ClinicalPractice

Urinary incontinence in the frail elderly: what do we still need to learn?

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Practice points

- Lower urinary tract symptoms and urinary incontinence are common, distressing, and under-reported.
- Active case finding is essential.
- The evidence for assessment and treatment in frail older people is limited.
- Clinicians need to use their judgment when extrapolating the evidence for management of lower urinary tract symptoms/urinary incontinence in younger people and pay due regard to the potential benefits and risks in the frail, while also seeking and paying attention to the views of both the patient and their caregivers.

Urinary incontinence and lower urinary tract symptoms are highly prevalent in older adults, and are strongly associated with frailty. Despite this, frail older persons are under-represented in the research evidence and much of the management of lower urinary tract symptoms in this patient group must be based on a pragmatic extrapolation of the data from community-dwelling younger or more robust older subjects. An increasing understanding of the role of central control and the impact of cerebral white matter hyperintensities on suppression of urgency is being developed and this may have an implication for mid-life prevention. Commonly used drugs for overactive bladder are often poorly tolerated in older persons; some data for newer agents exist for the 'medically complex' elderly. In this article, we review the current state of knowledge and look to the future of continence management in the frail older person.

Keywords: behavioral management • frailty • old age • overactive bladder • urge • urgency • urinary incontinence

Lower urinary tract dysfunction, including incontinence, is increasingly prevalent in late life [1]. Epidemiological studies around the world note the association with increasing age in the accretion of symptoms and incontinence subtypes [1–4]. More recent data from longitudinal cohorts reveal the temporal association with accumulation of symptoms and, in particular, overactive bladder (OAB) and urgency incontinence [5,6]. The absolute distribution in samples does however vary; this is most often due to variation in definition, sampling technique, and setting. There is a portion of our society that continues to be ignored in terms of inclusion in both epidemiological and interventional studies in the continence field; the frail elderly, some of whom may reside in institutional settings and have high care needs associated with coexisting chronic disease and cognitive impairment. This paper will review the current state of knowledge around the causes, diagnosis, and treatment of incontinence and lower urinary tract symptoms (LUTS) in the frail elderly, and identify the significant gaps in the current research.

Who are the frail elderly?

Societal aging has been described as one of the greatest challenges of the 21st century and forecasts suggest that, for many developed countries, the number of people over

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the age of 65 will shortly outnumber those under the age of 20 [7]. The greatest expansion will be in the proportion of the oldest old in the population, those in their ninth decade of life [8]. Whereas aging for many is characterized as 'a progressive, generalized impairment of function resulting in a loss of adaptive response to stress (loss of biological reserve) and in a growing risk of age-associated disease' [9], there has been a change in the physical wellness of older people in the 'baby boomer' generation which has led to reductions in late-life disability [10]. There are, within the entire population of older people, many to whom the term frail may be applied. Frailty as a concept has a been defined by Rockwood as 'the accumulation of impairments' [11], and Fried and colleagues as a phenotypic model, which defines frailty as 'biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes [12]. By either definition, greater frailty is strongly correlated with increased mortality and risk of institutionalization. Essentially, frailty can be encapsulated as 'a state of vulnerability to poor resolution of homeostasis following a stressor event and is a consequence of cumulative decline in many physiological systems during a lifetime' [13]. The frailty phenotype combines impaired physical activity, mobility, balance, muscle strength, motor processing, cognition, nutrition, and endurance [14–16]. Frailty is not synonymous with disability and the presence of co-existing disease (comorbidity). In a study of older people meeting Fried's 'phenotypic' criteria for frailty, only 22% of the sample also had both comorbidity and disability; 46% had comorbidity without disability; 6% disability without comorbidity and 27% had neither [15]. However, according Rockwood's model frailty may also be defined in a more mechanistic fashion, by adding up the total number of pre-existing biomedical and social comorbidities and assigning a value to these. By either definition, frail people do have a higher risk of intercurrent disease, increased disability, hospitalization, and death than those without frailty [17].

