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OVERACTIVE BLADDER (U LEE AND S ADELSTEIN, SECTION EDITORS)

Management of Overactive Bladder in the Young Man

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Abstract

Purpose of Review In this review, the current literature regarding idiopathic overactive bladder (OAB) in the young male will be discussed. We will also share the unique experience of providers at a single military institution in treating this specific patient population and their recommendations based on the unique etiologies, comorbidities, and treatment response and adherence.

Recent Findings Despite several studies addressing idiopathic OAB and providing the basis for existing guidelines, none offer guidance on how this syndrome affects a younger male population in whom OAB is less likely to be due to an obstructive etiology, nor is there guidance on the optimal approach to efficient assessment and management in this patient population.

Summary Adherence to the American Urological Association guidelines with more liberal use of adjunctive diagnostic measures with early escalation of therapy when symptoms are not adequately controlled may expedite OAB symptom management more appropriately in young men. Prospective studies focusing on OAB treatment in this patient population are needed to better understand and better treat OAB in this patient population.

Keywords Overactive bladder · Urinary urgency · Urinary frequency · Male lower urinary tract symptoms

Introduction

Lower urinary tract symptoms (LUTS) include a constellation of symptoms that are often divided into three categories based on their temporal relationship in the micturition cycle and include storage, voiding, and postmicturition symptoms. While women are almost exclusively bothered by the storage component of LUTS, men are at risk for symptoms throughout the micturition cycle given the risk for bladder outlet obstruction (BOO) often due to benign prostatic hypertrophy (BPH). Storage symptoms in the male when determined to be independent of an outlet obstruction usually fall within the overactive bladder (OAB) complex.

This article is part of the Topical Collection on *Overactive Bladder*

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The International Continence Society (ICS) defines OAB as a condition characterized by symptoms of urinary urgency, usually accompanied by frequency and nocturia, with or without urge incontinence, in the absence of infection or other pathologies [1]. The overall prevalence of OAB varies by age and sex as well as symptom severity, but has been shown to occur in approximately 11–36% of adults of which 10–27% are men [2–5].

OAB symptoms, especially urinary urgency and nocturia, frequently diminish health-related quality of life (HRQoL) and negatively impact social, psychological, occupational, physical, and sexual aspects of life [6–12]. Men suffering from OAB are more likely to have lower levels of overall health, concomitant mental health diagnoses including anxiety and depression, decreased work productivity, and less sexual satisfaction [7, 10].

Several well-performed studies on the epidemiology, assessment, and management of OAB have been reported and contribute to the current guidelines and practice patterns for this syndrome. However, the population addressed in most of these landmark studies includes men and women greater than 50 years of age. As a result, much less is known about OAB in men in their 3rd and 4th decades of life when storage symptoms are less likely to be due to BPH [13]. In a complex, heterogeneous syndrome like OAB, it is impractical to have a one-size-fits-all approach for its management.

As part of a military health care system, the vast majority of our patient population includes young, healthy males. Although typically considered a disease of the aging and more often afflicting females, we have the unique opportunity to care for young men who suffer from OAB.

In this review, we perform a comprehensive examination of the literature addressing idiopathic OAB in the young male and discuss the nuances that should be considered when treating this patient population. We will also present our experience with the use of sacral neuromodulation in this population.

Literature Review

Search Strategy

The PubMed, Embase, Medline, and Web of Science databases were searched systematically for full text, English language articles and abstracts published between 1998 and 2018 using the query OAB, urge incontinence, male, and young adult. References were manually reviewed to find additional studies of interest. Given our objective to explore idiopathic OAB in young men, we chose men 40 years of age and younger to define our population of interest given the relatively low incidence of LUTS due to BPH in this age group and is consistent with age stratification in previous epidemiologic studies (EPIC) [2, 13].

