

Do we understand urinary retention in women? Current understanding and future perspectives: ICI-RS 2017

Running title: Urinary retention in women

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Abstract

Aims

Urinary retention in women is poorly understood, compared to the equivalent condition in men, and was the subject of a dedicated session organised at the International Consultation on Incontinence Research Society (ICI-RS) in Bristol, United Kingdom, 2017.

Methods

The current understanding of the pathophysiological correlates of idiopathic voiding dysfunction in women, the role of urodynamics, neurophysiology, and non-invasive tests in characterising functional bladder outlet obstruction due to a non-relaxing urethral sphincter, and poorly defined diagnosis of detrusor underactivity were reviewed.

Results

Putative factors underlying the pathogenesis of urinary retention following urinary tract infections were discussed. Further research is required to explore the association between bladder wall inflammation and alterations in detrusor contractile functions. The complex interrelationship between urinary retention and psychological co-morbidities and sexual trauma were explored, and the overlap between these and psychological co-morbidities and functional neurological problems with functional urological problems were recognised. Understanding the mechanism of action of sacral neuromodulation, often a successful treatment for urinary retention, would provide insight into the underlying factors that may be responsible for urinary retention. Specifically, there is a

need to understand the role of the endogenous enkephalinergic system in the pathogenesis of urinary retention and to identify predictors of successful treatment with sacral neuromodulation. Based on current understanding and potential directions of research in the future, an algorithm for the evaluation of women with voiding dysfunction was proposed.

Conclusions

In the future, recommendations for research should lead to a better understanding of urinary retention in women and its treatment.

Key words: voiding dysfunction, Fowler's syndrome, dysfunctional voiding, opiates, psychological co-morbidities, sexual abuse, sacral neuromodulation, urinary tract infections

Introduction

Urinary retention is not an uncommon problem in women, but to date this condition has been poorly studied ¹⁻³. In the EpiLUTS study, a sensation of incomplete bladder emptying was reported by 27.4% and a weak flow by 20% of women aged >40 years ⁴. Urodynamic and imaging studies help to delineate the pathophysiological correlates to urinary retention such as bladder outlet obstruction (BOO, reported in 2-23%) ¹ or detrusor underactivity (DU, reported in 12-45% of older women) ⁵ in women investigated for lower urinary tract (LUT) symptoms. The lack of accurate definitions and appropriate diagnosis for either condition may be largely responsible for the apparent epidemiological discrepancies, but also reflect the lack of studies of female urinary retention to date.

Methods

At the International Consultation on Incontinence Research Society (ICI-RS) in Bristol, United Kingdom, 2017, a panel of clinicians and scientists participated in a think-tank discussing female voiding difficulty / urinary retention. The aim was to identify current problems with the diagnosis and treatment of female urinary retention and to produce a consensus view within this subject area in the form of a proposed algorithm to encourage a consistent approach for these patients.

The panellists reviewed the literature regarding the pathophysiology of voiding dysfunction in women, different triggering factors for urinary retention, diagnostic potential of invasive (urodynamics, neurophysiology) and non-invasive (imaging) tests

and the current understanding of the mechanisms by which sacral neuromodulation works. From the discussions at the meeting and subsequent e-mail iterations, the panel proposed priority areas of further research to advance the current understanding as well as an algorithm for the evaluation of female voiding dysfunction.

Voiding dysfunction in women

Voiding dysfunction in this document implies abnormally slow, intermittent micturition and/or incomplete bladder emptying, and is a diagnosis that is made following the recording of symptoms and analysis of urodynamic investigations ⁶. There are a few established causes for voiding dysfunction in women (table 1).

Voiding dysfunction is rather heterogeneous in women, and urodynamic studies are considered mandatory in order to provide useful information regarding the alterations in LUT function contributing to voiding dysfunction such as detrusor underactivity (DU) and bladder outlet obstruction (BOO).