Older people tend, on average, to have multimorbidity. A recent systematic review by Salive found reported prevalence of two or more conditions in those aged between 75 and 85 of 75% in the Medicare population [18]. Nonspecific presentation of disease in these older people is not the atypical scenario once taught to clinicians, but is a typical occurrence; such people take a high number of prescription medications [19] and are at increased risk of treatment associated adverse events. In a recent prospective study of attendees over the age of 65 years in a single emergency department, 45% of those attending over the age of 75 were on five or more drugs, and the median number taken was six [20]. In institutionalized persons, this may be much higher – in some studies, up to 10% of late-life emergency admissions are said to be due to unwanted effects of medications [21].

The state of the art in continence care for the frail elderly

As noted by the committee designated to address urinary incontinence (UI) in frail older people under the auspices of the 5th International Consultation on Incontinence note: 'There is probably no reason to assume that interventions which work in community-dwelling older people should not do so in the frail elderly' [22]. There are, of course, caveats when applying this assumption, and any planned treatment should take into account the wishes of the patient and, where the patient lacks capacity, their caregiver, and the relative risks and harms of the proposed treatment in relation to the remaining life expectancy of that individual. For example, assisted toileting and containment for social continence may be more appropriate for an immobile frail older person than pharmacotherapy. Wherever possible, measures should be taken to deal with sensory or communication impairment to engage patients in discussion about their proposed treatments.

The impact of comorbidity

In a large population-based observational study, UI (defined as use of pads) was associated with the presence of one or more other geriatric syndromes (cognitive impairment, injurious falls, dizziness, vision impairment, hearing impairment) in 60%, two or more conditions in 29% and three or more in 13% [23]. A decline in physical health has been associated with an increase in the incidence of incontinence. In an observational study of 6361 community-dwelling women, aged 65 and older, participating in a study of osteoporotic fractures, after adjusting for confounders, women with a recent worsening of 1 standard deviation from baseline in physical function were more likely to report weekly incontinence (OR: 1.3) for a decline in walking speed over 6 m and (OR: 1.4) in the ability to stand from sitting [24]. Likewise, impaired cognition is associated with an increased likelihood of UI. There is a moderate association in the community-dwelling elderly but a strong association with UI and cognition for those with impairment of orientation, living in institutions. For example, in a UK cross-sectional survey of over 15,051 people, those with cognitive impairment (Mini-Mental State Exam score ≤3, prevalence 18%) were significantly more likely to have UI (adjusted odd ratio [OR]: 1.3), impaired hearing (OR: 1.7), poor vision (OR: 1.7), have had at least two falls in the previous 6 months (OR: 1.4) and report poorer health (OR: 1.9) [25]. Comorbid conditions can also affect continence status and the likelihood of successfully toileting through multiple mechanisms, for example, diabetes mellitus. Approximately 40% of citizens of the USA have diabetes or impaired glucose tolerance [26], 13.92% of the over-60 age group in the UK are diabetic [27] and, in Canada, the incidence is estimated at 12% in the community and 17.5% in those living in institutions [28]. The association between long-standing type II diabetes mellitus of over 20 years duration and UI is well described [29]. Neurological conditions in the elderly commonly associated with UI include stroke, Alzheimer's disease, multi-infarct dementia, mixed dementia and the akinetic-rigid syndromes. Each of these conditions is associated with the development of brain lesions that can interfere with the normal ability to inhibit voiding as well as affecting cognition. These conditions are associated with impaired mobility and also affect the ability to toilet independently.

More recently, the concept of cerebral ischemic load, reflected in the extent of white matter hyperintensities on MRI, has come to the fore [30,31]. The white matter hyperintensity burden appears to be associated with the presence of the typical geriatric syndromes of impaired mobility and cognition as well as urinary urgency, urgency incontinence, detrusor overactivity and difficulty in maintaining continence during cystometry [32–35].