Selection of Eligible Studies

A single investigator screened all articles. Articles pertaining to neurogenic bladder, BPH, and female patients were excluded. Of the articles screened for management and treatment of idiopathic OAB in the male population, the mean age ranged from 50 to 70 years of age for most articles which were thus excluded. Only one article of the entire search addressed OAB in a mixed male and female cohort with a mean age less than 40 years old [14] (Fig. 1).

Pathophysiology

The pathophysiology of OAB is complex and, although not completely understood, several theories have been proposed.

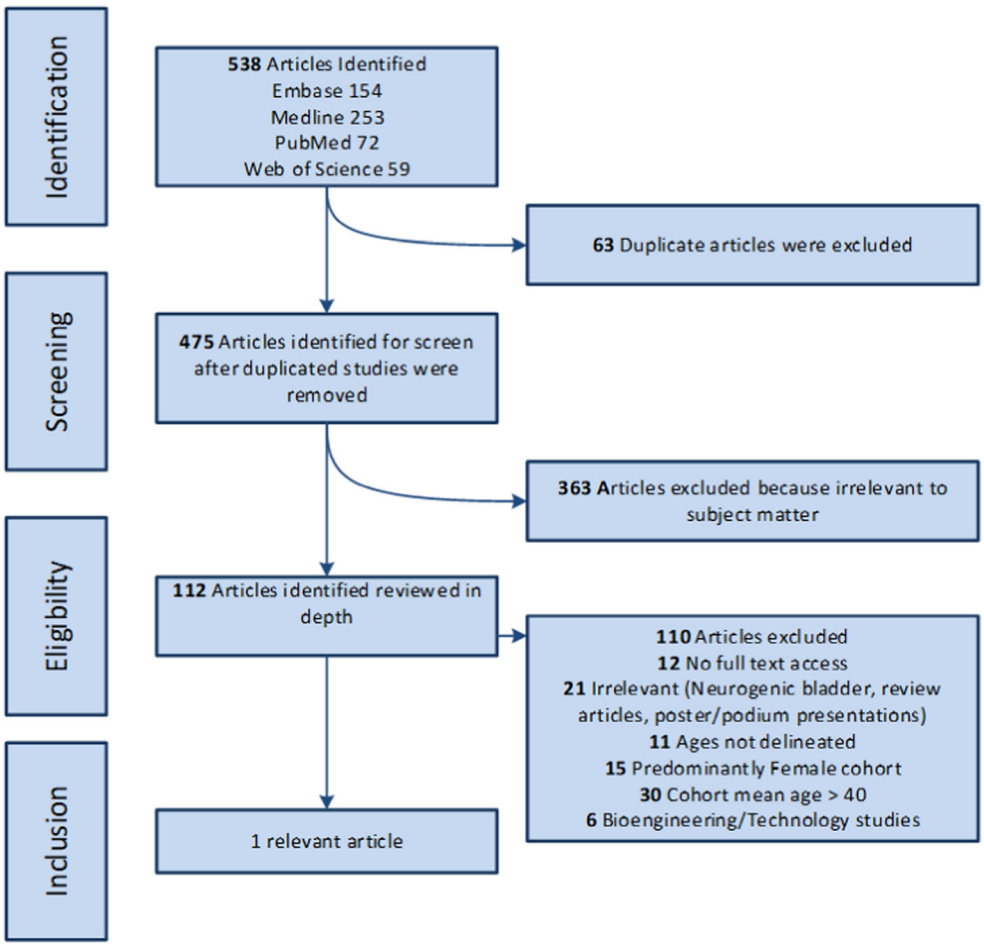

Fig. 1 Literature search results

A neurogenic mechanism suggests that a reduction in inhibitory neural impulses and enhanced excitatory transmission in the micturition reflex pathway along with increased afferent input from the bladder result in OAB symptoms [15, 16]. The myogenic theory, which applies mostly to patients with bladder outlet obstruction (BOO), suggests that chronic rises in intravesical pressure result in partial denervation of the bladder smooth muscle; this denervation causes an increase in spontaneous action potentials resulting in small detrusor contractions and increased intravesical pressures which then sends messages back to the central nervous system (CNS) causing the sensation of OAB [16]. The autonomous bladder theory suggests that detrusor overactivity results from overexpression of excitatory peripheral autonomic nerves causing increased sensory awareness as the bladder fills resulting in early detrusor contractions [17]. Lastly, an afferent signaling theory proposes that non-synchronized detrusor contractions occurring during bladder filling may result in increased afferent output to the CNS with subsequent OAB symptoms [18].

