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ORIGINAL ARTICLE

Long-term management of luminal urethral stricture in women

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Abstract
Introduction and hypothesis The objective was to report our long-term experience of luminal urethral stricture (LUS) in women treated with dilation under general anesthesia.
Methods Following institutional review board approval, charts of women who underwent urethral dilation (UD) under general anesthesia for LUS and had over 6 months' follow-up were reviewed. LUS was confirmed by urethroscopy. UD was performed using female dilators with guidewire and Heyman dilators when required. Outcome measures included the number of UD procedures and the duration and frequency of clean intermittent catheterization (CIC). Success was defined as the ability to void without repeat UD and with no need for CIC 1 year after UD. Possible predictive variables were analyzed.
Results Between 2000 and 2013, a total of 30 out of the 32 women who underwent UD for LUS met the inclusion criteria. Mean follow-up was 59 (range: 7 to 151) months. Thirteen women in the success group showed improvement in the mean maximum flow rate (pre 11 ml/s to post 27.8 ml/s) and post-void residual (pre 85 ml to post 43 ml). In the failure group of 17 patients, 2 required chronic CIC 1 year after a single UD. Fifteen opted for repeat UD. After second ($n=5$), third ($n=2$), and fourth ($n=2$) UD, 9 patients came off CIC and reported durable satisfaction. Four women remained on regular CIC. Two required a permanent suprapubic catheter.
Conclusion At a mean follow-up of 5 years, UD for LUS produced durable resolution in 43 % of our patients. Another 30 % fully benefited from repeat UDs. Shorter duration of symptoms before presentation was significantly associated with success.

Keywords Luminal urethral stricture · Urethral dilation · Women · Long-term outcome

Introduction

The incidence of bladder outlet obstruction (BOO) in women who present with lower urinary tract symptoms has been reported to be between 3 and 23 % [1–4]. Among etiologies for BOO, luminal urethral stricture (LUS) is infrequent, with a reported incidence of 4–18 % in BOO series, and thus have been relatively understudied [1, 5–7]. Etiology of LUS includes previous instrumentation of the urethra, pelvic trauma, inflammation, and/or radiation [3, 8, 9]. Presenting symptoms of LUS commonly include voiding lower urinary tract symptoms suggestive of BOO, namely slow stream, intermittency, hesitancy, straining, and terminal dribbling, in addition to intermittent recurrent urinary tract infections secondary to urinary stasis and irritative voiding symptoms such as frequency and urgency [8]. Diagnosis relies primarily on cystourethroscopy (defining the site of LUS and the inability to pass through the LUS) with support from urodynamic studies and voiding imaging, including voiding cystourethrogram (VCUG) and/or videourodynamic studies [8, 9]. These studies usually exhibit a narrowing of the urethral lumen in the mid to distal region with proximal ballooning [8].

Urethral dilation (UD) is typically the first intervention for LUS, although it is used for a range of other urethral conditions in women as well [10–14]. While UD in the office has been popular, the data regarding UD under general anesthesia is limited. Smith et al. advocated the efficacy of office UD followed by long-term clean intermittent self-catheterization

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(CIC) for urethral stricture disease [15]. Urethrotomy is generally less favored because of the increased risk of sphincter compromise and new-onset incontinence [14–17]. Surgical reconstruction of the strictured female urethra has also been reported using a variety of flaps, but in cases of LUS, these more complex procedures run the risk of traumatizing the sphincteric mechanism and risking secondary incontinence as well [3, 18]. Worsening or new-onset stress urinary incontinence (SUI) is a concern with UD, although markedly less than with urethrotomy or surgical reconstruction [12–14]. As the evidence for the different treatment modalities in addressing urethral stricture is limited, we reviewed our long-term experience with the management of nonradiated and nontraumatic LUS in women.