Bladder outlet obstruction in women

The characteristic findings of bladder outlet obstruction (BOO) are an increased detrusor pressure, reduced urine flow rate and often the presence of a raised post-void residual (PVR) ⁶. BOO is relatively uncommon in women, and there are a few structural and functional causes (Table 1). In the 1980s, Fowler et al. described a cohort of young women presenting in complete urinary retention with the finding of a specific electromyographic (EMG) pattern recorded from the striated urethral sphincter,

characterised by complex repetitive discharges (CRDs) and decorating bursts (DBs), and often with accompanying clinical features of polycystic ovaries ⁷. The syndrome has since become known as Fowler's syndrome (FS) and routine cystometry may not always demonstrate BOO, but rather a large capacity bladder without the usual sensations during the filling phase. The maximum urethral closure pressure (MUCP) is found to be elevated, with values typically above 100 cm H₂O and the urethral sphincter volume often enlarged in transvaginal ultrasonography. It is thought that the abnormal EMG activity prevents relaxation of the striated sphincter and abnormally high urethral pressure, and, through an exaggerated pro-contenance guarding response, poor bladder sensations and contractile function ⁸. CRDs have been reported from other pelvic floor muscles in women presenting with isolated urinary retention ⁹, and in apparently asymptomatic women ^{10,11} and therefore the association between the abnormal EMG signal and voiding dysfunction requires further exploration. Recently, EMG abnormalities have been shown to be associated with a pulsatile pattern in the UPP, and the underlying pathophysiological basis for this observation requires further study ¹².

Detrusor underactivity

Detrusor underactivity (DU) is common, especially in elderly women, with a prevalence of up to 45% ⁵. Defined as "a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span", there has been an increased interest in the clinical characteristics of DU, to diagnose the condition ^{13 14}. The common causes for DU in women are listed in Table 1.

There is a need to further understand the pathophysiological correlates to voiding dysfunction and longitudinal studies are needed to answer some of the unanswered questions:

- Do the clinical features, natural history and treatment outcomes differ between women with functional BOO and DU?
- Does the clinical profile of women with voiding dysfunction due to a primary disorder of urethral sphincter relaxation differ from women with non-relaxing pelvic floor, where biofeedback is an effective treatment?
- What is the contribution of the smooth muscle present at the bladder outlet to the development of obstructed voiding in women with evidence of a non-relaxing urethral sphincter?
- What is the role of the endogenous enkephalinergic system in the pathogenesis of urinary retention in women with a primary disorder of urethral sphincter relaxation?

Assessment

Figure 1 provides an overview of the assessment of women presenting in urinary retention ¹⁵. The ability to predict whether voiding dysfunction is due to BOO or DU based on symptoms alone is low ¹³. Voiding symptoms are common in both, and while storage symptoms commonly co-exist in patients with DU due to voiding in low urine volumes, the finding of detrusor overactivity (DO) is common in older patients with DU ⁵. In women with dysfunctional voiding, characterized by an intermittent and/or fluctuating

flow rate due to involuntary intermittent contractions of the peri-urethral striated or levator muscles during voiding in neurologically normal women ⁶, storage symptoms were twice as prevalent as voiding symptoms (67.9% vs. 32.1%) in women with dysfunctional voiding, urinary frequency being the most common complaint (41%), followed by dysuria (32.1%) and urgency incontinence (15.5%)¹⁶. The presence of a high PVR alone is also non-diagnostic with low sensitivity (13–57%) and specificity (18–38%) ³. Women with BOO due to a poorly relaxing urethral sphincter from FS are typically young and have attained menarche. Residual volumes are often demonstrated to exceed 1 litre at some stage and although they may experience pain, they do not report the expected urgency at such a large bladder capacity. Straining does not help emptying, and performing intermittent self-catheterisation is often painful, particularly on removal of the catheter, with many women complaining of a sensation of “something gripping” as the catheter is withdrawn ¹⁷.

Attempts have been made to recognise symptoms that may distinguish BOO from DU and an older age, enuresis, stress incontinence and impaired sensations of bladder fullness may occur more frequently in DU, whereas a “gripping sensation” during attempted catheter removal is characteristically described in functional BOO especially due to Fowler’s syndrome ^{13 17 14}. Preliminary results from a cohort of women with voiding symptoms present in 75% suggested a lower Qmax and higher bladder voiding efficiency upon free-flow to be more predictive of BOO ¹⁸.