These findings may offer interesting opportunities for mid-life intervention, in terms of prevention of these lesions, but as yet there are no interventional studies which look at clinical outcomes. A *post hoc* analysis of a single intervention using high dose HMG-CoA reductase inhibitors demonstrated that, over 2 years, in those affected with the highest ischemic load, a regression in white matter hyperintensities could be demonstrated [36]. Likewise, control of mild hypertension in midlife may offer benefits in terms of continence in later life, whereas a lack of benefit in terms of cardiovascular morbidity and mortality has led to the benefits of intervention being questioned [37].

Likewise, there is an epidemiological association between urinary urgency, urgency incontinence and nocturia and falls in older people, with weekly episodes of urgency incontinence having an increased relative risk of falls of 1.26 [38–40]. The mechanism underlying this is unclear, but there are a number of plausible hypotheses, including common risk factors with frailty and excessive cognitive load leading to gait instability. Rather than avoiding antimuscarinic agents for the management of falls in older persons with OAB for fear of anticholinergic-associated falls, treatment of OAB with either oxybutynin or tolterodine does not appear to be associated with an increase in falls, suggesting a beneficial effect [41]. However, despite now being included in some national and international guidelines [42], there are no formal intervention trials which specifically examine the impact of continence treatment on the incidence of falls.

There is relatively little evidence for the management of UI in frail older people which is specifically targeted at amelioration of the comorbid condition, measuring improvement of UI as an outcome.

A survey of stroke unit practice in Australia showed that less than half had a formal plan for continence care, and two-thirds of respondents would use a catheter to manage post-stroke incontinence [43]. In the UK, as part of the national sentinel audits of stroke, there was little advance in continence care [44,45]. A comparative study of stroke nursing found a dearth of evidence and treatment focused on containment and social continence, highlighting the need for systematic assessment and management [46]. In Parkinson's disease, where anticholinergic treatment may lead to cognitive decline, a recent exploratory study of exercise-based behavioral interventions resulted in a clinically meaningful reduction in symptoms and an improvement in quality of life [47].

Behavioral and lifestyle interventions

The maintenance of continence in the frail elderly population is not only a function of the bladder and pelvic floor, but also relies on complex interplay between the brain, the body, the bladder, and the environment. Interventions to improve continence in frail older people, particularly the institutionalized elderly are therefore multifactorial. Exercise, both general and pelvic floor, has been shown to promote continence in this population [49,50]. Behavioral interventions have been developed for frail older people with UI, and these revolve around the reinforcement of desirable behaviors to promote continence. Although programs vary in their detail, they have in common the fact that they all require active participation by both patients and caregivers. These include prompted voiding, where prompts to toilet and positive reinforcement of successful toileting are used to promote continence through increased requests for toileting and self-initiated toileting. This has been shown to be effective and a response in the first three days is predictive of response at 9 weeks [51]. Habit retraining involves identifying a patient's usual bladder routine and providing assistance to toilet before an episode of incontinence occurs, with no attempt to influence a person's voiding habits. Timed voiding is the practice of toileting residents on a fixed schedule, with no reference to their individual toileting needs or attempts to alter them.

There is little evidence for the effectiveness of either approach [52], and both could be considered as aimed at the convenience of staff rather than the benefit of the patient. There is a dearth of high-quality evidence as to the best model of providing continence promotion programs, and studies have identified challenges to implementation [53]. There is also evidence that the compliance with the intervention studied in many trials is not continued past the end of the study period [54].

Although we have evidence of efficacy for behavioral interventions, there are significant implementation barriers and a dearth of knowledge about the minimal dose of intervention required to either achieve or sustain benefit within the confines of available resources in the institutional environment.

