EUROPEAN UROLOGY xxx (2022) xxx

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Female Urology – Incontinence

*Editorial by XXX on pp. x–y of this issue*

# European Association of Urology Guidelines on the Management of Female Non-neurogenic Lower Urinary Tract Symptoms. Part 2: Underactive Bladder, Bladder Outlet Obstruction, and Nocturia

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**Article info**

***Article history:***
Accepted January 26, 2022

***Associate Editor:***
James Catto

***Keywords:***
Female lower urinary tracts symptoms
Underactive bladder
Bladder outlet obstruction

**Abstract**

***Context:*** Female lower urinary tract symptoms (LUTS) are a common presentation in urological practice. Thus far, only a limited number of female LUTS conditions have been included in the European Association of Urology (EAU) guidelines compendium. The new non-neurogenic female LUTS guidelines expand the remit to include these symptoms and conditions.

***Objective:*** To summarise the management of underactive bladder (UAB), bladder outlet obstruction (BOO), and nocturia in females.

***Evidence acquisition:*** The literature search was updated in September 2021 and evidence synthesis was conducted using modified GRADE approach as outlined for all EAU guidelines. A new systematic review on BOO was carried out by the panel for purposes of this guideline.

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https://doi.org/10.1016/j.eururo.2022.01.044


Please cite this article as: S. Arlandis, K. Bø, H. Cobussen-Boekhorst et al., European Association of Urology Guidelines on the Management of Female Non-neurogenic Lower Urinary Tract Symptoms. Part 2: Underactive Bladder, Bladder Outlet Obstruction, and Nocturia, Eur Urol (2022), https://doi.org/10.1016/j.eururo.2022.01.044

Nocturia
Conservative management
European Association of Urology guidelines

***Evidence synthesis:*** The important considerations for informing guideline recommendations are presented, along with a summary of all the guideline recommendations.
***Conclusions:*** Non-neurogenic female LUTS are an important presentation of urological dysfunction. Initial evaluation, diagnosis, and management should be carried out in a structured and logical fashion on the basis of the best available evidence. This guideline serves to present this evidence to practising urologists and other health care providers in an easily accessible and digestible format.
***Patient summary:*** This report summarises the main recommendations from the European Association of Urology guideline on symptoms and diseases of the female lower urinary tract (bladder and urethra) not associated with neurological disease. We cover recommendations related to the treatment of underactive bladder, obstruction of the bladder outlet, and nighttime urination.


## 1. Introduction

Part 2 of the European Association of Urology (EAU) guideline summary on non-neurogenic female lower urinary tract symptoms (LUTS) presented here focuses on the sections relating to underactive bladder (UAB), bladder outlet obstruction (BOO), and nocturia. This summary relates primarily to the patient pathway from presentation through diagnostics and to management of the specific conditions. The best available evidence is summarised and the main recommendations from the full version of the guidelines are presented in a concise and easily digestible format.

## 2. Evidence acquisition

The scope of the EAU guidelines on non-neurogenic female LUTS was expanded, so a new literature search was carried out, with expansion of the terminology and criteria. The full details of the search strategy are available on the EAU website (https://uroweb.org/wp-content/uploads/2021-EAU-Non-neurogenic-Female-LUTS-Guidelines-Search-Strategy.pdf).

The EAU Guidelines Office uses a modified GRADE approach for evaluating the relevant literature on each topic area. High-quality systematic reviews (SRs) are referenced when available, and lower-quality evidence is evaluated if SRs are not available. For this edition of the guideline, new SRs on overactive bladder (OAB) and female bladder outlet obstruction (BOO) were conducted by the panel.

Evidence summary statements and assessments of the quality of the evidence available are reinforced by certainty ratings (ranging from very low to high). Recommendations are then produced in accordance with these certainty ratings, the benefit/harm balance, and consideration of patient values and preferences, where feasible, to give an overall recommendation with a strength rating of "strong" or "weak". It should be noted that the balance between "strong" and "weak" recommendations is related to these three factors rather than just the evidence base for the intervention. Our panel recommendations are reinforced by the inclusion of patient representatives in the panel to provide a valuable input into discussions regarding patient values and preferences.

## 3. Evidence synthesis

### 3.1. *Underactive bladder*

UAB is a common condition, defined by the International Continence Society (ICS) as "a symptom complex characterised by a slow urinary stream, hesitancy, and straining to void, with or without a feeling of incomplete bladder emptying sometimes with storage symptoms" [1].

Detrusor underactivity (DU) is a diagnosis based on urodynamic studies and defined by the ICS as "a detrusor 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" [2].

#### 3.1.1. *Diagnostic evaluation*

*3.1.1.1. Symptoms associated with DU.* According to current data, a pivotal symptom or collection of symptoms to specifically identify DU patients has not been identified. The ICI Questionnaire-Underactive Bladder (ICIQ-UAB) is a research tool that needs further validation before use as a patient-reported outcome measure in routine clinical practice [3].