Non-invasive Urodynamics

The predictive value of uroflowmetry for the diagnosis of BOO and DU has been investigated in an effort to standardize diagnostic criteria. Voiding dysfunction has been defined as a urine flow below the 10th maximum flow rate centile of the Liverpool nomograms, or as a maximum flow of ≤ 15 mL/s and/or a PVR ≥ 50 mL. A cross-sectional multicentre study of women with pelvic organ prolapse aged >55 years reported 39.7% with voiding symptoms, and using the above mentioned cut-off, it was demonstrated that the nomograms may be more predictive of voiding dysfunction than the combination of uroflow parameters and PVR¹⁹. These results conflicted with an earlier study, which reported the odds of diagnosing voiding difficulty as 3.7 (95% CI, 1.9-7) using uroflowmetry compared to 2.8 (95% CI, 1.6-5.2) using the Liverpool nomogram. Uroflowmetry was found to have a specificity of $>70\%$ but with a wide range of sensitivities (50-100%) depending on the cut-offs chosen²⁰.

Invasive urodynamics

The role of cystometry in the evaluation of urinary retention in women is not well defined. Most studies have focussed on the urodynamic diagnosis of BOO with various criteria proposed which are based on voiding pressure, urine flow rate and fluoroscopic appearances. These are summarised in Table 2^{21 22 23 24 25 26}.

No consensus exists on which of these criteria are most accurate and a “gold standard” is yet to be established.

Fluoroscopy in combination with cystometry can be invaluable in certain circumstances for instance primary bladder neck obstruction, urethral stricture and extrinsic outlet

compression. Consequently, most clinicians would routinely advocate these of video urodynamics.

Urethral Pressure Profilometry (UPP)

The UPP can be helpful in delineating the cause of female urethral retention and is of particular relevance when the pressure-flow measurements and radiological appearances suggest a large maximum cystometric capacity and impaired ability to mount detrusor pressures. These are findings that are common for both DU²⁷ and Fowler's Syndrome²⁸, however the finding of a high maximal urethral closure pressure would suggest the latter⁸.

Cystoscopy

Cystoscopy is useful to assess the bladder outlet and exclude anatomical causes for obstruction, as well as to identify structural bladder alterations or complications of BOO such as trabeculations, diverticula and dilated ureteric orifices which may suggest vesico-ureteric reflux. Cystoscopy is routinely performed in the investigation of women presenting with voiding difficulties, however the usefulness of this test needs to be researched.

Pelvic Neurophysiology

Concentric needle electromyography (EMG) of the striated urethral sphincter may reveal abnormal signals in women presenting with urinary retention due to BOO. Over the audio-amplifier of the EMG machine, complex repetitive discharges (CRDs) produce

a sound similar to helicopter sounds, and the decelerating component of a CRD, known as decelerating bursts (DB), produce a characteristic sound akin to the sound of underwater recording of whale songs²⁹. Other pelvic neurophysiology tests recording the anal sphincter EMG, bulbocavernosus reflex and pudendal sensory evoked potentials assess the integrity of the somatic S2,3,4 nerve roots. These tests however are performed only at specialist centres and are indicated particularly in situations where an obscure lesion of the sacral roots or conus medullaris is suspected to be the cause for retention, though their clinical utility needs to be better defined.

Emerging non-invasive tests

Magnetic resonance imaging (MRI) of the pelvic floor allows for precise evaluation of ligaments, muscles, and pelvic organs and provides accurate information about the three compartments of the pelvic floor^{30,31}. However, these techniques are mostly used diagnostically in conditions of a 'weak' pelvic floor: cystoceles, rectoceles, enteroceles, fascia damage, ligament damage, bowel dysfunction. The high resolution of images, the ability to acquire dynamic sequences during voiding, and the lack of radiation makes MRI an attractive tool to study functional disorders of the pelvic floor. Moreover, MRI may have applications in the evaluation of functional BOO, as an enlarged urethral sphincter is seen in women with FS⁸. Dynamic MRI studies during the voiding phase may help to study pelvic floor descent and identify differences in bladder and bowel configuration during straining. These studies may be combined with simultaneous urodynamic recordings, however is not available for routine clinical use at present.

Ultrasonography of the pelvic floor has emerged as a non-invasive technique to examine the pelvic floor in women with incontinence and pelvic organ prolapse (POP). 2-D, 3-D and 4-D techniques with application of the probe translabially^{32 33-35 36}, transabdominally³⁷ and transvaginally have been evaluated³⁰. Results are conflicting, however, and despite the known association between levator ani abnormalities and an underactive pelvic floor, no relation to incontinence or POP was identified³⁸.

Contradictory findings have also been reported in studies evaluating bladder wall thickness (BWT) ultrasonographically in patients with functional LUT disorders^{39,40}.

