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Journal
Current Urology Reports, 19(11)

ISSN
1527-2737

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Publication Date
2018-11-01

DOI
10.1007/s11934-018-0845-5

Peer reviewed

HHS Public Access

Author manuscript

Curr Urol Rep. Author manuscript; available in PMC 2019 July 30.

Published in final edited form as:

Curr Urol Rep. ; 19(11): 92. doi:10.1007/s11934-018-0845-5.

Management of Overactive Bladder in Older Women

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Abstract

There are many unique challenges and complexities associated with the management of overactive bladder in older women. Although treatment guidelines that provide a framework for the management of overactive bladder in adults exist, there are limited recommendations on clinical factors (i.e. frailty, functional and cognitive impairment, multimorbidity, polypharmacy, estrogen deficiency, and remaining life expectancy), which impact symptom management in older women. This review will highlight our current understanding of age-related changes in bladder function and propose important clinical considerations in the management of overactive bladder specific to older women.

Keywords

frailty; elderly; pharmacotherapy; botox; sacral neuromodulation; geriatric syndromes

Introduction

Overactive bladder (OAB) is a symptom complex that affects over 45% of women ages 65 and older [1]. Defined as urinary urgency (with or without urinary incontinence), frequency and nocturia, OAB in older women is associated with an increased risk of falls, hip fractures, anxiety/depression, and social isolation, all leading to a significant reduction in quality of life [2,3]. OAB also carries a significant economic burden with societal costs totaling over $14 billion in older women [4].

While treatment guidelines that clearly define appropriate first-, second-, and third-line treatment strategies for OAB exist [5, •6], there are reasons to believe that these guidelines reflect more of a “one size fits all” model that may not be appropriate for use in all older adults. For example, older women with special considerations such as frailty, poor functional status, cognitive impairment, multimorbidity, polypharmacy and estrogen deficiency may respond differently to certain therapies or experience a higher rate of treatment related side effects compared to younger women. This review will summarize our current understanding

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of age-related changes in bladder function and will highlight unique clinical considerations for the management of overactive bladder in older women.

Age-related changes in bladder function

Aging induces neurologic, anatomic, and biochemical alterations to bladder function which can predispose to the development of OAB symptoms (Figure 1.) Functional brain-imaging (fMRI) studies in older women have illustrated increased activation of the dorsal anterior cingulate cortex (dACC) associated with heightened sensory perception of urinary urgency. [7, 8]. Bladder ischemia, commonly induced by atherosclerosis in older individuals, can cause nerve injury and smooth muscle damage leading to detrusor overactivity, as well as impaired contractility. [9]. Stretch induced non-neuronal release of acetylcholine (ACh) and adenosine triphosphate (ATP) from the detrusor muscle has been shown to be altered with increasing age. When compared to younger individuals, patients ages 65 and older release roughly three times the amount of stretch-induced ACh, which contributes to detrusor overactivity [10]. Similarly, inflammatory mediators released from the urothelium can trigger bladder contractions potentially independent from neurologic control, resulting in increased urgency and frequency.

Estrogen receptors have been identified in the squamous epithelium of the urethra, bladder urothelium, and pelvic floor musculature [11–13]. Estrogen directly affects detrusor function through modifications in muscarinic receptors and inhibition of calcium ions into muscle cells. Estrogen deprivation following menopause has been associated with increased basal and stretch-induced ACh release, urothelial damage, and muscular atrophy. Thus, postmenopausal women often have reduced bladder capacity, impaired detrusor contractility, and decreased urine flow rates predisposing them to OAB symptoms [•14].

Clinical considerations for older women with OAB

Older women are a heterogenous group and can embody several unique factors that should be taken into consideration during the workup and management of OAB (Figure 2). Age alone is not a good measure of individual functionality and well-being. Rather, factors such as frailty, functional impairment, cognitive impairment, multimorbidity, polypharmacy, postmenopausal estrogen status, and remaining life expectancy, more accurately depict overall health more than age alone. Thus, when evaluating and managing OAB symptoms in older women a boarder, more holistic focus is recommended to incorporate the complexities within this population.