Assessment

In 2014, the American Urological Association (AUA) and Society of Urodynamic, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) published clinical guidelines for the diagnosis and treatment of non-neurogenic OAB and is the current basis for which urologists approach this symptom complex [19].

History and Physical Exam

The assessment of OAB in the young male starts with a comprehensive history. Baseline bladder storage and voiding symptoms along with symptom severity are elicited and recorded using a symptom scoring mechanism such as the AUA symptom score. Medical comorbidities with review of current medications and surgical history should be discussed with consideration of possible contributions to their bladder symptoms.

In addition to the history described above, we inquire about childhood voiding dysfunction. A history of painful urination, urinary retention, urinary frequency (or infrequency), incontinence, enuresis, and holding maneuvers as well as any subsequent intervention (successful and unsuccessful) should be elicited. Although frequently assessed in the pediatric population, a history of constipation in an adult presenting with LUTS is not as dogmatic. However, because this population may include now adult childhood dysfunctional voiders, we verify healthy bowel habits and treat constipation if present. Even in the absence of childhood voiding dysfunction, eliciting a history of constipation is relevant as medical management of OAB can cause or worsen constipation as will be addressed below.

Occasionally, we have men present with nocturnal enuresis along with daytime OAB symptoms. Some of these men have never achieved consistent continence at night, whereas others experience a return or worsening of their nocturnal enuresis symptoms after exposure to an acute stressor—often boot camp in our population. Although infrequently encountered, it is important to screen for nocturnal enuresis in this population presenting with OAB not only because it may be uncomfortable for the patient to initiate this discussion but also because it can influence future management.

Unique to this population, it is also important to elicit a history of physical, psychological, or sexual trauma. The onset of LUTS after stressful exposure has been well established in multiple animal models [20, 21]. Furthermore, the association of OAB with post-traumatic stress disorder (PTSD) and other mental health diagnoses is well reported, often with a bidirectional relationship where an exacerbation of one symptom set can adversely affect the others [22, 23, 24•, 25•]. Several of our patients who have required third-line management also carry a mental health diagnosis. It is important to inquire about these diagnoses, educate the patient of the correlation between OAB and mental health disorders, and ensure patients are getting appropriate mental health care in order to most effectively treat their OAB symptoms.

Lastly, the degree of bother and the impact of LUTS on other domains of life (physical, mental, sexual, and social well-being) should be assessed. These men are often otherwise healthy with their OAB symptoms being the sole contributors to and negatively impacting their HRQoL. OAB can interfere with work, social relationships, and sexual function—all of which are extremely important in this age group. In the military, some of our patients cannot stand certain duties if they frequently require a relief to use the bathroom, which can ultimately lead to job disqualification and negatively impact future promotion. An Active Duty member distracted from his post because of his LUTS poses a security threat. Other occupations, including pilots and surgeons, place similar demands on men where they cannot easily nor safely make frequent bathroom breaks. For a young man with professional aspirations, this can be extremely stressful.

A focused physical exam should be performed next. A genitourinary exam should assess for meatal stenosis, scars, masses, hernias, and urinary distention [26••]. Although a patient may deny such surgical history, the presence of penile scars or a narrow urethral opening may suggest a prior hypospadias repair with subsequent stricture or fistula formation resulting in inadequate bladder emptying and new OAB symptoms in a young man.