Transabdominal measurement of BWT was found to correlate with both BOO and DU in a series of 167 women with LUTS⁴⁰, whereas in a larger cohort of women, detrusor wall thickness in symptomatic women was no different from asymptomatic women, and was not associated with parameters of voiding function, or urodynamic indices of BOO³⁹.

Promising novel techniques for the future include dynamic ultrasonography performed during voiding, and shear wave elastography (which aims to provide a quantitative assessment of bladder neck elasticity)⁴¹, however findings have not been correlated with voiding symptoms or urodynamic findings.

Other exploratory non-invasive tests include measurement of urinary nerve growth factor (NGF) levels⁴², surface EMG of the pelvic floor⁴³ and cardiovascular testing for occult dysautonomia⁴⁴. To date there have been no studies showing correlation of these techniques with symptoms or urodynamic findings.

The results from tests provide some insight into the LUT dysfunction, however to what extent they contribute to our understanding of female voiding dysfunction has been poorly researched and there are several unanswered questions:

- Are the currently established tests- (video)cystometry and urethral pressure profile (UPP)- sufficient to characterise the LUT dysfunction responsible for urinary retention in women? Which women with voiding dysfunction should have UPP measurements?
- What is the role of pelvic neurophysiology testing in the evaluation of women presenting with voiding dysfunction?
- How do the findings of abnormal EMG signals in the urethral sphincter (decelerating bursts and complex repetitive discharges) correlate with the clinical and urodynamic findings of Fowler's syndrome (FS)?
- Can the presence of abnormal EMG signals in otherwise asymptomatic women serve as a marker of susceptibility for developing urinary retention at a later stage?
- What is the role for non-invasive tests such as sphincter imaging (ultrasound, routine MRI), dynamic MRI and urinary biomarkers (eg. NGF) in the evaluation of urethral sphincter and pelvic floor functions in women presenting with bladder outlet obstruction?
- Is there evidence for more generalised autonomic dysfunction (eg. cardiovascular, sweat, pupillary abnormalities) in women presenting with idiopathic urinary retention?

- Are there techniques to evaluate the afferent signalling pathway from the urethra of women and its role in the pathogenesis of “detrusor failure”?
- What are the predictive associations between non-invasive urodynamics with invasive pressure-flow urodynamic studies?
- Can a multicentre study be designed to develop and test an acceptable diagnostic index for female bladder outlet obstruction?

Factors known to be associated with urinary retention in women

Different triggering factors and co-morbidities seem to be associated with retention.

Urinary tract infections

Urinary tract infections (UTI) are often reported as a triggering factor for retention in women. The basis for this is uncertain but a link between inflammatory changes and the development of DU involving the ‘mechanosensitive transducer’ comprising urothelium, interstitial cells, detrusor and ganglia of the bladder has been postulated. During inflammation, different mediators of the ‘mechanosensitive transducer’ are altered such as elevation of TNF- α , suppression of NGF and lower expression of E-cadherin. Together with oxidative stress, altered expression of receptors (lower expression of M₂-, M₃-, P2X₃-receptors; higher expression of β ₃-receptors), and activation of different cells-types (increased mast cells, macrophages and apoptotic cells in the suburothelial layer) may significantly influence afferent activity from the bladder ^{45 46}. The role of afferent signalling in modulating the strength, velocity, and duration of detrusor contraction is now being recognised ⁴⁷ in type 2 diabetes mellitus

(DM), where age and recurrent urinary tract infections were identified as independent factors for developing impaired voiding function ⁴⁸.

Changes in detrusor contractile strength follow a dynamic course ⁴⁹, exhibiting a possible biphasic response in some, with initial changes of overactivity, followed by sequelae such as DU. The evidence so far in diabetic patients and the elderly suggest that both histological changes of the detrusor muscle, as well as the cascade of inflammatory reactions, may have a major contribution to the development of DU.