Medication management

The evidence for pharmacological management of urgency incontinence in frail older people is lacking and much data come from the robust community-dwelling elderly. However, surveys of nursing home residents suggest that incontinence is massively undertreated [55]. Until recently there were no planned prospective trials of drug management in older people. Of late, there have been studies in the community-dwelling elderly [56,57] and in the 'medically complex elderly' [58], which may allow the case for extrapolation to more frail individuals to be made. The mainstay of pharmacological treatment for OAB continues to be the use of antimuscarinic drugs. These act at the level of the detrusor and urothelium to increase bladder storage capacity and reduce the impact of urinary urgency [59]. They are associated with numerous adverse drug effects (ADEs), commonly xerostomia and constipation [60]. Adherence to treatment is poor, with high discontinuation rates; around half of patients stop treatment by three months [61]. Cognitive impairment, particularly with oxybutynin, is an under-reported, under-appreciated, yet potentially significant ADE [62–64]. Other anticholinergics, including fesoterodine [65], darifenacin [66], and solifenacin [67], have been shown not to affect cognition, and those that do not cross the blood–brain barrier, such as trospium [68,69] may be less likely to have central nervous system ADEs. A small trial of solifenacin in subjects with mild cognitive impairment has also demonstrated no effect on cognition versus placebo [70], although no data are available for frail older people. The safety and efficacy of anticholinergics in people with cognitive impairment has not been well studied. In a study of nursing home residents with dementia, co-prescription of anticholinergics (specifically oxybutynin and tolterodine) with a cholinesterase inhibitor (ChI) was associated with a 50% greater rate of functional decline in Minimum Data Set – Resident Assessment Index physical function scores for the most independent in ADL at baseline than in those taking ChI alone [71]. In other studies of co-prescription, there has been an improvement of continence outcomes and no deterioration in cognition [72,73]. Nevertheless, the potential benefits of medication on continence outcomes need to be carefully weighed in terms of the likely benefits, potential reduction in need for care and improvements in quality of life for frail older people. Newer agents, such as the β_3 receptor agonist mirabegron, are effective in reducing incontinence and LUTS, but data are limited to pooled analysis in those >65 years of age from registration trials, and specific cognitive studies have not been performed [74,75]. In intractable urgency urinary incontinence, onabotulinumtoxin A can be injected into the bladder to good effect, and low dose treatment has been shown to be effective in older people with lower risks of urinary retention [76], but again there are no data available for frail older people and the probability of such individuals being offered this more invasive therapeutic option is, on balance, minimal without careful selection and advocacy.

Recent developments in the understanding of urothelial function may provide new targets for pharmacological action. Several subtypes of the transient receptor potential vanilloid (TRPV) receptor are expressed in bladder epithelium. $TRPV4^{-/-}$ knockout mice have enlarged bladder capacities and dysfunctional voiding [77], and agents which block TRPV1 channels, such as capsaicin, can reduce the symptoms of urgency [78]. However, the ubiquity of TRPV channels may make the development of a bladder-specific drug challenging. Other emerging targets include the prostaglandin E receptor EP1, although a recent trial of an EP1 receptor agonist did not show any improvement in LUTS [79]. The development of targeted drugs for detrusor overactivity, OAB, and LUTS is an emerging area of research.

There are still relatively few data on pharmacological management of incontinence in frail older people, who tend to be excluded from clinical trials. There is a definite need for their prospective inclusion in treatment trials and careful note taken of not only efficacy and tolerability but also the impact on symptom burden, quality of life and caregiver burden, plus the use (or saving) of healthcare resource use. Recommendations for rational use of medications in this group are few.

Sacral neuromodulation (SNS) has been used for OAB where pharmacotherapy has failed. A Cochrane review in 2009 concluded that 'implantable neurostimulators have benefits for some patients with OAB symptoms, retention without organic obstruction, and in those for whom other methods of treatment have failed' [80]. However, there are no trials, or even case reports, of SNS in the frail elderly, and given the cost and high rate of complications, their use can only be considered in very carefully selected cases.