Frailty

Frailty is a decline in physiologic reserve that leads to increased susceptibility to adverse events. The phenotypic definition of frailty is met when three or more of the following criteria are present: weakness based on grip strength, slow walking speed, low physical activity level, low energy or self-reported exhaustion, and unintentional weight loss [15, 16]. The presence of frailty and OAB have both been shown to increase with age. In one study, frailty, as measured by the Timed Up and Go Test (TUGT), was significantly associated with a diagnosis of OAB (when adjusted for age) among older adults presenting to an academic

non-oncologic urologic practice. Age (when adjusted for frailty), on the other hand, was not significantly associated with a diagnosis of OAB. This finding challenges our prior understanding that OAB is an age-related condition, suggesting that frailty may have a more significant and dynamic association with OAB than age alone. [17].

In addition to frailty being associated with a diagnosis of OAB, frail older adults are known to be at heightened risk of nighttime falls, making it particularly dangerous for them to get up at night to void. A study of frail older adults demonstrated that 27% of falls occur at night, with more than half (54%) related to toileting [18]. With this in mind, frail older adults with OAB symptoms have a higher risk of morbidity when compared to asymptomatic older adults, making proper diagnosis and management of frailty a health priority. Given the clinical implications, a frailty assessment should be considered in the evaluation and management of OAB and frail older adults should be considered to be at a heightened risk of falls.

Functional impairment

Functional impairment pertains to medical and/or physical ailments which can interfere with a person's ability to perform basic activities of daily living (ADL) such as transferring, dressing, bathing, eating, toileting, and continence. Patients may also exhibit deficits with instrumental activities of daily living (IADL) such as managing medications, managing money, shopping for groceries or personal items, performing housework, doing laundry, and using the telephone, all of which require more complex thinking skills. Impairment of ADLs among older women with OAB can compromise safe transfers to the restroom, again increasing their fall risk. Difficulty with grooming and self-care can affect hygiene management in the setting of incontinence, increasing potential morbidity and diminishing quality of life. Pharmacotherapies for OAB, specifically anti-muscarinics, can cause blurred vision or dizziness, further hindering safe mobility. Patients may also have difficulty making it to OAB therapy/treatment appointments. To ensure patient safety and improve treatment compliance, a baseline assessment of functional status and support is important when selecting an OAB treatment option. A patient's ability to dress independently is a quick and simple way to assess motor skills related to toileting habits and can be easily incorporated in standard OAB evaluation in older adults [5].

Cognitive impairment

The national prevalence of dementia (including Alzheimer's disease) among women ages 71–79 years is roughly 5%, with more than a five-fold increase at age 80 years and older [19]. Mild cognitive impairment and dementia have been associated with deficits in IADLs. [20, 21]. Older women with OAB and cognitive decline may have difficulty with articulating the presence and impact of their symptoms. They may also have a harder time understanding the treatment plan or adhering to recommendations. For example, behavioral therapies such as bladder and pelvic floor muscle training, require a level of comprehension and active patient participation which may be limited in patients with cognitive deficits. Managing OAB medications may also be an issue leading to noncompliance. Lastly, procedures for OAB including percutaneous tibial nerve stimulation (PTNS), sacral neuromodulation, and intra-detrusor onabotulinumtoxinA require informed consent and patient feedback to assess

clinical improvement, aspects which may be difficult to obtain depending on one's cognitive status.

Multimorbidity

Multimorbidity, the presence of two or more chronic medical conditions, is associated with aging and can affect both the development and management of OAB symptoms. The average geriatric patient with OAB is likely to have 3 to 5 concomitant diseases [22], with diabetes, hypertension and hyperlipidemia being most prevalent. Among poorly controlled diabetics, prolonged hyperglycemia can induce oxidative stress causing damage to the detrusor muscle and bladder innervation [23, 24]. Women can subsequently develop diabetic cystopathy described as a triad of decreased bladder sensation, increased bladder capacity, and poor bladder emptying, all of which can exacerbate pre-existing OAB symptoms [24]. In addition to optimizing glucose control, recommended management of diabetic cystopathy coincides with OAB guidelines.

Conditions requiring careful monitoring of fluid volume such as hypertension and congestive heart failure are of great importance in OAB management, as certain medications such as diuretics and/or alpha blockers can counteract the efficacy of OAB treatment. For instance, an older woman with bothersome nocturia and on a diuretic for hypertension may be better served taking the diuretic in the morning instead of the evening in an effort to decrease night time voiding due to medication induced diuresis. Compression stockings, ambulation (if able), and elevation of feet above the level of the heart during the day are also recommended to assist in fluid mobilization which can help decrease OAB symptoms, particularly at night.