Opiate use

Opiates exert a suppressor effect on LUT function through spinal μ - and δ -opioid receptors that induce bladder relaxation by activating descending inhibitory systems, as well as possibly through direct effects ⁵⁰. Furthermore, opiates peripherally impair the perception of bladder sensation of fullness by inhibiting the parasympathetic outflow and increasing the (internal) sphincter tone by sympathetic over-stimulation, resulting in increased bladder outlet resistance ⁵¹. Epidurally administered morphine has been shown to be associated with marked relaxation of the detrusor in simultaneously performed urodynamic studies and was associated with an increase in maximal bladder capacity and urinary retention ⁵². Studies have demonstrated a much stronger inhibitory effect on bladder function following spinal administration of opiates, compared to intraventricular, intravenous or intramuscular routes ⁵³. A meta-analysis of 94 studies with pooled data of 12,513 patients showed that the highest retention rate (mean 29.1%) occurred with epidural analgesia, strengthening the association between postoperative pain management and the risk of urinary retention ⁵⁴. A double-blind

study evaluating the urodynamic effects of μ -agonists (fentanyl, morphine) and partial μ -agonist-antagonist (buprenorphine) showed that the administration of fentanyl and buprenorphine resulted in altered bladder sensations, increased PVRs and reduced detrusor contractions in men. Compliance and urethral pressures did not change ⁵⁵. The effects in women however are uncertain. Tramadol was reported to cause transient impairment of voiding, which resolved after stopping the drug ⁵⁶. There is also evidence that orally administered opiates play a role in developing urinary retention in women, often in the context of Fowler's syndrome. It is hypothesized that Fowler's syndrome is due to an up-regulation of spinal cord enkephalins, and that exogenous opiates may compound functional abnormalities and thereby predisposing young women to urinary retention ⁵⁷.

Psychological co-morbidities and sexual abuse

The relatively high prevalence of psychological co-morbidities observed in women with urinary retention raises questions around the association between psychological and sexual trauma and LUT dysfunction. A retrospective chart review of 61 women with FS suggested that 24% reported medically unexplained/"functional" symptoms, including loss of consciousness, limb weakness, sensory disturbance and memory impairment. Furthermore, almost a third (31%) had psychological co-morbidities such as anxiety/depression or obsessive compulsive symptoms ⁵⁸. Furthermore, several questionnaire-based studies have demonstrated an association with depression requiring hospitalisation, hysteria, depression, risk of somatisation, definitive somatoform disorder and unspecified psychiatric disorders ^{59 60 61 62}. However despite

the evidence to suggest increase rates of psychological co-morbidities in this group, the impact of these co-morbidities on treatment outcomes has yet to be elucidated.

Sexual abuse can result in psychological trauma, but also pelvic floor damage. A higher prevalence of abuse is reported amongst women with psychological co-morbidities, as well as with LUT dysfunction, however the nature of these associations is poorly understood. Prevalence figures of abuse amongst women in a western population is considerable, ranging between 12% to 25%^{63 64}. A community based survey found a strong correlation between abuse and symptoms of voiding dysfunction, such as urinary frequency, urgency and nocturia⁶⁵. 20% of a large cohort of children reporting a history of sexual abuse complained of one or more urogenital symptoms⁶⁶. In a smaller study, 72% of individuals with a history of sexual abuse reported voiding dysfunction, compared to 22% of controls⁶⁷. In addition, 23% of patients attending a pelvic floor center reported a history of abuse. Patients with multiple urogenital complaints were more likely to have a history of abuse than patients with isolated complaints⁶⁸. Whether addressing psychological trauma related to sexual abuse helps to ameliorate voiding symptoms requires further study.

The association between triggering factors and the pathogenesis of urinary retention needs further exploring:

- How does the inflammatory response in the bladder wall triggered by a UTI influence detrusor contractile functions?

- Which are the opiate receptor sub-types involved in the central inhibition of LUT functions following exogenously administered opiates?
- Are there any phenotypic/genetic characteristics which can help to prognosticate the risk for developing urinary retention following exposure to prescription opiates?
- What is the role of the enkephalinergic system in the midbrain and other regions of the brain stem in the pathogenesis of urinary retention following exposure to opiates?
- Do exogenous opiates influence lower urinary tract functions peripherally- at the level of ganglia in the pelvic splanchnic nerves or directly through receptors in the urothelium, suburothelium or detrusor?
- What are the different types of functional disorders/ psychological co-morbidities seen in women with urinary retention?
- How does the profile of functional symptoms/ psychological co-morbidities differ between women with urinary retention and women with other types of lower urinary tract symptoms, ie. predominantly overactive bladder
- What is the nature of the association between lower urinary tract dysfunction and medically unexplained symptoms in women with idiopathic urinary retention or with Fowler's syndrome?
- Is there a role for psychological assessment when selecting women in urinary retention for sacral neuromodulation?
- Is there a role of managing concomitant psychological co-morbidities using psychological treatments (eg. cognitive behavioural therapy (CBT), systematic

desensitisation, biofeedback) for women in retention for whom sacral neuromodulation is being planned? What effects do these psychological treatments have on voiding dysfunction?