Stress UI

Stress UI (SUI), the complaint of involuntary loss of urine during coughing, sneezing or exertion, is more common in women. Risk factors include increasing age, obesity and smoking, as well as multiparity [81]. In men, it is most commonly seen following prostate surgery.

Initial management is conservative, with pelvic floor muscle training (PFMT). A Cochrane review in 2010 [82] found significant heterogenicity in the trials of PFMT in women, with a range of outcome measures. In general, the studies found an improvement in continence, however defined, an increase in quality of life and a reduced likelihood of requiring surgery, compared with no intervention. Outcome measures considered included self-reported symptoms, quantification of symptoms such as urine lost, clinical observations, quality of life measures and socioeconomic impact. In men, PFMT prior to prostatectomy has been shown to be of benefit in reducing postoperative incontinence [83]. Trials of postoperative PFMT have shown inconsistent results, and the 5th International Consultation on Incontinence (ICI) report concluded that PFMT may be helpful.

Since the mid-1990s, the surgical treatment of choice for SUI in women has been the mid-urethral sling [84], a minimally invasive procedure which can be performed as a day-case under local anesthesia. They have been shown to be as safe and effective in older women as younger women [85], and their introduction leads to a large decrease in the number of invasive operations performed. However, there has not been an increase in the proportion of such procedures performed in older women, and the reasons for this are unknown [74]. Injection of urethral bulking agents, such as autologous fat or silicone beads, is used to increase urethral closing pressure and thereby reduce SUI [86]. Recent advances in methods using fibroblast-derived growth-factor-loaded plasmids to encourage urethral redevelopment are promising [87] but remain at an early stage. It is not yet known whether such techniques will deliver on their early promise, and there are no data in the frail elderly as yet [88].

In men, SUI occurs predominantly as an adverse consequence of prostatectomy with rates varying from 2.5 to 87%, depending upon the type of procedure, age of the patient, definition of incontinence and sampling time frame [89]. Surgery for benign prostate disease is being performed less frequently than previously, with a reduction of 60% in the last decade of the last century, as a direct result of the introduction of effective medical therapy for benign prostatic enlargement [90]. However, radical prostatectomy for localized prostate cancer is performed more frequently that it was 20 years ago, and is now commonly performed using the robot-assisted laparoscopic technique [91]. For men who remain incontinent post-prostatectomy despite PFMT, the treatment of choice is either the implantation of an artificial urinary sphincter (AUS) or the use of a suburethral sling. The AUS was first introduced in 1973, and comprises a reservoir, urethral cuff and control pump. Up to a third of implants require revision [92]. Newer devices in development may provide more automated control systems and allow use in frailer or more cognitively impaired people with severe stress or post-prostatectomy incontinence, as they are less reliant on manual dexterity than the traditional system [93]. Mid-urethral slings in men are an emerging area of interest. The 5th ICI concluded that, in the intermediate term, slings appear to perform well [22]. AUS remains the gold-standard treatment, and it remains to be seen if sling procedures will surpass it.

Bladder underactivity

Detrusor underactivity (DU) is defined as contraction of either reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to complete bladder emptying within a normal time frame [94]. The changes to the bladder in normal aging are complex and poorly understood. Some studies have shown the muscle-to-collagen ratio to reduce [95] and maximum bladder contraction strength declines [96]. In patients with DU, changes to the muscle and urothelium occur, including loss of contractile proteins, beyond that seen in normal aging [97]. However, an age-related degradation in detrusor contractility has not been confirmed as the primary contributor to DU, and the role of ischemic insult and changes to the neural innervation of the bladder also have a role [98]. It should be borne in mind that DU is a clinical syndrome and is not synonymous with impaired detrusor contractility. Treatment of DU is currently limited to the relief of bladder outlet obstruction (BOO), either with drugs such as alpha blockers or 5α-reductase inhibitors, or intermittent or indwelling urinary catheterization. In many older patients with DU, there is no evidence for significant BOO [97], and there are currently no data on the best treatment for these patients. There is a need for a well-characterized model for the pathophysiology of DU-linking urodynamic findings to alterations in structural and molecular pathology in order to begin to piece together a hypothetical model upon which potential treatments can be based. In an ongoing study of older peoples' expectations from treatment, intermittent catheterization is high on the list of most unwanted treatments [Unpublished Data].