Neurologic diseases such as cerebrovascular accidents, Parkinson's disease (PD), and multiple sclerosis are also important to consider, as these conditions significantly contribute to OAB symptom presence and severity. All conditions can confound effective treatment due to the imposed functional limitations and concerns with drug interactions. Specific to PD, cholinesterase inhibitors (ChIs), such as donepezil, are the predominate treatment drugs used in older women. Concomitant use of a ChI with an anti-muscarinic medication is cautioned as it can diminish ChI therapy and potentially exacerbate cognitive decline. In a 2011 retrospective study on concomitant use of ChI and anti-muscarinics in older adults, 64% of concomitant users were women with a mean age of 79 years. [25]. Thus, in this subpopulation, lifestyle modifications and third-line therapies may be preferred over pharmacotherapy.

Constipation is another common condition among older women and can worsen OAB symptoms due to overlapping neural pathways between the bowel and bladder, in addition to a pressure effect of a dilated sigmoid colon on the bladder. A study assessing the association between OAB symptom severity and chronic constipation in women older than 40 years of age demonstrated that women with chronic constipation had four times the odds of reporting moderate to severe OAB symptoms [26]. Alleviation of constipation through diet modification and pharmacotherapy can significantly improve urinary frequency and urgency and is thus advised.

Lastly, older persons have a higher prevalence of visual and hearing impairment, dementia, and falls, all of which are independently associated with urinary incontinence and conditions which can complicate effective health care management. For frail older women with multiple comorbidities and shared risk factors, co-management with a geriatrician is recommended to improve treatment efficacy and safety.

Polypharmacy

Polypharmacy affects approximately 40% of older women and is a significant health concern given the risk of severe adverse events [27, 28]. Drugs commonly prescribed to older women can alter normal bladder function, worsen OAB symptoms, or adversely interact with standard OAB pharmacotherapy. Certain drugs used in combination can also alter drug bioavailability and metabolism. The Beers Criteria for Potentially Inappropriate Medication Use in Older Adults are a set of guidelines to help guide prescribing practices to reduce polypharmacy and its associated risks [29]. A detailed review of the patient's medication list and co-management with their primary care physician and/or geriatrician is advised prior to prescribing OAB medications especially in high risk individuals.

Estrogen deficiency

Hypoestrogenism causes urogenital atrophy and is associated with urinary urgency, frequency, nocturia, incontinence, and recurrent urinary tract infections in postmenopausal women. Previous studies have implicated estrogen deficiency as a trigger for lower urinary tract symptoms, with 70% of women relating the onset of urinary incontinence with their final menstrual period [30].

Estrogen use for the management of OAB symptoms has been investigated. In animal models, estrogen receptor activation reduced the amplitude and frequency of spontaneous rhythmic detrusor contractions [31, 32]. Estradiol has been shown to suppress inflammatory cell infiltration and reverse bladder atrophy by way of vascular endothelial growth factor; findings which support the therapeutic properties of estrogen (33, 34]. Although systemic estrogen therapy has been associated with worsening incontinence, low dose vaginal estrogen has been shown to decrease heightened bladder sensory activity resulting in improved urinary urgency, frequency, and bladder capacity [11]. In clinical trials, use of vaginal 17β-oestradiol tablets (Vagifem) decreased OAB symptoms and improved urodynamic parameters including cystometric capacity, strong desire to void, and reduction in uninhibited detrusor contractions [35, 36]. The synergistic effects of anti-muscarinics and vaginal estrogen have also been investigated with conflicting results [37–39].

Local estrogen therapy including vaginal estrogen cream, vaginal tablets or the ring is recommended for urogenital atrophy and its use among women with OAB may be beneficial in combination with other recommended treatment options [•14, 40]. Low dose vaginal estrogen is currently not included in national guidelines for OAB and is not standard of care. However, given previous findings and the known physiologic effects of estrogen in the lower urinary tract, further research is warranted.

Life expectancy

As of 2016, the average female life expectancy in the United States is 81.1 years, a 0.2-point drop from 2014 with a slight increase in age-adjusted death rates from Alzheimer's disease and unintentional injury [41]. Quality of life is often prioritized among those with limited life expectancy whether due to medical illness or due to natural age progression. Given the impact of OAB on quality of life, knowledge of life-expectancy may influence treatment decisions and can be calculated using easily accessible online prognostic tools (www.eprognosis.ucsf.edu). Remaining life expectancy calculators and life tables have clinical utility among frail older women with OAB, especially given its shared burden with other chronic medical conditions. Such tools can be used to help weigh the pros and cons of more invasive OAB treatment modalities especially among older women in which the standard OAB algorithm may not apply.