Materials and methods

Following Institutional Review Board approval, a retrospective chart review of all patients who underwent UD under general anesthesia at one institution by the same surgeon (PZ) from 2000 to 2013 was performed by a third party reviewer not involved in patient care (SP) using an electronic record system (EPIC, vCDR). LUS was defined on urethroscopy by visualization of a circumferentially narrowed and distorted urethral lumen (Fig. 1b) [3]. Urethroscopy was performed with a flexible cystoscope in the office setting or a 17.5-Fr Wolff blunt end rigid female urethroscope (Fig. 1a) in the operating room to confirm the fixed and anatomical nature of the LUS. Luminal stricture locations included the mid- (Fig. 1b), mid-to-distal, and mid-to-proximal urethra. Patients were excluded if they had a history of meatal stenosis, bladder neck contracture, primary bladder neck obstruction, urethral diverticulum (present or repaired), neurogenic bladder, pelvic radiation, pelvic trauma, or gynecological, urethral, or bladder malignancy. Patients with less than 6 months' follow-up were also excluded.

Pre-operative evaluation involved history, including demographics, previous urethral procedures, and presenting symptoms; physical examination findings; non-invasive flow rate; and post-void residual (PVR) according to a bladder scan. Additional studies were obtained as clinically indicated, including standing lateral VCUG (Fig. 2) to confirm the site of the LUS, urethral magnetic resonance imaging (MRI) to exclude a urethral tumor or diverticulum, and/or multichannel invasive urodynamic testing to confirm obstruction (high voiding pressures with a low flow) [11]. Such additional testing was limited in patients with extremely narrow urethras that could not be catheterized and in those who were concerned with provoking urethral pain.

Urethral dilation was performed under general anesthesia with female dilators up to 39–43 Fr, with guidewire and Heyman dilators when required by a very narrow LUS (Fig. 3). Often, a catheter was left in place for variable periods of time (ranging from a few days to a few weeks depending on LUS severity, history of previous UD, intra-operative urethral wall bleeding, and/or the presence of concurrent urinary tract infection). Of note, UD was routinely performed under perioperative i.v. antibiotic coverage, with daily oral antibiotic prophylaxis coverage extended as long as the catheter remained indwelling.

Primary outcome measures included the number of urethral dilations and duration and frequency of CIC. Success was defined as the ability to void after first UD without the need for another UD or for CIC at 1 year following UD. Failure was defined as recurrent LUS requiring repeat UD, chronic CIC, and/or urinary diversion (suprapubic tube).

Variables that could affect success versus failure were investigated to assess predictive factors that could determine the optimal candidate for UD. One of our hypotheses was that patients with a long history of repeated UD, menopausal women not on hormone replacement therapy (HRT), and those with strictures that were very narrow and required the use of Heyman dilators might not respond successfully to urethral dilation.

Post-operatively, patients were seen at 6 weeks, 3 months, 6 months, and then yearly thereafter. Post-operative evaluation included follow-up history (including assessment of symptom recurrence and need for CIC), physical examination, flow rate, and PVR by bladder scan in addition to VCUG and cystourethroscopy, as indicated. After the first UD, many

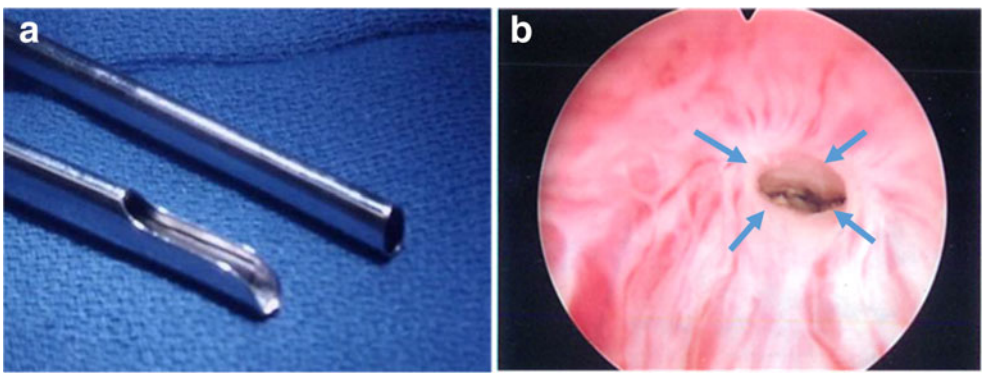

Fig. 1 **a** 17.5-Fr Wolff female urethroscope (*right*) adjacent to a male urethroscope (*left*). **b** Pinpoint luminal urethral stricture (LUS; less than 1 mm) visualized on urethroscopy. *Arrow*s denote site of luminal stricture