Laboratory Studies and Adjunctive Tests

After the history and physical exam, adjunctive tests are performed. We adhere to AUA guidelines for OAB assessment in

young men with a few nuances. Urinalysis, urine culture, and post void residual (PVR) are routinely checked to rule out infection, hematuria, and urinary retention. Although a great tool for assessment and symptom management, we find that most young men are unable or unwilling to complete an accurate bladder diary. Carrying a urinal for volume recording is not practical during the work or school week nor during the weekend for most of these men. This is distinct from our older female population who often present with a highly detailed bladder diary.

Although not routinely used in an older patient with LUTS and OAB, we commonly use adjunctive diagnostic tools early in the assessment of our younger male population. LUTS secondary to obstructive causes must be discerned prior to initiating management for OAB. To do so, we obtain a uroflow with a PVR to rule out incomplete emptying. If the uroflow is inconclusive, we may consider proceeding with a cystoscopy and/or retrograde urethrogram to further assess for an anatomic abnormality. Although BPH does not play a significant role in LUTS for this population, an elevated bladder neck detected on cystoscopy could contribute to incomplete bladder emptying and OAB symptoms similar to LUTS associated with BPH. In these cases, we have had men undergo incision of the bladder neck with marked improvement in both obstructive and storage symptoms; this is performed only after a thorough discussion of the possible associated surgical risks with emphasis on the risk of retrograde ejaculation is completed. Urethral stricture disease resulting in LUTS is not uncommon in this population vulnerable to urethritis and urethral or perineal trauma. Distinction of this pathology with the above adjuncts is critical as the treatment for OAB can worsen symptoms due to stricture disease.

Multi-channel filling cystometry with pressure flow studies is used judiciously in young men with OAB and reflect the AUA/SUFU adult urodynamics (UDS) guidelines [27•]. These studies are typically obtained to determine the presence of abnormal bladder compliance, detrusor overactivity, detrusor external sphincter dyssynergia (DESD), or elevated voiding pressures prior to performing any morbid or irreversible treatment which may not maximally benefit patients. For example, dysfunctional voiding demonstrated by pseudo DESD on UDS is best managed with PFPT. Without UDS, this diagnosis would be difficult to make and can result in inappropriate escalation of treatment when first-line therapy with PFPT is most effective in this patient. UDS can also diagnose functional urinary obstructions with findings of elevated voiding pressures and decreased urinary flow; this in turn can prompt the provider to perform further diagnostic studies to evaluate for an anatomic obstruction as described above or can confirm an obstructive etiology as the cause of LUTS when other tests are equivocal. Because the diagnosis of an elevated bladder neck on cystoscopy can be subtle and difficult to anatomically discern with certainty, we often use UDS to confirm a functional obstruction in these patients prior to recommending surgical treatment.

In addition to the above criteria, we often use urodynamic studies early in the assessment of young men with urinary incontinence. This is distinct from our older population in whom a degree of urinary incontinence will be tolerated as management is titrated for optimal symptom control with UDS reserved for patients with refractory symptoms. In younger men, however, urinary incontinence to any degree is concerning for underlying pathology and can cause severe stress to the patient. For these reasons, we feel a more aggressive evaluation with early UDS may hasten symptom control and is thus justified.

Lastly, the absence of concerning findings on UDS such as the presence of detrusor overactivity does not necessarily exclude its existence and thus does not prevent us from recommending further therapy [27•].

Management

When managing OAB in the young male, noninvasive treatment strategies should be implemented and exhausted before introducing more invasive strategies as outlined in the AUA guidelines. Furthermore, prior to starting any treatment, it is critical that patient education on the natural history of OAB ensues and appropriate expectations and treatment goals are established early.

Non-Pharmacological Treatment

First-line treatment for OAB includes therapies aimed at modulating patient behavior or environment to improve symptoms [19]. We explore all aspects of the young male's life for consideration for changes that may impact their symptoms. Tobacco cessation, weight loss, dietary and fluid intake modifications, bowel regulation to prevent constipation, and routine exercise can mitigate symptoms [28, 29]. Decreased fluid intake or cessation in the hours preceding bedtime should be implemented for patients with bothersome nocturia. Excessive caffeine intake via coffee, energy drinks, etc. as well as other bladder irritants should be elicited during the history followed by patient education and goals to reduce their intake.