- How does the management of urinary retention fit within the biopsychosocial model of managing medically unexplained functional disorders?

Sacral Neuromodulation

Sacral neuromodulation (SNM) is a well-established successful treatment for idiopathic urinary retention in women, and may serve as a tool to understand the cause for voiding dysfunction. An exaggerated pro-contenance guarding response is thought to inhibit bladder afferent and efferent activity in FS and SNM may work by restoring functions via these signalling pathways ⁶⁹. A functional MRI study in women with FS suggested alterations of activation in different regions of the brain, and these changes were reversed when the stimulator was switched on ⁷⁰. Bladder filling was shown to elicit abnormally strong urethral afferent signals that inhibit bladder afferent activity in the sacral cord, preventing input to the periaqueductal grey and higher brain centres. Thus, SNM seems to act at the level of the sacral cord, by modulating urethral afferents. Recent evidence suggests that modulating the enkephalinergic system plays a role in inhibition of bladder overactivity during SNM ⁷¹.

In patients with DU, SNM may target bladder contractile function rather than the bladder outlet. Bladder contractility significantly improved following SNM in a cohort with

detrusor underactivity who had “detrusor hypocontractility” on urodynamics ⁷². In a cohort of patients with detrusor overactivity with impaired contractility (DHIC), a typical condition in the elderly, 70% undergoing test stimulation showed a treatment response and both DO during filling and DU during voiding improved ⁷³.

Not all women with idiopathic retention respond to SNM however, and recognizing prognostic factors may highlight underlying mechanisms responsible for developing retention. Women with BOO due to FS have a longer duration of benefit, as well as lower revision rates ⁶¹. Better outcomes have been shown in patients with urinary retention who are able to void at least more than 50 mL ⁷⁴, whereas patients with worse detrusor function assessed using the Maastricht-Hannover nomogram were found less likely to respond to SNM ⁷². The finding of acontractility at ambulatory urodynamics is also associated with poor outcomes ⁷⁵. A recent review of 356 patients found no relationship between age and treatment success and suggested that age reduces the need for surgical revision by 3% per additional year of age ⁷⁶.

A history of mental health problems such as hysteria, depression and hypochondria has been shown to be associated with shorter duration of effect ^{77 59 78, 62}, and furthermore, higher revision rates have been observed in patients prescribed antidepressants and analgesics ⁷⁹. Conversely, no association was found between an abnormal Hospital Anxiety and Depression Score and efficacy or safety outcomes following SNM ⁸⁰.

Very little is known regarding sacral neuromodulation and its mechanism of action in urinary retention:

- What role do endogenous endorphins play in the effects of sacral neuromodulation?
- What are the factors that influence outcomes following SNM in women with urinary retention?
- Does the pattern of LUT dysfunction (ie. detrusor underactivity or bladder outlet obstruction), degree of detrusor underactivity (urodynamic findings of underactivity versus acontractility) or concomitant use of opiates influence outcomes following SNM?

Future direction

On the basis of our current understanding, and potential future directions of research, an algorithm to evaluate the cause for voiding dysfunction in women is proposed (figure 1). Currently available investigations recognise a cause in only a proportion of cases, and in the rest the cause remains “idiopathic”. There is a need to further understand the pathophysiological correlates to voiding dysfunction and whereas urodynamic testing provides some information, emerging non-invasive tests, and neurophysiology, may provide further insight into the causes and expand our understanding, and our ability to effectively treat voiding dysfunction in women. It is possible that there exists a cohort of women with a susceptibility to develop urinary retention based upon a putative phenotypic (such as an abnormal urethral sphincter EMG) and genetic characteristics. Further research is required to identify these factors so that in the future it may be possible to define this susceptibility and develop a “scoring system” of different factors

to define risk. Urinary retention may then manifest only in those with the greatest score (susceptibility) when exposed to different triggering factors. Moreover, understanding how these different triggers can precipitate urinary retention opens new directions for treatment. The role of the endogenous enkephalinergic system in the pathogenesis of urinary retention is of particular interest as it may emerge as target for new treatments. Sacral neuromodulation responses may also allow for a better understanding of the causes of voiding dysfunction.

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Figures

Figure 1. Proposed clinical approach to women presenting with voiding difficulties

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