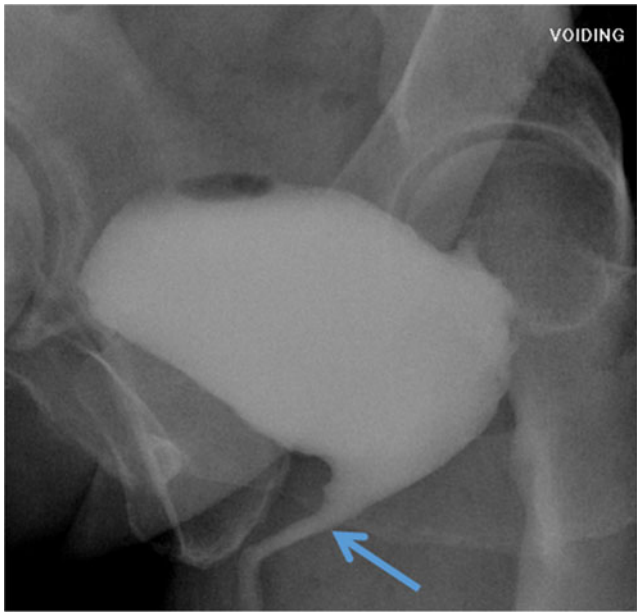

Fig. 2 Lateral standing voiding cystourethrogram (VCUG) indicating a trabeculated bladder, a ballooning proximal urethra and bladder neck, and a sharp transition at the site of the LUS in the mid-urethra (*blue arrow*)

patients experienced no recurrent symptoms and never performed CIC. Those who began experiencing mild recurrence of voiding symptoms were taught CIC by a nurse in clinic and instructed to do so on a daily basis. Some were able to gradually reduce CIC to every other day, 2–3 times weekly, monthly, and then discontinue if their symptomatology durably improved. Among the failures, some patients opted for a repeat UD when they felt that their first UD had produced significant improvement, but was not sustained. Some women, on the other hand, opted for regular CIC rather than undergoing an additional procedure. After their second UD, patients were advised to consider CIC to maintain urethral patency. However, because of discomfort or difficulty catheterizing (owing to obesity, arthritis, etc.), a few chose either a third of a fourth UD, whereas others elected for permanent suprapubic tube placement.

Using a structured telephone interview, attempts were made to contact patients with less than 6 months' follow-up to seek information on long-term results and satisfaction.

A literature review of comparative studies included a PubMed search using combinations of keywords such as "urethral stricture," "urethral dilation," "urethral dilatation," "female," and "women" with restrictions for articles in English and on human subjects. Articles focusing on male or pediatric patients, stricture secondary to trauma or neurogenic bladder, obstruction at the level of the bladder neck or external meatus, or alternative urethral procedures (urethrotomy, urethroplasty, etc.) were excluded.

Descriptive statistics used means and ranges for continuous measures and frequencies and percentages for categorical measures. Characteristics of the success and failure groups were compared using a two-sample t test assuming unequal variances, with $p < 0.05$ considered statistically significant.

Results

From 2000 to 2013, a total of 30 out of the 32 women who underwent UD for LUS met all the inclusion criteria. Four out of 6 patients with less than 6 months' clinic follow-up responded to structured telephone questionnaire and were therefore included in analysis. Two could not be contacted and remained lost to follow-up: these two patients were excluded from the analysis.

Among the 30 women with more than 6 months' follow-up, mean follow-up was 59 (standard deviation: 39, median: 50, range: 7 to 151) months. Nineteen patients (63 %) were followed for 3–13 years. Table 1 lists the baseline characteristics of patients. Common presenting symptoms included frequency ($n = 20$), recurrent urinary tract infections ($n = 16$), urgency ($n = 13$), feeling of incomplete emptying ($n = 12$), urinary incontinence ($n = 10$) and hesitancy ($n = 9$), intermittency ($n = 7$), and weak urinary stream ($n = 5$). Of 15 women who underwent multichannel invasive UDS, all were found to be obstructed. Twenty of the 24 patients with VCUG showed narrowing of the urethra; 4 could not void during the study. Finally, 10 patients underwent MRI because of a suspected tumor or diverticulum. None was found to have tumor or diverticulum; 7 showed urethral wall fibrosis and narrowing