*3.1.1.2. Urodynamic studies.* Noninvasive studies such as uroflowmetry, postvoid residual (PVR) volume measurement, and bladder voiding efficiency determination are potentially useful in identifying women who might have DU. There is considerable symptomatic overlap with BOO, and uroflowmetry and PVR findings may also be similar. Only invasive urodynamics with pressure-flow studies can reliably distinguish DU from BOO and these urodynamic diagnoses can co-exist. In addition, diagnosis in women is particularly difficult as females can void by relaxing the pelvic floor, that is, without a detectable detrusor contraction during the pressure-flow study and without an increase in abdominal pressure [4]. The simplest methods for defining and diagnosing DU involve the use of cutoff values for the maximum flow rate ($Q_{max}$) and the detrusor pressure at $Q_{max}$ ($P_{det}Q_{max}$). There is no consensus on which threshold values should be used [5] and consequently the prevalence of DU depends on the criteria used [6].

Several proposed measures of contractile strength exist. Watt's factor estimates the power generated by the detrusor per unit area of bladder [7]. Projected isovolumetric

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pressure (PIP) is a gross simplification of the bladder output relation and estimates the maximum detrusor pressure that can be generated by the bladder when the outlet is closed, the isovolumetric detrusor pressure. The bladder contractility index is simply a reduction of PIP to an index [8]. PIP also estimates the isovolumetric detrusor pressure, but was developed in an entirely female population via an experimental method [9]. These parameters do not necessarily reflect what the detrusor might potentially achieve under optimum conditions [10].

### 3.1.2. Disease management

Treatment of female DU includes strategies to ensure bladder drainage, increase bladder contraction, decrease urethral resistance, or a combination [11]. The management goals for UAB are to improve symptoms and quality of life (QoL) and reduce the risk of complications.

#### 3.1.2.1. Conservative management.

*3.1.2.1.1. Behavioural interventions.* Regular or timed voiding should be encouraged in women with impaired bladder sensations. Assisted voiding via abdominal straining with adequate relaxation of the pelvic floor muscle (PFM) has been recommended, as well as double or triple voiding, in an attempt to improve bladder emptying. None of these manoeuvres have proven efficacious in any randomised study. There is a possible association between voiding via excessive abdominal straining and the risk of pelvic organ prolapse (POP) or rectal prolapse [12]. A small retrospective study in neurogenic patients showed that Valsalva voiding may increase the risk of rectal prolapse when compared to clean intermittent self-catheterisation (CISC) [13].

*3.1.2.1.2. PFM relaxation training with biofeedback.* There are no randomised controlled trials (RCTs) examining PFM relaxation training in adult women with UAB. One study found significant relaxation of the PFM after PFM contraction [14] and another study found that PFM relaxation training over time increased the speed of relaxation after a single contraction [15]. In the absence of RCT data for women, the findings of an RCT for children with non-neuropathic UAB and voiding dysfunction comparing the effect of PFM relaxation and biofeedback plus combined treatment (hydration, scheduled voiding, toilet training, and diet) versus combined treatment alone can be cautiously extrapolated to an adult population [16]. The paediatric trial showed that additional PFM relaxation led to significant increases in the mean number of voiding episodes and $Q_{max}$ and decreases in PVR volume and voiding time [16].

*3.1.2.1.3. Clean intermittent self-catheterisation.* CISC has proven efficacy in patients who are unable to empty their bladder and remains a gold standard for reducing the adverse consequences of a high PVR and incomplete voiding, despite the low level of evidence supporting this approach.

*3.1.2.1.4. Indwelling catheter.* An indwelling urinary catheter may be an option for some women for whom all other treatments have failed and who are unable to perform CISC. Complications include urinary tract infection (UTI), stone formation, and urethral damage. Suprapubic catheterisation may be preferable over urethral catheterisation to minimise the risk of urethral trauma and pain [17].

*3.1.2.1.5. Intravesical electrical stimulation.* According to a retrospective study [18], intravesical electrical stimulation may be useful in some patients after prolonged bladder overdistension. However, this must be investigated in high-quality RCTs.

#### 3.1.2.2. Pharmacological management.

*3.1.2.2.1. Parasympathomimetics.* An SR on the use of parasympathomimetics in patients with UAB included ten RCTs [19]. The SR did not support the use of parasympathomimetics for treating UAB, especially when frequent and/or serious adverse effects are taken into account.

*3.1.2.2.2. α-Adrenergic Blockers.* There is limited evidence regarding the effectiveness of α-blockers. One prospective study showed similar improvements in uroflowmetry parameters (specifically in the percentage of patients who had a good therapeutic response) with tamsulosin in women with BOO (39.4%) or DU (32.7%) [20]. Another longitudinal study including 14 women with DU showed clinical and urodynamic improvements after tamsulosin [21]. A prospective single-blind RCT in female patients with DU compared the efficacy of α-blockers, cholinergic drugs, and combination therapy, with the latter exhibiting the best results [22].