Detrusor hyperactivity and underactivity can coexist, leading to a common but underdiagnosed condition, detrusor hyperactivity with impaired contractility [99]. First described by Resnick in 1987, it presents with symptoms of OAB and impaired voiding, and may cause urinary retention and complicate pharmacological treatment of OAB if not recognized.

Functional incontinence

The maintenance of continence is reliant not only on a functional lower urinary tract and pelvic floor but also on sufficient cognition to interpret the desire to void and locate a toilet, adequate mobility and dexterity to allow safe and effective walking to the toilet, and an appropriate environment in which to allow this [74]. Functional incontinence occurs where this fails and can be seen in the context of a completely normal lower urinary tract – for example, if an older person is admitted to hospital and not told where the toilets are, or the required assistance or devices to enable them to get there are unavailable. Coexisting disease, such as dementia, arthritis and visual impairment can impair the ability to locate and get to an appropriate place to void, and the 5th ICI concluded that an effort should be made to 'identify treatable, potentially reversible conditions and other factors that can cause or contribute to UI'. Amelioration may improve UI directly, make UI more amenable to other interventions, and overall improve the patient's (and caregivers') quality of life [100].

Nocturia & nocturnal enuresis

Nocturia, the complaint of waking one or more times at night to void, and nocturnal enuresis, the loss of urine during sleep [94], are prevalent in frail elderly people[1], although people tend not to seek help unless they wake three times or more, as it is at this level that significant bother occurs [101,102]. Nocturia is often multifactorial; one large study in Finland found that half of older adults with nocturia had more than one cause [103]. Underlying contributing factors include OAB, obesity, congestive cardiac failure, BOO and sedative drugs. In addition, during normal aging the proportion of the total daily urine output produced at night rises even in the absence of pathology [105]. The use of desmopressin in frail elderly people is not recommended, due to the risk of hyponatremia [100]. Nocturnal enuresis, the passing of urine during sleep, is also common in old age, with prevalence of around 2% in community-dwelling older people [106], rising to 43% in institutionalized elders [107]. Despite this, there is no good quality evidence to guide the management of nocturia or nocturnal incontinence in frail older people in any care setting [100].

Conclusion

The maintenance of continence in frail older people relies on a complex interplay of many factors, both personal and environmental. There are significant gaps in the knowledge as to how normal aging affects the urogenital tract, the prevalence and impact of LUTS and incontinence in older people, and especially in older men. There is a continued dearth of high-quality evidence to guide best practice, particularly for the management of continence in the context of cognitively impaired, frail older people living in long-term care facilities. The currently available pharmacological treatments for OAB are often poorly tolerated, and the safety and efficacy of available newer agents in frail older people has yet to be established, and attempts to find drugs for other therapeutic targets have been fruitless thus far. Where complex, multicomponent interventions have been developed, there best way of maintaining the intervention in the face of challenging care environments remains elusive.

Future perspective

Modern medicine is extremely good at creating old people. As people survive into their 9th decade and beyond, the prevalence of frailty, institutionalization, and UI is only going to rise. There is an increasing need for high-quality evidence in both the basic science of the aging urinary tract and its control, as well as the holistic management of LUTS and UI in frail older people. Barriers to care, such as the erroneous belief that UI is a normal part of aging, or that treatment is not available, must be overcome, and a greater understanding of the impact and importance of good-quality continence care should be developed and used. Greater understanding of the pathophysiology of OAB and the role of the urothelium will lead to new pharmacological agents becoming available and hopefully surgical treatments for SUI more widely used in the older population.

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