Bladder training is another first-line treatment option where OAB symptoms are mitigated by modifying bladder function. Patients void at regular intervals despite earlier voiding urges with the intention to increase bladder capacity and thus decrease urinary frequency. Voiding intervals can initially be as short as 30 min with gradual incremental increases to achieve control of 3–4 h. Although bladder training offers a non-pharmaceutical treatment option with no adverse side effects, we find that this is rarely a practical management strategy in young men. Our Active Duty patients are often in environments where toilets are not easily accessible or are standing

watches that cannot be vacated to urinate. Similar occupational constraints are placed on an executive during a long meeting, a surgeon in the operating room, a college student in a seminar, etc. In these situations, the frequent interruptions that are required for bladder training or timed voiding are not a realistic option, and so more aggressive therapy may be considered first.

Pelvic floor physical therapy (PFPT) focuses on the bladder outlet and urge suppression. Patients are taught to contract the pelvic floor muscles during involuntary detrusor contractions which can lead to decreasing episodes of urgency and urge incontinence [30].

Pharmacological Treatment

Pharmacological therapy is second-line in OAB treatment and can be used in conjunction with behavioral therapy.

Anticholinergic (i.e., antimuscarinics) medications are the most common class of drugs used in the treatment of OAB. Detrusor relaxation occurs through competitive inhibition of muscarinic receptors at the neuromuscular junction of parasympathetic nerves innervating the bladder as well as inhibition of afferent urothelial receptors [31]. Dry mouth and constipation are the most common and bothersome side effects [32]. Unfortunately, the side effect profile of these medications often outweighs their perceived benefit with discontinuation rates reported to be 43–83% in the first 30 days of treatment and more than 50% of patients quitting during the initial prescription [33].

Mirabegron, a β-3 adrenergic receptor agonist which enhances detrusor muscle relaxation, was approved by the FDA in 2012 for the treatment of OAB. Multiple systematic reviews demonstrate this drug to be as effective as antimuscarinic therapy at reduction of OAB symptoms with fewer bothersome side effects [34–36]. The most common potential dosage-dependent side effects include hypertension and arrhythmia; however, this medication is generally well tolerated [34].

In patients interested in pharmacological treatment, we typically start with an extended release anticholinergic medication. If symptoms are not sufficiently reduced after an adequate trial, we may consider augmenting with mirabegron to maximize conservative treatment in this population without evidence of BOO and concern for urinary retention. If the anticholinergic initially used is poorly tolerated, we will consider trying a different anticholinergic medication as heterogeneity in response to this drug class is well established [37–39].

Poor compliance with these medications has been widely reported and this certainly holds true for this population. Compared with our female or older male patients, we find that our younger male patients with OAB are less likely to complete an adequate trial of medication, are more bothered by the side effects, and often fail to follow-up for prescription renewal.

Third-Line Treatment

Third-line treatment and referral to a urologist should be initiated in patients with symptoms refractory to first- and second-line management, in patients who cannot tolerate pharmacological therapy, or for whom first- or second-line therapy is inappropriate.

Onabotulinumtoxin A (Botox) cystoscopic detrusor injections were FDA-approved in 2013 for treatment of refractory OAB. Botox blocks the release of acetylcholine at the neuromuscular junction of nerves innervating the detrusor muscle, thereby decreasing detrusor contractility while also causing atrophy of muscle at the injection site. Side effects include urinary tract infections and urinary retention; patients must be educated on this and be willing and able to perform clean intermittent self-catheterization (CIC) in the event temporary retention ensues.