*3.1.2.2.3. Prostaglandins.* Prostaglandins E2 and F2 have been used intravesically to treat urinary retention after surgery. A Cochrane SR showed a statistically significant association between intravesically administered prostaglandin and successful voiding among postoperative patients with urinary retention. However, the success rate was low (32%) compared to placebo, with very low certainty of evidence [23].

#### 3.1.2.3. Surgical management.

*3.1.2.3.1. Sacral nerve stimulation.* An RCT included 37 patients in the implantation arm and 31 in the standard medical therapy arm, showing a mean decrease in PVR volume in the implantation group [24]. A meta-analysis of seven studies (one RCT and six observational studies) showed a mean difference in PVR volume reduction of 236 ml and a mean voided volume increase of 299 ml [25]. The response rate during the trial phase ranged from 33% to 90% (mean 54.2%) and the success rate for permanent implantation ranged from 55% to 100% (mean 73.9%), highlighting that patient selection is crucial [26]. A subgroup of women with idiopathic urinary retention (Fowler's syndrome) had a higher response rate of 68–77% [27]. Sacral nerve stimulation (SNS) is a valid option for female patients with DU, with proper patient selection. Patients with evidence of anatomical BOO, suspected loss of intrinsic detrusor contractility, or neurogenic bladder dysfunction showed lower response rates [28].

*3.1.2.3.2. OnabotulinumtoxinA.* There is low-level evidence that onabotulinumtoxinA injections to the external striated urethral sphincter may improve voiding in patients with DU by reducing outlet resistance and suppressing the guarding reflex. Retrospective case studies have shown improvements in voiding symptoms, recovery of sponta-

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neous voiding, and improvements in urodynamic parameters [29,30]. The duration of symptomatic relief is typically 3 mo.

*3.1.2.3.3. Transurethral incision of the bladder neck.* Transurethral incision of the bladder neck has been described in short series of women with refractory DU. In a retrospective case study, 40/82 women (48.8%) achieved satisfactory outcomes (spontaneous voiding with voiding efficiency ≥50%), but five (6.1%) of the patients developed stress urinary incontinence (SUI) and two (2.4%) developed a vesicovaginal fistula (VVF) [31].

*3.1.2.3.4. Other procedures.* Reduction cystoplasty and myoplasty are uncommon procedures with very limited evidence regarding their effectiveness.

Recommendations for the management of UAB are provided in Table 1.

### 3.2. Bladder outlet obstruction

BOO is defined by the ICS as "obstruction during voiding, characterised by increased detrusor pressure and reduced urine flow rate" [2].

*3.2.1. Diagnostic evaluation*

*3.2.1.1. Clinical history.* Evidence regarding the clinical utility of symptoms in the diagnosis of BOO is inconclusive. In a single-centre retrospective study including women with BOO, the authors concluded that symptom assessment alone was insufficient for diagnosis and a full urodynamic evaluation was essential [32]. Studies have found that significant proportions of women presenting with symptoms of urinary incontinence (UI) also have concomitant voiding symptoms and BOO on urodynamics [33,34].

**Table 1** – Recommendations for underactive bladder

| Recommendation | Strength rating |
|---|---|
| Encourage double voiding in women who are unable to completely empty their bladder. | Weak |
| Warn women with UAB who use abdominal straining to improve emptying about the risk of pelvic organ prolapse. | Weak |
| Use CISC as a standard treatment in patients who are unable to empty their bladder. | Strong |
| Thoroughly instruct patients in the technique and risks of CISC. | Strong |
| Offer indwelling transurethral catheterisation and suprapubic cystostomy only when other modalities for urinary drainage have failed or are unsuitable. | Weak |
| Do not routinely recommend intravesical electrical stimulation in women with UAB. | Weak |
| Do not routinely recommend parasympathomimetics in the treatment of women with UAB. | Strong |
| Offer α-blockers before more invasive techniques. | Weak |
| Offer intravesical prostaglandins to women with urinary retention after surgery only in the context of well-regulated clinical trials. | Weak |
| Offer onabotulinumtoxinA external sphincter injections before more invasive techniques as long as the patient is informed that the evidence to support this treatment is of low quality. | Weak |
| Offer sacral nerve stimulation to women with UAB refractory to conservative measures. | Strong |
| Do not routinely offer detrusor myoplasty as a treatment for detrusor underactivity. | Weak |

CISC = clean intermittent self-catheterisation; UAB = underactive bladder.

*3.2.1.2. Clinical examination.* There are no studies evaluating the clinical utility of physical examination in women with suspected BOO; nevertheless, this is universally considered a key part of the medical assessment.

*3.2.1.3. Uroflowmetry and PVR volume.* Studies have shown reasonable correlation between low flow rates, significant PVR volume, and urodynamic BOO [34–37].

*3.2.1.4. Ultrasound.* The major utility of ultrasound scanning in women with BOO is in detecting possible complications such as bladder wall thickening or upper tract dilatation/hydronephrosis. One study reported that transvaginal ultrasonography was able to demonstrate a closed bladder neck during attempts at micturition and concluded that this modality was useful for the evaluation of possible causal factors in female BOO [38].