Treatment for OAB in Older Women

Current management guidelines for OAB serve to provide evidence and consensus-based treatment options, with the best approach guided by the clinician and patient. The hierarchy of current therapies is based on the invasiveness of the treatment and potential for adverse events. Few specific guidelines for the management of OAB in older women exist and current guidelines largely represents a "one size fits all" approach. Table 1 depicts the current American Urologic Association and Society of Urodynamics, Female Pelvic Medicine, and Urogenital Reconstruction (AUA/SUFU) guidelines on treatment of non-neurogenic OAB in adults and is augmented with our proposed modifications for use in this special and potentially vulnerable population of older women.

First-line treatment: behavioral therapies

First-line treatments consist of behavioral therapies with the aim of reducing urinary frequency and increasing bladder volume. Behavioral therapies include bladder training (timed voiding, urge suppression techniques), fluid management, and pelvic floor muscle training (PFMT). In our opinion, a patient's level of frailty, functionality, and cognitive status (a factor currently included in AUA/SUFU guidelines in the discussion of second-line therapy) should be considered when recommending behavioral therapies. For example, a frail older woman with functional limitations may have difficulty with timed voiding since she may not be able to safely transfer to the restroom every three hours. Women with cognitive impairment may require active involvement of their caregiver for prompted voiding or assistance with fluid management. The clinician is encouraged to ask about patient ADLs and IADLs in addition to the patient's home environment and level of caregiving and/or support available, in an effort to achieve success with behavioral therapies in the face of such limitations.

Physical activity has been investigated as a way to help overcome functional limitations. Increased physical activity alone, or combined with behavioral therapies, has been shown to reduce incontinence episodes in older persons by way of improving mobility and functional independence [42–45]. A study of frail older women (mean age 85 years old) without dementia demonstrated a reduction in incontinence episodes by 50% after undergoing a 12-

week combined physical and behavioral therapy urinary incontinence program [46]. With this in mind, increased physical activity should be encouraged especially among frail older women with OAB.

PFMT involves intentional contraction of the pelvic floor muscles to suppress detrusor overactivity and strengthen urethral support, helping to decrease urine loss associated with urgency. Controlled trials on urge suppression using PFMT alone have shown reductions of incontinence ranging from 60 to 80% [47]. However, these methods require continued motivation and effort by the patient and/or caregiver. Even functionally intact older women with urgency urinary incontinence who are compliant with PFMT have illustrated treatment failure in part due to impaired cortical activation of the brain region responsible for bladder control [48]. This highlights the impact of age-related physiologic changes that can compromise symptom improvement with behavioral therapies alone.

Clinicians should also encourage older women to optimize comorbid conditions which can exacerbate OAB symptoms and preclude success with behavioral therapies. This may involve active discussion between the patient, caregiver, and primary care provider or geriatrician. Fluid restriction should also be cautioned in frail older women, due to the increased risk of mortality and disability associated with dehydration [49].

Second-line treatment: oral anti-muscarinics or β3-adrenoreceptor agonist

Oral anti-muscarinic (also known as anti-cholinergic) therapy has been the mainstay for OAB management but presents a challenge in older women due to the risk of polypharmacy, increased side effects, and medication noncompliance. The guidelines outline that common medications such as warfarin, ranitidine, digoxin, codeine, and diazepam have anti-muscarinic properties, increasing the anti-muscarinic load and risk of side effects if used concomitantly with OAB medications. Current guidelines also caution against prescribing anti-muscarinics in patients using other medications with similar properties. Table 1 includes a list of additional commonly prescribed medications to consider.

A higher anti-muscarinic load can predispose older patients to cognitive decline, dementia, and delirium [50–53]. Anti-muscarinic risk scales (referred to as anti-cholinergic risk scales in the literature) have been developed for research and clinical use in an effort to quantify the anti-muscarinic burden. Currently, the Anti-cholinergic Cognitive Burden (ACB) scale, a four-point system developed using published data and expert opinion, is the most frequently validated anti-cholinergic scale on adverse outcomes [54, 55]. This scale, among others, has potential for clinical application in older women when considering the risks and benefits of medication management for OAB.