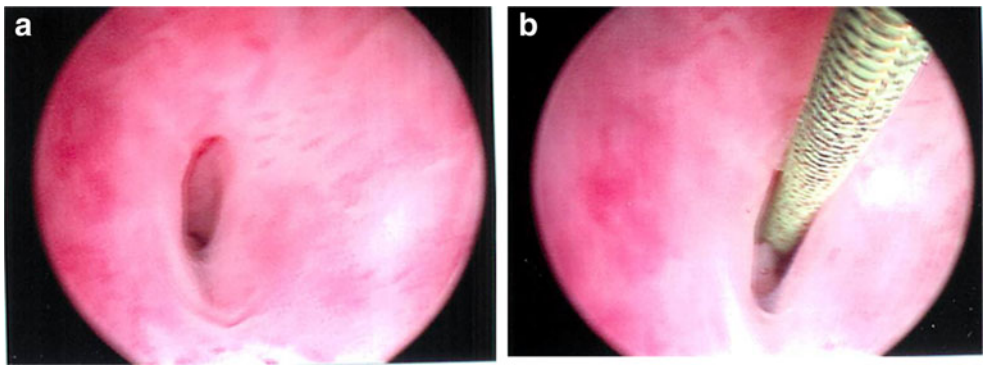

Fig. 3 **a** Very narrow ring-like LUS. **b** Use of Heyman dilators for safe dilation (compare with Fig. 1, where the use of Heyman dilators was not required)

Table 1 Baseline demographics

Variable	Number of patients	Percentage
Age (mean/range)	55	23–86
BMI (mean/range)	29	20–50
Race		
Caucasian	23	77
African–American	4	13
Hispanic	3	10
Gravidity (median/range)	3	0–7
Parity (median/range)	2	0–7
Previous urethrotomy	1	4
History of previous urethral dilations	10	33
Duration of symptoms (years; mean/range)	8.4	0.5–30
Presenting symptoms		
Frequency	20	67
Urgency	13	43
Hesitancy	9	30
Feeling of incomplete emptying	12	40
Incontinence	10	33
Recurrent urinary tract infections	16	53
Presenting with >1 symptom	24	80
Additional testing		
Voiding cystourethrogram	24	
Multichannel urodynamic studies	15	
Magnetic resonance imaging	10	

of the urethra. All 30 women underwent cystourethroscopy showing circumferentially narrowed urethral lumen.

The average total operating room time was 27 (standard deviation: 10, median: 27, range: 10–50) min. Following UD, 14 patients had indwelling catheters for a mean of 11 (standard deviation: 11, median: 7, range: 1–40) days. Median catheter size was 22-Fr (range: 18–24). No perioperative complications were recorded based on a review of the operative notes and follow-up clinical visits.

Figure 4 depicts a flow chart of patient outcomes. Of 30 women, 13 patients (43 %) had a successful outcome according to the above-mentioned criteria. Twelve of the 13 voided well after their first UD and never needed CIC. One patient required short-term CIC owing to a mild recurrence of symptoms, but because she gradually ceased CIC within several months and her voiding pattern remained satisfactory, she was counted as a success.

Post-operatively, 4 patients (31 %) in the success group reported persistent frequency, and 5 had urgency (38 %). Consistent with previous studies of UD [12, 13], the 13 women in the success group had improvement in the mean maximum flow rate and a reduction in mean PVR. Mean maximum flow rate increased from 7 ml/s (standard deviation: 3.6, median: 7, range: 1.3–13.2) pre-operatively to 17.2 ml/s (standard deviation: 8.5, median: 14.7, range: 9.3–42.3) post-operatively ($p = 0.0001$). Mean PVR decreased from 85 ml (standard deviation: 93, median: 50, range: 0–310) pre-operatively to 43 ml (standard deviation: 71, median: 22, range: 0–293) post-operatively ($p = 0.08$).