*3.2.1.5. Magnetic resonance imaging.* There are no reports on the clinical utility of magnetic resonance imaging (MRI) in the diagnosis of female BOO. MRI in patients with a urethral stricture can reveal the degree of periurethral fibrosis, although the prognostic and clinical significance of such a finding has not been established [39].

*3.2.1.6. Electromyography.* Abnormal electromyography (EMG) activity may be associated with nonrelaxation of the striated sphincter, abnormally high urethral pressure, poor bladder sensation, and reduced detrusor contractile strength [40,41]. Complex repetitive discharges and decelerating bursts are specific EMG abnormalities (using periurethral concentric needles) that have been described for patients with high-tone nonrelaxing sphincter, although these abnormalities also occurred in asymptomatic volunteers [42,43]. A review of voiding dysfunction in women showed that increased EMG activity of the PFM using surface electrodes during voiding or nonrelaxation, coupled with pressure-flow information from urodynamics, may be useful in differentiating between functional and anatomical obstruction [44].

*3.2.1.7. Cystourethroscopy.* Cystourethroscopy can be useful for visualising anatomical/mechanical obstruction and providing information regarding its nature, location, and calibre. Given that pelvic malignancy may cause anatomical BOO, cystourethroscopy is considered an essential part of the diagnostic pathway.

*3.2.1.8. Urodynamics and video-urodynamics.* Pressure-flow studies are the mainstay of BOO diagnosis and the characteristic abnormalities are a combination of low flow and high voiding pressure [45]. The urodynamic definition of female BOO remains controversial [46]. The Blaivas-Groutz nomogram is one of the most popular urodynamic criteria for female BOO [47] but it has been suggested that it overestimates obstruction [48]. The addition of fluoroscopic imaging introduces a video-urodynamic criterion for obstruction [49]. However, both methods lack data supporting their clinical validity, especially regarding their predictive value for treatment outcomes [50].

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Several urodynamic cutoff values have been proposed to optimise the diagnostic accuracy of video-urodynamic studies [36]:

- $P_{det}Q_{max} \geq 30$ cm $H_2O$ for differentiating BOO from bladder dysfunction and normal studies (area under the receiver operating characteristic curve [AUC] 0.78);
- Abrams-Griffiths number >30 for differentiating anatomical from functional BOO (AUC 0.66); and
- $P_{det}Q_{max} \geq 30$ cm $H_2O$ for differentiating dysfunctional voiding from poor sphincter relaxation (AUC 0.93).

More recently, Solomon et al [51] devised a nomogram for calculation of the female BOO index (BOOIf) using the formula BOOIf = $P_{det}Q_{max} - 2.2Q_{max}$:

- BOOIf <0: <10% probability of obstruction;
- BOOIf 5–18: equivocal, ≥50% likelihood of obstruction; and
- BOOIf >18: >90% likelihood of obstruction,

Voiding cystourethrography alone or in conjunction with concomitant pressure-flow studies may be useful in delineating the site of the obstruction [49].

### 3.2.2. Disease management

Therapeutic interventions for BOO aim to decrease outlet resistance and increase urinary flow, improve bladder emptying, and reduce LUTS [46,50,52]. Treatment choice is dictated by the nature of the underlying cause of the obstruction.

#### 3.2.2.1. Conservative management.

*3.2.2.1.1. Behavioural modification.* Behavioural modification aims to improve or correct maladaptive voiding. It can include elements such as education regarding normal voiding function, self-monitoring of symptoms, changes in lifestyle factors, avoidance of constipation, and alteration of voiding technique. Ultimately, techniques aim to improve the coordination and synergistic action between the detrusor and sphincter [46,50,52]. General interventions such as those listed above may help with symptoms resulting from BOO, but no quantification of their effect is possible from existing published data.

*3.2.2.1.2. PFM training ± biofeedback.* PFM relaxation training with biofeedback may result in relaxation of the PFM/urethral sphincter in women with dysfunctional voiding. A case series involving women with pelvic muscle or external urethral sphincter hyperactivity during voiding showed improved relaxation and voiding function following PFM training (PFMT) with biofeedback [53]. High-quality RCTs are needed to confirm such observations.

*3.2.2.1.3. Vaginal pessaries.* In a prospective study of 18 women with grade 3 or 4 cystoceles and urodynamic BOO, normal voiding was noted in 17 (94%) following placement of a vaginal pessary [54].

*3.2.2.1.4. Urinary catheterisation.* In a series of 20 patients with voiding dysfunction after tension-free vaginal tape surgery who adopted a CISC programme, 59% had a consistent residual volume <100 ml and 50% were voiding normally within 12 wk [55].

*3.2.2.1.5. Intraurethral inserts.* In a study among women with voiding dysfunction who received an intraurethral insert, device removal within 7 d of insertion occurred in 60% of cases because of discomfort, pericatheter leakage, or technical difficulty. The 20% who continued to use the device in the long term were satisfied, with PVR volumes remaining <100 ml. Adverse events included device migration and symptomatic UTI [56,57]. There is no convincing evidence from RCTs to support the use of intraurethral inserts.