AUA/SUFU guidelines for OAB caution against prescribing medications in frail older women, given the risk of progression to mild cognitive impairment and/or Alzheimer disease. Additionally, depending on the level of cognitive impairment, use of anti-muscarinics in patients with dementia may also be contraindicated. The guidelines recommend obtaining a baseline assessment of patient cognition using the Mini-Mental State Examination (MMSE), a 30-point questionnaire used to assess the presence, severity and progression of cognitive decline, is recommended especially among those at increased

risk of cognitive impairment [5]. The results of the MMSE can be used, in addition to other clinical factors, to help individualize a more safe and effective treatment plan. Repeating the MMSE periodically is also advisable especially for patients who exhibit changes in cognition, ADL performance, and/or are on long-term therapy.

In regards to specific OAB medications, oxybutynin is a well-studied anti-muscarinic agent available in several preparations and doses. Oral oxybutynin may confer the highest risk of cognitive impairment, with the transdermal preparation being more favorable in older persons due to avoidance of first pass metabolism [53]. Extended release formulations of oxybutynin and tolterodine are recommended due to lower rates of dry mouth. Fesoterodine use in older populations has illustrated good efficacy with similar side effect profiles when compared to a younger population [56, 57]. Trospium is unique due to its structure and hydrophilic properties, and it is least likely to cross the blood brain barrier and contribute to cognitive impairment. A recent clinical trial looking at the effects of trospium chloride on cognitive function in women ages 50 or older found no changes in cognitive function between those taking trospium and placebo [•58]. Thus, trospium may be preferred over other anti-muscarinic formulations in older women with OAB. As stated in current guidelines, anti-muscarinics should not be used in patients with narrow angle glaucoma unless approved by the treating ophthalmologist [5].

Mirabegron, the only clinically approved β3-adrenoreceptor agonist, stimulates the β3 receptor in the bladder causing detrusor relaxation. Although 97% of the β3 receptors are expressed in the bladder, this subtype (along with β1 and β2 receptors) is also expressed in the cardiovascular system and mediates vasodilation and increases atrial contraction. [59, 60]. The cardiovascular safety of mirabegron at various doses has been previously reviewed with minimal increases in blood pressure (BP) and heart rate (HR) reported [59]. There are no published data on the use of mirabegron in frail older adults. With this in mind, close BP and HR monitoring after starting mirabegron is recommended.

Age-related changes that could affect pharmacokinetics/drug metabolism are also important to consider in older women. Increasing age can be associated with slow gastric emptying, which may reduce drug absorption. Decreased serum albumin in older women can lead to increased plasma levels of free drug, which is particularly important for tolterodine metabolism [50]. Patients with hepatic dysfunction have altered cytochrome P450 metabolism which is needed for drug clearance specifically for oxybutynin, tolterodine, darifenacin, and solifenancin. Additionally, reduced renal function should be considered with drugs renally excreted such as trospium and tolteradine. Discussions between medical specialists are encouraged if there are any concerns for adverse drug interactions with other medications and/or medical conditions in an effort to prevent any undue risk to the patient. The prescribing physician is encouraged to proactively and closely monitor older adults after the start of pharmacotherapy to minimize adverse events and evaluate for treatment efficacy.

Lastly, with the limitations and risks associated with pharmacotherapy discussed herein, it is our opinion that third-line treatments for OAB, particularly PTNS, may be considered as second-line treatments when appropriate. While this statement does not strictly follow the AUA/SUFU guidelines, we believe that the potential systemic side effects associated with

pharmacotherapy make the traditional second-line treatments potentially less attractive in certain older adults, particularly among those with cognitive impairment. Further research on third-line OAB therapies in older adults is needed to add to our knowledge of outcomes specific to this special population.

Third-line treatment: PTNS, sacral neuromodulation, and intra-detrusor onabotulinumtoxinA

Standard guidelines recommend consideration of third-line treatments [PTNS, sacral neuromodulation, intra-detrusor onabotulinumtoxinA] in patients who are refractory to behavioral or pharmacotherapy following comprehensive evaluation to rule out other disease processes. However, in older women with known treatment barriers, we believe there may be more flexibility in the standard treatment algorithm and patients may experience improved treatment efficacy if third-line therapies are considered sooner, particularly in the case of PTNS. Although third-line treatments are more invasive, in the appropriate patient, they have the potential to alleviate treatment barriers and provide similar efficacy to pharmacotherapy with a potentially lower side effect profile when it comes to systemic side effects.