Neuromodulation via intermittent peripheral tibial nerve stimulation (PTNS) or continuous sacral nerve stimulation (SNS) is another option for refractory OAB. Electrical stimulation of sacral nerve roots or peripheral nerves has been shown to modulate afferent detrusor nerve signaling leading to symptom relief [40–42]. PTNS is usually performed over the course of 3 months on a weekly basis through a small needle inserted into the tibial nerve for about 30 min per session. With SNS, an impulse generator is implanted in the operating room. This is typically performed as a staged procedure where a temporary percutaneous generator is implanted for one week first to confirm symptom control prior to implanting the permanent generator. Both therapies are generally well tolerated with minimal side effects. However, it is important to note that the use of MRI is FDA-approved only for 1.5 Tesla (T) head scans with the most current model of InterStim™, and so a thorough history eliciting the possible need for future MRI should be taken. Additionally, patients should be counseled that SNS is not FDA-approved for scuba diving below 30 ft of water as it has not been tested in environments greater than 1 atmospheric pressure.

Our Experience with SNS

Twenty-three patients who were males less than 40 years of age were implanted with the InterStim™ System from 2015 to 2019 at a single institution. All patients except for one had a staged procedure. Test stimulation success was defined as at least 50% improvement in symptoms from baseline based on patient reporting. Those with successful symptom improvement were implanted with the neurostimulator. One patient underwent a single stage redo implantation due to suspected lead migration from the initial procedure; this was not staged given successful results from the previous implant.

Table 1 lists baseline demographics. The average age at the time of implant was 31.6 (± 6.7) years. Most patients were Caucasian and married. Urinary urgency, urinary frequency,

Table 1 Baseline demographics

No. of patients	23	
No. of race (%)		
Caucasian	11	(47.8)
Black	4	(17.4)
Asian or PI	2	(8.7)
Other	6	(26.1)
Mean ± SD age at implantation	31.6 ± 6.7	
No. of LUTS (%)		
Urgency	21	(91.3)
Nocturia	21	(91.3)
Frequency	21	(91.3)
Urge incontinence	11	(47.8)
Enuresis	4	(17.4)
Previous LUTS therapy (%)		
PFPT	2	(8.7)
Anticholinergic	22	
> 1 anticholinergic	8	(34.7)
Mirabegron	3	(13.0)
Hydrodistension	2	(8.7)
Alpha adrenergic blocker	5	(21.7)
PTNS	8	(34.7)
Transurethral incision prostate	1	(4.3)
Cystometry and pressure flow findings (%)		
DO	15	(65.2)
Obstructive voiding pattern	3	(13.0)
Marital status (%)		
Married	15	(65.2)
Single	5	(21.7)
Divorced	0	(0)
Unknown	3	(13.0)
Medical comorbidities (%)		
Mental health diagnoses (depression, anxiety, PTSD)	10	(43.4)
Musculoskeletal pain	5	(21.7)
Chronic pain	2	(8.7)
Gastrointestinal issues (GERD, constipation)	4	(17.4)
Obstructive sleep apnea	4	(17.4)
Hypertension	2	(8.7)
Hyperlipidemia	1	(4.3)
Erectile dysfunction	2	(8.7)
Hypothyroid	1	(4.3)
Atrial fibrillation	1	(4.3)

and nocturia were equally reported occurring in almost all patients. Eleven patients experienced urge incontinence. Four patients reported enuresis. All patients underwent urodynamic studies prior to implantation. Fifteen patients (35%) demonstrated detrusor overactivity on UDS. The most common comorbidity in this group was a mental health diagnosis followed by a diagnosis of musculoskeletal or chronic pain.

All patients except for one had a trial of at least one anticholinergic medication with eight patients having tried more than one. Anticholinergics were avoided in one patient diagnosed with idiopathic neurogenic bladder with inadequate bladder emptying on UDS and was primarily treated with SNS. Alpha adrenergic blockers were used in three patients in whom a BOO was suspected. One of these patients underwent a transurethral incision of the prostate for cystoscopic concern for anatomic obstruction. Two patients with dysfunctional voiding patterns completed a trial of PFPT. Finally, eight patients had a trial of PTNS prior to SNS.