*3.2.2.1.6. Extracorporeal magnetic stimulation.* In a small prospective nonrandomised trial, alfuzosin was compared to electromagnetic stimulation and to the combination of both in women with functional BOO. Significant increases in $Q_{max}$ and decreases in symptoms were observed in all groups, with greater improvements in the combination therapy group [58].

#### 3.2.2.2. Pharmacological management.

*3.2.2.2.1. α-Adrenergic blockers.* In the only placebo-controlled RCT reporting subgroup analyses among women with urodynamically proven BOO, no significant difference was observed in symptoms, $Q_{max}$, or PVR after 8 wk of alfuzosin versus placebo [59]. A small nonrandomised trial compared the use of tamsulosin and prazosin. More patients treated with tamsulosin experienced a decrease in symptoms and treatment satisfaction. More adverse events were reported with prazosin [60].

*3.2.2.2.2. Striated muscle relaxants.* A randomised placebo-controlled crossover trial investigated oral baclofen in 60 women diagnosed with BOO. The results showed a lower number of voids and improvements in $Q_{max}$ and $P_{det}$-$Q_{max}$ with 4 wk of baclofen in comparison to placebo [61].

*3.2.2.2.3. Sildenafil.* A placebo-controlled, randomised crossover trial in women with BOO showed that sildenafil is not superior to placebo in improving symptoms or urodynamic parameters of female BOO [62].

*3.2.2.2.4. Thyrotropin-releasing hormone.* A small RCT including women with voiding problems of mixed aetiologies showed no difference in urodynamic outcomes between intravenous thyrotropin-releasing hormone and placebo [63].

#### 3.2.2.3. Surgical management.

*3.2.2.3.1. Intrasphincter botulinum toxin injection.* A SR in women with dysfunctional voiding showed improvements in symptoms and reductions in residual volume as well as voiding pressure. Larger series in adults describe success rates of 86–100% [64]. In a randomised study, 100 U of onabotulinumtoxinA resulted in a significantly lower International Prostate Symptom Score (IPSS) and larger voided volume in adults with voiding dysfunction [65]. Two small case series of women with BOO who received an intrasphincter injection of onabotulinumtoxinA (100 U) showed improvements in symptoms, a significant reduction in PVR, an increase in $Q_{max}$, and an improvement in static urethral pressure profile [40,66]. The average symptom-free duration was 16.8 wk [66]. Adverse events included UTI and a temporary need for CISC. No SUI was reported.

*3.2.2.3.2. Sacral nerve stimulation.* A cohort study of women who underwent SNS for urinary retention associated with outlet obstruction showed an overall spontaneous voiding rate of 72% over mean follow-up of 4 yr [67]. In a

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single-centre series of patients with idiopathic urinary retention who underwent SNS, 62.5% achieved a >50% reduction in CISC rate [68].

*3.2.2.3.3. POP surgery.* A multicentre prospective study involving women with grade ≥2 symptomatic POP who underwent surgery demonstrated a significant reduction in voiding symptoms and PVR volume at 1 yr after surgery [69]. A retrospective study of women who underwent laparoscopic sacrocolpopexy for POP showed a significant increase in mean postoperative $Q_{max}$ and decreases in $P_{det}$-$Q_{max}$ and PVR volume in those aged ≥65 yr [70].

*3.2.2.3.4. Urethral dilatation.* Pooled analysis of data from an SR of retrospective studies of females with urethral stricture showed a mean success rate of 49% after urethral dilation to 41 Fr at mean follow-up of 46 mo. The mean time to failure was 12 mo. Among treatment-naïve patients, the success rate was 58%, compared to 27.2% among patients who had undergone previous dilatation [39]. Significantly greater improvements in $Q_{max}$ and PVR were seen with intermittent urethral dilatation compared to on-demand dilation for primary urethral stricture [71]. Worsening or new-onset SUI, frequency, and urgency after dilatation have been reported [72].

*3.2.2.3.5. Urethrotomy.* A prospective study of women with urethral strictures who underwent Otis urethrotomy to 40 Fr followed by 6-weekly dilatations demonstrated improvement in IPSS, QoL, voided volume, $Q_{max}$, and PVR volume at 6 mo. Only the improvements in PVR volume and QoL were maintained on long-term follow-up [73].

*3.2.2.3.6. Bladder neck incision or resection.* A review of case studies on bladder neck incision for the treatment of bladder neck obstruction in women reported success rates of 76–100% [45]. Several prospective case series consistently reported significant improvements in IPSS, QoL, $Q_{max}$, $P_{det}Q_{max}$, and PVR after treatment, regardless of the site of the incision, type of energy used, or length of follow-up [74–77]. Complications reported included VVF (3.6%), SUI (4.7%), and urethral stricture (3.6%). Complications of VVF and SUI were noted in the cohort of patients who had their incisions at the 5- and 7-o'clock positions, and not in those who had their incisions at the 2- and 10-o'clock positions [77].