The efficacy of PTNS in frail, older women is unknown since studies specific to this population are sparse. Despite this limitation, the procedure is typically well tolerated with minimal side effects. A meta-analysis on the effectiveness of PTNS for OAB reported a pooled subjective and objective success rate of 60%, which is comparable to oral therapy, but with very few side effects [61]. One of the downsides of PTNS is related to the need for weekly 30-minute treatments for a course of twelve weeks, followed by monthly maintenance sessions.

In regards to sacral neuromodulation (SNS) one small study evaluated its use in older patients with a reported efficacy of 48% following test stimulation [62]. However, only 17% of the older cohort achieved complete dryness following permanent implantation, compared to a rate of 40% among younger persons. Contrarily, a recent study looking at the impact of age on the use of SNS, reported no difference in test stimulation or permanent implantation success rates by age [•63]. Such findings suggest that age alone should not be a predictor of SNS treatment response. However, patients who are unable to operate the neurostimulator device or those who anticipate the need for future magnetic resonance imaging are not candidates for SNS. Additionally, evaluation of cognitive status among older women considering SNS, both for their ability to assess efficacy during the trial phase and ability to make adjustments thereafter is another important factor to consider.

Based on current treatment guidelines, intra-detrusor onabotulinumtoxinA (BoNT-A) injections (100 U) are recommended for carefully-selected patients refractory to first and second-line therapies. In a recent study, the rate of urinary retention requiring clean intermittent self-catheterization two weeks after BoNT-A injections was 6.2% among female OAB patients [64]. Thus prior to proceeding with treatment, patients must be able and willing to return for post-void residual (PVR) evaluations and perform self-catheterization if indicated [5]. BoNT-A injections should be avoided in frail older adults with an elevated PVR.

There is also an increased risk of urinary tract infection (UTI) after BoNT-A injections, which is important to consider, especially in older patients with baseline renal dysfunction. A recent study comparing symptom control and adverse events in women following BoNT-A or SNS treatments illustrated beneficial reductions in daily urge incontinence episodes for both treatments, however the rate of UTIs were higher among women ≥ 65 years [•65]. The higher rate of UTIs in older women could be related to their increased risk of post-void residual volumes > 150 mL, longer duration of urinary retention following BoNT-A injection, and urogenital atrophy [66]. Women with a higher body mass index also have a higher risk of treatment failure with BoNT-A injections [67]. These are all factors to keep in mind for patient counseling and post-procedure expectations. Further research is needed to elucidate factors specific to older women and its impact on treatment outcomes.

Conclusions

Overactive bladder is commonly diagnosed in older women and is associated with significant morbidity and decreased quality of life. With increasing age comes higher rates of comorbid conditions, functional decline, and physiologic changes which adversely impact effective management of OAB in older women. Due to the complexity within this population, the standard AUA/SUFU treatment algorithm may not always be applicable. Third-line therapies, particularly PTNS, may be preferable over second-line therapy in some cases, thus management of OAB in older women must have a boarder scope. Continued research with the inclusion of older adults and those with geriatric syndromes including frailty, cognitive deficits and functional impairments in relation to OAB treatment options is needed in an effort to optimize treatment efficacy and compliance in this growing and vulnerable population.

