoms may be an early symptom of a yet to be diagnosed neurological disorder and the elderly patient will first be seen by a health care professional specializing in continence rather a neurologist [55]. Elements of the history, clinical assessment and test findings may raise the suspicion for a neurological cause (Table 2).

6. Practice recommendations

Treatment is aimed at improving symptoms and maximizing the quality of life with minimal complications. Conservative treatment options recommended for overactive bladder are applicable and must be offered to all patients before and alongside drug therapy. All drugs carry the risk of adverse events and these risks can be substantially exacerbated by concomitant medications (which often increase the antimuscarinic burden), and concomitant health conditions (such as an increased risk of postural hypotension with alpha adrenergic blockers). There are also concerns regarding the impact on cognition (both short-term, as well as long term dementia) with antimuscarinics and the risk of hyponatremia with the use of desmopressin in the elderly [10,38]. Hence, the underlying philosophy must usually be one of using the minimum number of medicines to alleviate the patient's symptoms. It is also important to remember that up to one-third of men might experience a spontaneous resolution of their symptoms without any therapy, medical or surgical [56].

There needs to be low threshold for neurological evaluation in these men [55]. Geriatric neuro-urological conditions can often accompany or result in LUTS. Failure to identify some of these conditions can result in unsatisfactory outcomes. Suspicion of conditions such as MSA might trigger the need for video-urodynamics.

Clinically, men with storage-dominant LUTS can often be triaged into those without any voiding problems, or those with severe abnormality of voiding after application of non-invasive testing including uroflow, PVR, and void%. The former group of men having a normal flow, low PVR and high void% can often be safely treated along the OAB pathway. The latter group of men, showing poor flow, large PVR and low void% can often go on to bladder outlet obstruction reduction surgery directly, without resorting to invasive urodynamics. However, a substantial group remains where there is either a less severe voiding problem or there are concerns with regard to detrusor contractility.

Table 1
Neuropsychiatric changes occurring in dementia can contribute to storage urinary symptoms.

- •Impaired ability to perceive sensations of bladder fullness
- •Poor coping strategies when presented with unpleasant stimuli
- •Impaired ability to initiate tasks in response to unpleasant endogenous or exogenous stimuli
- •Lack of awareness about incontinence

Table 2
When to suspect an underlying neurological cause when an elderly patient presents with LUT symptoms.

- • LUT symptoms- recent onset, storage+ voiding dysfunction/ urinary retention
- • Other concomitant pelvic visceral dysfunction- eg. new onset slow transit constipation, sexual dysfunction (erectile dysfunction, anejaculation)
- •Urodynamics- detrusor overactivity + Detrusor underactivity
- •Observe the patient during the consultation:
- •Walking into the consultation room- unsteady, requires assistance
- •Handshake- tremulousness, weak grip, cold hands
- •Poor dexterity
- •Do they require the partner's help for simple tasks?
- •Forgetfulness
- •Postural giddiness- grey-outs or black-outs
- •Dryness of the mouth, eyes
- •Poor thermoregulation
- •Cold extremities

It should be possible to stratify most men following urodynamics into one of two groups: those who are candidates for further invasive treatment for refractory OAB, and those that are candidates for bladder outflow resistance reduction surgery (despite their storage-dominant LUTS) [57]. Men with severe or moderate obstruction (BOOI ≥80 or ≥40 respectively), would generally be offered bladder outflow resistance reduction surgery. It might be prudent to offer men with intermediate obstruction (BOOI 20–40) such surgery as well. As mentioned earlier, such men have a good chance of long-term resolution of their storage symptoms. For men who fail to improve, surgery can allow a re-challenge with medication (potentially allowing use of combined OAB medication) as well as enable use of botulinum toxin therapy should patients remain refractory.

Men with a complete lack of obstruction on urodynamics (BOOI <20) and a good detrusor voiding contraction should be candidates for intravesical botulinum toxin therapy. Such men are likely to have a normal uroflow and low PVR. Men with a lack of obstruction on urodynamics and an underactive detrusor voiding contraction are likely to demonstrate slow flow and/or elevated PVR. In such men, the decision is more problematic. These men often have mixed detrusor overactivity with detrusor underactivity and might be at risk of poorer outcomes. Mixed detrusor overactivity with detrusor underactivity has been noted in 12.5% men undergoing urodynamics and can be seen across the age-spectrum, although prevalence rises with age [58]. Botulinum toxin injection in such men might be associated with much higher rates of retention and is perhaps best avoided at the outset, unless the patient is willing to catheterize. There is some potential for improved voiding in these men with bladder outflow obstruction resistance surgery despite the lack of obstruction.[59,60] Improvement in voiding can be associated with some improvement in storage LUTS and might enable a re-challenge with medical therapy [25]. Sacral neuromodulation offers the potential for improvement in both voiding and storage LUTS. However, it might be prudent to address any (even intermediate or 'mild') obstruction before offering such therapy.

7. Conclusions

The management of mLUTS requires good clinical medicine with judicious use of investigations. The underlying philosophy of management is alleviating the patient's symptoms using the minimum number of medicines. Invasive urodynamics are useful before escalation to invasive therapies for refractory storage-dominant mLUTS. There is an urgent need to direct research to answer questions that are fundamental to the management of mLUTS.

CRediT authorship contribution statement

Sanjay Sinha: Concept, Manuscript. **Anne P. Cameron:** Concept, Manuscript. **Vincent Tse:** Concept, Manuscript. **Jalesh Panicker:** Concept, Manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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