Bladder neck incision and V-Y reconstruction using Nesbit's technique in women with BOO showed similar rates of improvement in symptoms and postoperative PVR volume. V-Y plasty had longer operating and catheter times, a lower improvement rate, a higher transfusion rate, and a higher adverse event rate [78].

*3.2.2.3.7. Urethroplasty or urethral reconstruction.* Retrospective studies reporting outcomes for urethroplasty detail success rates of 57–100% [39,79]. Pooled analysis from studies using vaginal or labial flaps showed a mean success rate of 91% over mean follow-up of 32 mo. Vaginal or labial graft urethroplasty had a success rate of 80% at mean follow-up of 22 mo. Oral mucosal grafts had a mean success of 94% after mean follow-up of 15 mo [39]. A later review of retrospective studies on dorsal buccal mucosal grafts reported success rates of 62–100%, with a pooled success rate of 86% [80]. A long-term study with mean follow-up of 32 mo showed a stricture recurrence rate of 23.1% [79].

A retrospective study comparing women who underwent urethral dilatation or urethroplasty with a dorsal-onlay pedicled labium flap reported significant improvements in both groups. The urethroplasty group had significantly better QoL scores and $Q_{max}$ at follow-up in comparison to the dilatation group [81]. Adverse events associated with urethroplasty include new-onset SUI and urgency and worsening of urge UI.

*3.2.2.3.8. Urethrolysis.* Case series show improved voiding and lower PVR volumes, improvement or resolution of symptoms and QoL, and improvement of urodynamic parameters after urethrolysis treatment [82–84]. De novo SUI was reported in 39% of cases in one study [84]. A greater delay in performing urethrolysis was associated with persistent bladder symptoms [85].

*3.2.2.3.9. Removal, excision, section, or loosening of mid-urethral slings.* Several small retrospective reviews of cases using different techniques for sling revision (incision, partial excision, or excision) showed good success rates in terms of symptom reduction, resumption of voiding with a significant reduction in PVR volume, and improvement of urodynamic parameters. SUI recurs in a small proportion of patients and often to a lesser degree than before the sling procedure. Studies have shown long-term efficacy, including preservation of continence.

No significant difference in success rates was demonstrated on comparison of different techniques. There was a greater need for surgery for recurrent SUI after partial sling excision in the group without an anti-SUI procedure [86].

One study showed that patients who underwent surgical release >180 d after initial anti-SUI surgery had significantly less recurrent SUI in comparison to patients who underwent the release sooner [87].

Recommendations for the management of female BOO are provided in Table 2.

### 3.3. Nocturia

Nocturia was defined by the ICS in 2002 as "the complaint that the individual has to wake at night one or more times to void" and quantified in an updated document in 2019 as "the number of times an individual passes urine during their main sleep period, from the time they have fallen asleep up to the intention to rise from that period" [88].

#### 3.3.1. Diagnostic evaluation

Evaluation of nocturia should include a thorough medical history and physical examination, with particular reference to history of sleep disorders, fluid balance, associated LUTS, cardiovascular and endocrine comorbidity, renal disease, current medications, and history of urological disease [89].

A bladder diary is a vital initial investigation in patients complaining of nocturia. A low nocturnal bladder capacity or global bladder capacity will be highlighted by lower voided volumes. Global polyuria is defined as 24-h urine production >40 ml/kg [90] and may be present in conditions such as diabetes mellitus and diabetes insipidus. The definition of nocturnal polyuria is age-dependent and the thresholds for this diagnosis range from 20% (in younger individuals) to 33% (age >65 yr) of the 24-h urine volume

Please cite this article as: S. Arlandis, K. Bø, H. Cobussen-Boekhorst et al., European Association of Urology Guidelines on the Management of Female Non-neurogenic Lower Urinary Tract Symptoms. Part 2: Underactive Bladder, Bladder Outlet Obstruction, and Nocturia, Eur Urol (2022), https://doi.org/10.1016/j.eururo.2022.01.044