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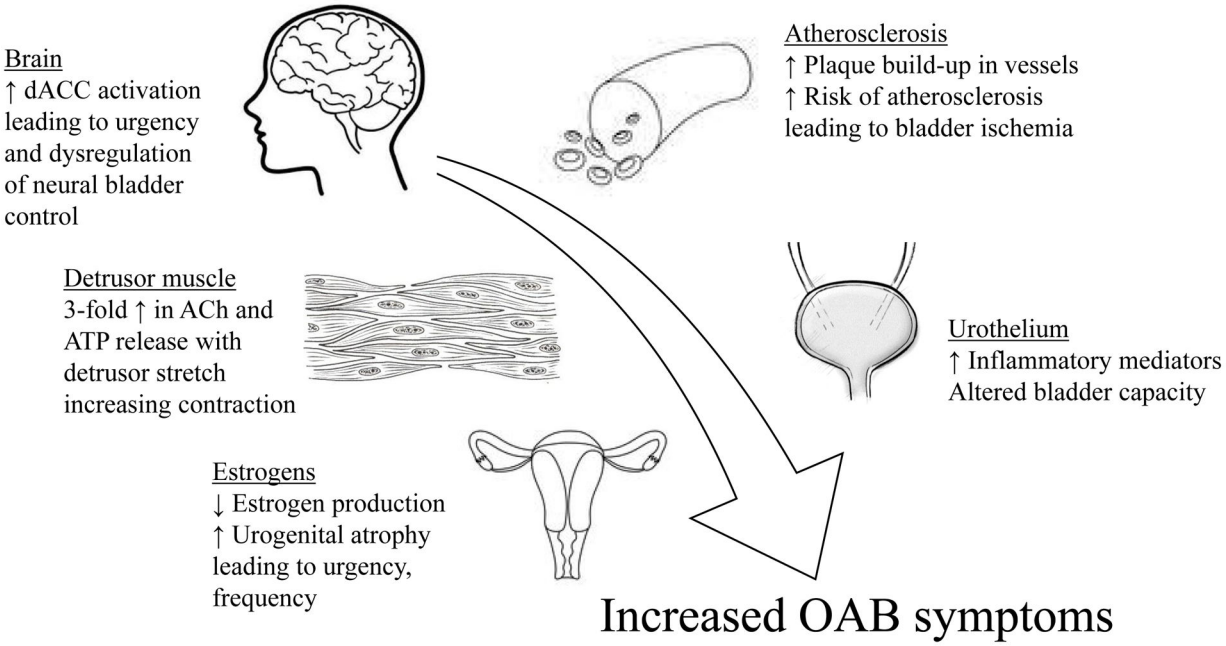

Figure 1.
Neurologic, anatomic and biochemical alterations associated with OAB in older women