InterStim™ implant was safe and effective. One patient experienced a wound infection that was treated with oral antibiotics and did not require device explant; no other complications were reported. One patient required device explant to obtain an MRI. Symptom improvement was noted in all patients at the time of the last clinic follow-up.

Discussion

Although the epidemiology, assessment, and management of OAB in older adults are well described in the literature, an exhaustive literature review was performed confirming that no such studies exist for young men with this symptom complex. As such, we reviewed our current practices with treating OAB in men less than 40 given our unique opportunity to care for these patients within a military health care system.

The AUA/SUFU guidelines on non-neurogenic OAB and adult urodynamics are followed during the assessment and management of this population with some nuances. Inquiry into a history of childhood voiding dysfunction as well as any previous trauma exposure should be made, as well as the specifics regarding their urinary complaints. Additionally, the degree of symptom bother and any collateral adverse effects on quality of life should be elicited. When a history of any of the above is present and/or the patient's HRQoL is severely affected, we tend to be more fastidious and aggressive during the assessment and management.

During the evaluation, adjunctive tests to include uroflow with PVR, cystoscopy, and retrograde urethrogram are frequently used to rule out an obstructive cause of their LUTS. Urodynamic studies are used to diagnose a functional

obstruction and assess for detrusor overactivity when the diagnosis is equivocal or in the setting of urinary incontinence.

Noninvasive treatment strategies should typically be initiated first with progression to more invasive and potentially morbid treatment strategies if symptoms are not adequately controlled. However, occupational or social considerations may exist that favor deviation from this algorithm. Furthermore, we find these patients are notoriously noncompliant with medications due to poor symptom control, intolerable side effect profile, or failure to follow-up for prescription refill. In these scenarios, we may consider starting with a more aggressive treatment strategy if we think it will improve patient compliance and symptom management.

Patients requiring third-line management are offered and thoroughly counseled on the benefits and side effect profiles of Botox, PTNS, and SNS. We often found that young men were uninterested in PTNS due to the weekly time commitment and subsequent maintenance therapy schedule. Additionally, in our experience, most men were reluctant to accept the low risk of urinary retention and potential need for CIC that may occur with intravesicular Botox injections. SNS, however, despite being viewed as a more invasive treatment option requiring a surgical incision, in our limited experience, was more frequently chosen by the patient in this age group for third-line management.

This review should be considered in the context of several limitations. Given the lack of existing data, the recommendations discussed here represent the experience of urologists at a single institution in treating a relatively small number of patients fitting the population of interest. Given this, along with the complexity of the OAB syndrome, our recommendations may not be generalizable. In addition, the chart review performed was retrospective and thus carries inherent limitations. Specifically, the definition of success for an InterStim™ trial was based on patient reporting as opposed to a more rigorous reporting method such as a voiding diary. Urodynamic studies were not available for review in all patients; in those missing, descriptions of the study results in the medical record were used. Patient followed-up varied likely reflecting patient relocation within the military or separation from the military.

Future work to define the epidemiology and prevalence of OAB in this population would be useful. Prospective studies comparing the efficacy of various treatment modalities as previously performed in older patients would help determine how this syndrome can be best managed in these young men. Finally, given this population's vulnerability to mental health disease, a prospective study comparing the effects of OAB treatment on overall mental health would be valuable.

Conclusion

Little is known about OAB in men less than 40 years old. This population is often severely negatively impacted by their symptoms and concomitant mental health diagnosis is common. The AUA guidelines are adhered to for assessment and management with some nuances; a slightly more aggressive evaluation with adjunctive tests is used to expedite evaluation and ultimately symptom control.

Compliance with Ethical Standards

Conflict of Interest Dr. Herforth and Dr. McLain declare that they have no conflict of interest. Dr. Choe participates as a Center of Excellence on behalf of Medtronic for the implantation technique of SNS. The US Navy, Naval Medical Center San Diego, and Dr. Choe cannot and do not accept any financial gains or fees for participation as a Center of Excellence.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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