**Table 2** – Recommendations for female BOO

| Recommendation | Strength rating |
|---|---|
| **Diagnosis** | |
| Take a full clinical history and perform a thorough clinical examination in women with suspected BOO. | Strong |
| Do not rely on measurements from urine flow studies alone to diagnose female BOO. | Strong |
| Perform cystourethroscopy in women with suspected anatomical BOO. | Strong |
| Perform urodynamic evaluation in women with suspected BOO. | Strong |
| **Conservative treatment** | |
| Offer PFMT aimed at PFM relaxation to women with functional BOO. | Weak |
| Prioritise research that investigates and advances understanding of the mechanisms and impact of PFMT on the coordinated relaxation of the pelvic floor during voiding. | Strong |
| Offer the use of a vaginal pessary to women with grade 3 or 4 cystocoeles and BOO who are not eligible/inclined towards other treatment options. | Weak |
| Offer urinary containment devices to women with BOO to address urinary leakage as a result of BOO, but not as a treatment to correct the condition. | Weak |
| Offer CISC to women with urethral strictures or post-UI surgery for BOO. | Weak |
| Do not offer an intraurethral device to women with BOO. | Strong |
| **Pharmacological treatment** | |
| Offer uroselective α-blockers as an off-label option to women with functional BOO following discussion of the potential benefits and adverse events. | Weak |
| Offer oral baclofen to women with BOO, particularly those with increased EMG activity and sustained detrusor contraction during voiding. | Weak |
| Only offer sildenafil to women with BOO as part of a well-regulated clinical trial. | Strong |
| Do not offer thyrotropin-releasing hormone to women with BOO. | Strong |
| **Surgical treatment** | |
| Offer intrasphincter injection of botulinum toxin to women with functional BOO. | Weak |
| Offer sacral neuromodulation to women with functional BOO. | Weak |
| Advise women with voiding symptoms associated with POP that symptoms may improve after surgery. | Weak |
| Offer urethral dilatation to women with urethral stenosis causing BOO, but advise on the likely need for repeated intervention. | Weak |
| Offer internal urethrotomy with postoperative urethral self-dilatation to women with BOO due to urethral stricture disease but advise on its limited long-term improvement and the risk of postoperative UI. | Weak |
| Do not offer urethral dilatation or urethrotomy as a treatment for BOO to women who have previously undergone mid-urethral synthetic tape insertion owing to the theoretical risk of causing urethral mesh extrusion. | Weak |
| Inform women of the limited long-term improvement (only in terms of PVR volume and QoL) after internal urethrotomy. | Weak |
| Offer bladder-neck incision to women with BOO secondary to primary bladder-neck obstruction. | Weak |
| Advise women who undergo bladder-neck incision on the small risk of developing SUI, VVF, or urethral stricture postoperatively. | Strong |
| Offer urethroplasty to women with BOO due to recurrent urethral stricture after failed primary treatment. | Weak |
| Caution women on the possible recurrence of strictures on long-term follow-up after urethroplasty. | Weak |
| Offer urethrolysis to women who have voiding difficulties after anti-UI surgery. | Weak |
| Offer sling revision (release, incision, partial excision, or excision) to women who develop urinary retention or significant voiding difficulty after tape surgery for UI. | Strong |
| Caution women about the risk of recurrent SUI and the need for repeat/concurrent anti-UI surgery after sling revision. | Strong |

BOO = bladder outlet obstruction; CISC = clean intermittent self-catheterisation; EMG = electromyography; PFM = pelvic floor muscle; PFMT = PFM training; POP = pelvic organ prolapse; PVR = postvoid residual; QoL = quality of life; SUI = stress urinary incontinence; VVF= vesicovaginal fistula; UI = urinary incontinence.

produced during sleep. A large study conducted across European and American centres involving ~2000 patients identified nocturnal polyuria as a contributory cause of nocturia in 89% of patients who were being treated for LUT abnormalities.

### 3.3.2. Disease management

*3.3.2.1. Conservative management.* Owing to the lack of high-quality evidence, most recommendations are derived from consensus methodology. Interventions that may help with nocturia include:

- Reduction of fluid intake at specific times;
- Avoidance/moderation of intake of caffeine or alcohol;
- Distraction techniques;
- Bladder retraining;
- PFMT;
- Review of medication; and
- Treatment of constipation.

In the EAU systematic review [91], three studies [92–94] were favourable for conservative treatment with PFMT, with another failing to confirm a benefit [95].

Individual and group PFMT approaches appear to be equally effective in reducing nocturia episodes [95]. Most studies evaluating PFMT for nocturia in women with additional urinary symptoms have shown positive results compared with placebo, transcutaneous electrical nerve stimulation (TENS), or anticholinergic drugs [92,93,95].

In patients with obstructive sleep apnoea who complain of nocturia, continuous positive airway pressure was shown to be effective in an SR and meta-analysis of five RCTs involving both sexes [96].

*3.3.2.2. Pharmacological management.*

*3.3.2.2.1. Desmopressin.* A recent SR [91] identified three trials of desmopressin specifically conducted in women. A dose-response relationship was observed. Significant changes in nocturnal urine volumes were reported in favour of higher desmopressin doses. Differences in the nocturnal polyuria index also tended to favour desmopressin over placebo. The level of certainty of the evidence from these trials is low. Desmopressin treatment for nocturia led to significant reductions in nocturnal urine output, nocturnal urinary frequency, and the nocturnal polyuria index [97–99]. Most

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nocturia patients tolerate desmopressin treatment without clinically significant hyponatraemia; however, the risk of hyponatraemia increases with increasing age and lower baseline serum sodium concentration [91].

Desmopressin treatment in elderly patients should include careful monitoring of serum sodium concentrations and should be avoided in patients with a baseline serum sodium concentration below the normal range [100].

Desmopressin can be safely combined with anticholinergics with significant additional benefit in women with OAB and nocturnal polyuria, as shown by a multicentre RCT of 97 patients [101].

*3.3.2.2.2. Anticholinergics.* A SR [91] identified three RCTs involving anticholinergics such as oxybutynin [94] and tolterodine [95,101]. Treatment of nocturia in OAB patients with anticholinergic drugs led to a reduction in nocturia episodes.