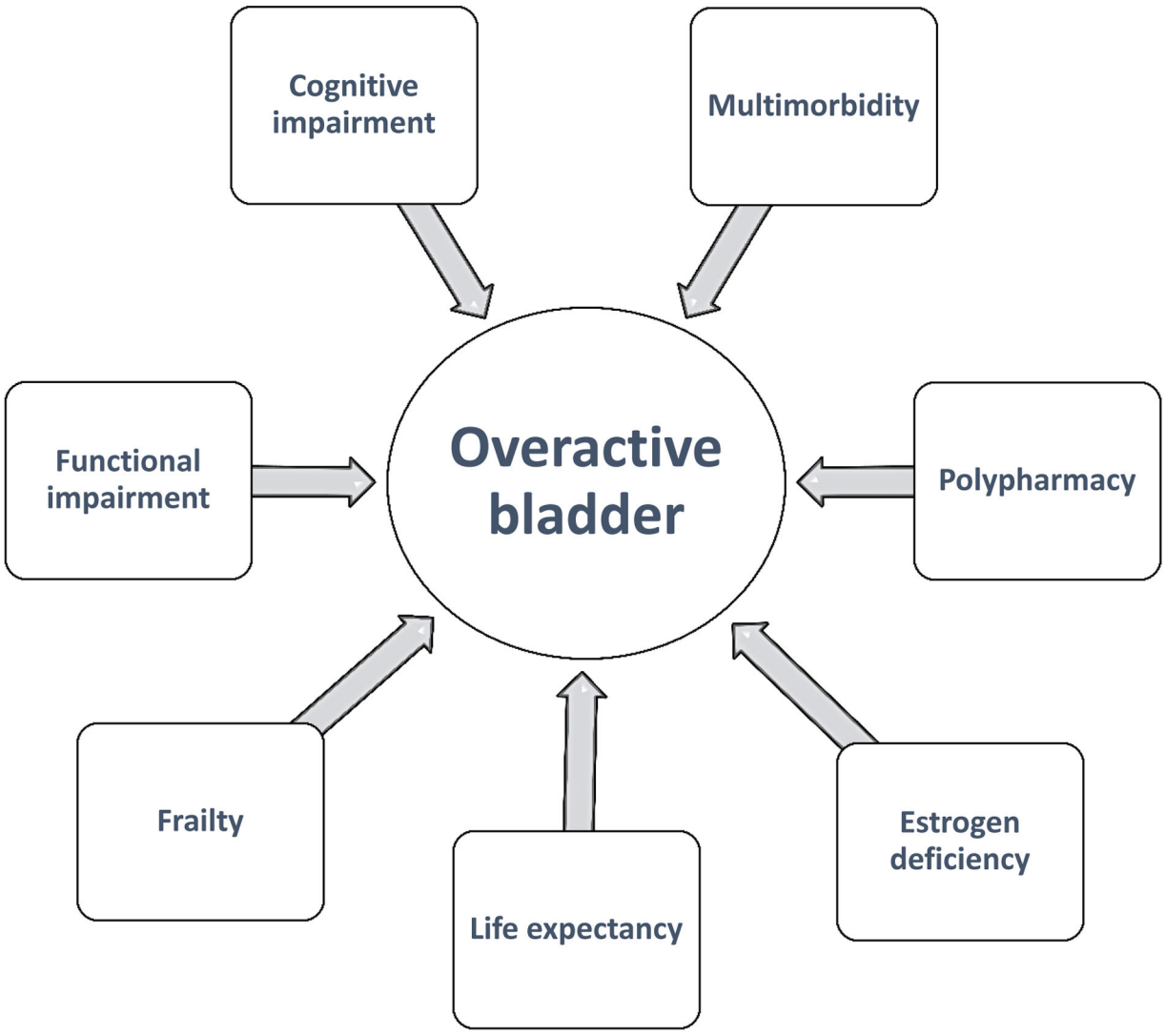

Figure 2.
Special Considerations In Older Women with Overactive Bladder

Table 1.

Summary of AUA/SUFU Guidelines for management of OAB and proposed modifications for use in older women/adults

	AUA/SUFU Guideline	Proposed modifications for older women/adults
First-line treatments	• Behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management)	• Consider frailty, functional and cognitive impairment in an individual's ability to perform and participate in behavioral therapies • Consider a patient's environment and level of caregiving/ support available to be successful with behavioral therapies • Encourage increased physical activity to improve mobility and functional independence • Assess co-morbid conditions which may directly impact bladder function and hinder behavioral therapies • Avoid fluid restriction in frail older adults
Second-line treatments	• Oral anti-muscarinics or oral ß3-adrenoreceptor agonists • Clinicians should use caution in prescribing anti-muscarinics in patients who are using other medications with anti-cholinergic properties. – Tricyclic antidepressants – Diazepam – Warfarin, ranitidine, digoxin, codeine – Medications used in the treatment of Parkinsonism, other extra-pyramidal disease and Alzhiemer's disease: benzotropine, biperiden HCl, galantamine, rivastigmine, and trihexyphenidyl HCl – Anti-nausea medications and those with atropine-like properties: trimethaphan, methscopolamine bromide, ipratropium – Donezepil • Clinicians should use caution in prescribing medications in the frail older patient. Use may be contraindicated entirely in those with dementia depending on the level of cognitive impairment. Clinicians should begin with the lowest possible dose and consider polypharmacy. No data on use of oral ß3-adrenoreceptor agonists in the frail older population exists • A MMSE should be conducted on all patients that may be at risk for cognitive impairment.	• Consider use of an anti-muscarinic risk scale or Beers Criteria to assess risk of concomitant anti-muscarinic medication use, especially in the setting of polypharmacy • When considering anti-muscarinic therapy, take into account age-related changes in pharmacokinetics, increased likelihood of adverse events, and drug-drug interactions • Work together with primary care physicians/geriatricians and other members of the individual's healthcare team when prescribing new medications • Proactively and closely monitor older adults once starting pharmacotherapy to evaluate for efficacy and adverse events • Consider PTNS, sacral neuromodulation, and OnabotulinumtoxinA in appropriate patients early in the treatment algorithm if risks of second-line treatments are too great.
Third-line treatments	• OnabotulinumtoxinA (100 U), PTNS, or sacral neuromodulation • For onabotulinumtoxinA, frail older adults may have lower success rates and may be more likely to have elevated PVRs compared to non-frail	• Consider evaluation of cognitive status among older women considering sacral neuromodulation both for their ability to assess efficacy during the trial phase and for ther ability to make adjustments thereafter.

	AUA/SUFU Guideline	Proposed modifications for older women/adults
	older adults or younger adults. No specific recommendations for use of this treatment in frail older adults is made.	• Avoid onabotulinumtoxinA in older, frail persons with an elevated PVR

PTNS: peripheral tibial nerve stimulation, OAB: overactive bladder, MMSE: mini-mental state examination, PVR: post-void residual