*3.3.2.2.3. Oestrogens.* In a recent SR [91] only a single RCT investigating the efficacy of oestrogen for nocturia was identified [102]. Vaginal oestrogen may be beneficial in the treatment of nocturia in approximately 50% of women, but the certainty of evidence for this outcome was low.

*3.3.2.2.4. Diuretic treatment.* A randomised placebo-controlled study investigating afternoon (timed) diuretic treatment with furosemide showed a reduction in nocturia episodes and nocturnal voided volume in men, but no similar studies have been conducted in women [103].

Recommendations for the management of nocturia are provided in Table 3.

**Table 3** – Recommendations for nocturia

| Recommendation | Strength rating |
|---|---|
| Take a complete medical history from women with nocturia. | Strong |
| Use a validated questionnaire during the assessment of women with nocturia and for re-evaluation during and/or after treatment. | Weak |
| Use a 3-d bladder diary to assess nocturia in women. | Strong |
| Do not use nocturnal-only bladder diaries to evaluate nocturia in women. | Weak |
| Offer women with LUTS lifestyle advice before or concurrent with treatment. | Strong |
| Offer PFMT for nocturia (either individually or in the group setting) to women with UI or other storage LUTS. | Strong |
| Offer women with nocturia and a history suggestive of obstructive sleep apnoea a referral to a sleep clinic for an assessment of suitability for continuous positive airway pressure treatment. | Strong |
| Offer a anticholinergic treatment for nocturia to women with UUI or other storage LUTS following appropriate counselling regarding the potential benefits and associated risks. | Strong |
| Inform women with nocturia that the combination of behavioural therapy and anticholinergic drugs is unlikely to provide greater efficacy than either modality alone. | Weak |
| Offer a combination of anticholinergics and desmopressin to women with OAB and nocturia secondary to nocturnal polyuria following appropriate counselling regarding the potential benefits and associated risks. | Weak |
| Offer vaginal oestrogen treatment to women with nocturia following appropriate counselling regarding the potential benefits and associated risks. | Weak |
| Offer timed diuretic treatment to women with nocturia secondary to polyuria following appropriate counselling regarding the potential benefits and associated risks. | Weak |

LUTS = lower urinary tract symptoms; OAB = overactive bladder; PFMT = pelvic floor muscle training; UUI = urge urinary incontinence.

## 4. Conclusions

Non-neurogenic female LUTS comprise a broad range of symptomatologies and conditions, and diagnostic uncertainty is common. A thorough history and a stepwise logical approach to investigation are required to arrive at an accurate diagnosis. Management should be guided by individual patient factors and a collaborative approach with patients to guide treatment decisions.

***Author contributions***: Salvador Arlandis had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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*Statistical analysis*: None.
*Obtaining funding*: None.
*Administrative, technical, or material support*: None.
*Supervision*: Arlandis, Harding, Lapitan.
*Other*: None.

***Financial disclosures:*** Salvador Arlandis certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Salvador Arlandis has received company speaker honoraria from Astellas Pharma S.A., Bayer Hispania S.L., and Lacer-Holliste; has received honoraria for consultation from Presurgy S.L., Boston Scientific Europe, and Coloplast Productos Medicos; has participated in clinical trials by GlaxoSmithKline, Astellas, Ipsen, and Urovant; has received travel grants from Astellas Pharma S.A., WellSpect, Lacer, and Rovi; and has been a company consultant for Lacer Laboratories. Christopher K. Harding is a company consultant for Teleflex Medical; has received speaker honoraria from Astellas, Allergan, and Medtronic; has participated in clinical trials by Medtronic; has received fellowship and travel grants from Medtronic; and has received research support from the National Institute for Health Research and The Urological Foundation. Marie Carmela Lapitan has received speaker honoraria from Astellas, AstraZeneca, and GSK. Elisabetta Costantini has received research support from S&R Farmaceutici. Jan Groen has participated in clinical trials by Neuspera Medical Inc. Veronique Phé has received speaker honoraria from Medtronic and Viatris and is a company consultant for Allergan and Coloplast. Huub van der Vaart has ownership interest in a patent with Ligalli B.V.; is a director of Berman Clinics; receives royalties from NVOG; is participating in clinical trials by UroGyn; and receives research support from ZonMw and NWO-TTW. Benoit Pey-

ronnet is a company consultant for Boston Scientific. Lazaros Tzelves receives research support from the National and Kapodistrian University of Athens and the ASCAPE Project and is participating in a clinical trial by the ASCAPE Project. The remaining authors have nothing to disclose.

***Funding/Support and role of the sponsor*:** None.

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Please cite this article as: S. Arlandis, K. Bø, H. Cobussen-Boekhorst et al., European Association of Urology Guidelines on the Management of Female Non-neurogenic Lower Urinary Tract Symptoms. Part 2: Underactive Bladder, Bladder Outlet Obstruction, and Nocturia, Eur Urol (2022), https://doi.org/10.1016/j.eururo.2022.01.044

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