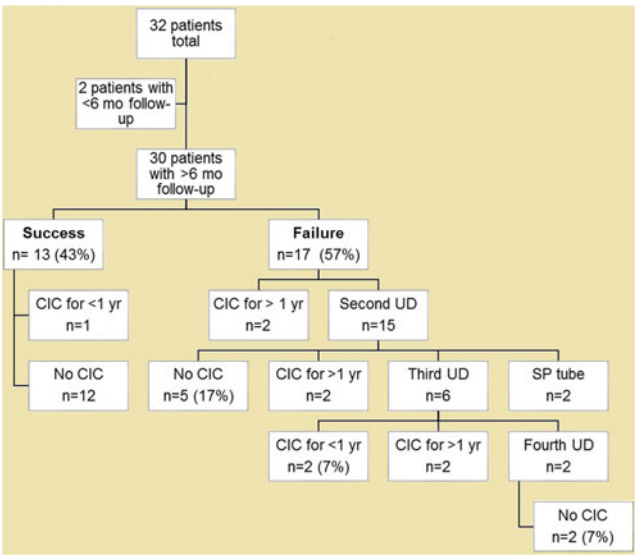

Fig. 4 Flow chart of the patient population and outcomes. *CIC* clean intermittent catheterization, *UD* urethral dilation, *SP* suprapubic

In the failure group consisting of 17 patients, 2 remained on chronic CIC for over a year after a single UD, as they wanted to avoid an additional procedure. The remaining 15 opted for a repeat UD because of temporary improvement in their voiding symptoms after their first UD. The mean time between first and second UD was 17 (standard deviation: 15, median: 12, range: 2–53) months. After a second UD, patients were advised to consider CIC to maintain urethral patency. Five of the 15 women elected not to perform CIC and still experienced durable satisfactory symptom improvement; mean follow-up for this sub-group was 55 (standard deviation: 34, median: 49, range: 16–109) months. Two of the 15 underwent placement of a permanent suprapubic catheter. Five of the 15 patients had elected CIC: 2 performed CIC for longer than 1 year after their second UD, whereas 3 patients had to discontinue CIC for technical reasons (back surgery, arm injury) and subsequently required repeat UD owing to a significant recurrence of symptoms. The remaining 3 of these 15 patients elected for repeat UD rather than for performing CIC. Therefore, a total of 6 women underwent a third UD.

After a third UD, 2 women were able to discontinue CIC within a year without experiencing recurrent LUS symptoms; follow-up for these 2 patients was 37 and 71 months. Two remained on chronic CIC for over a year. The remaining 2 women who remained opposed to CIC chose to undergo a fourth UD and experienced no recurrent symptoms afterwards.

For the 6 who remained on CIC for more than 1 year after their last UD, their CIC regimens included: daily ($n=1$), every other day ($n=1$), three times weekly ($n=1$), twice weekly ($n=2$) or monthly ($n=1$). No patients required urethrotomy or open urethroplasty during our follow-up.

Flow rate and PVR was closely monitored in the failure group approximately every 1–3 months. In these women, these values tended to improve initially after UD as patients usually reported a transient resolution of their lower urinary tract symptoms. But as the flow rate and PVR eventually worsened as did their symptoms, further therapy was considered.

With regard to our hypotheses, Table 2 describes outcomes versus several variables. The failure group was found to have significantly longer duration of symptoms before presentation ($p=0.03$). All other differences between the success and failure groups were found to be nonsignificant, including that of worsening or new-onset stress urinary incontinence (SUI) and the use of hormone replacement therapy (HRT). To elaborate, 4 patients in the success group reported SUI: 2 reported that it was persistent and unchanged compared with their pre-operative status, whereas 2 reported that it was new-onset but very mild, not requiring the use of pads. One patient in the failure group reported SUI, which was actually slightly improved compared with her pre-operative status. Three women in the success group reported using systemic HRT versus 2 women in the failure group.

Discussion

This retrospective analysis of long-term outcomes after dilation of female LUS under general anesthesia reports on 30 women with a mean follow-up of 5 years. In 43 % of patients, durable and satisfactory results were achieved after a single UD under anesthesia followed by CIC for less than a year, with no need for additional UD or CIC beyond 1 year.

Table 2 Comparison of success and failure groups after one urethral dilation (UD) for key variables

Variable	Success group; mean (range) ($n=13$)	Failure group; mean (range) ($n=17$)	p value
Length of follow-up (months)	51 (7–143)	65 (16–151)	0.33
Age, years (range)	58 (30–86)	52 (23–78)	0.32
BMI	28 (21–43)	29 (20–50)	0.71
Gravidity, median (range)	3 (0–5)	3 (0–7)	0.9
Parity, median (range)	2 (0–4)	2 (0–7)	0.9
Smoking, number of patients (%)	2 (15)	1 (6 %)	0.44
Menopausal, number of patients (%)	9 (69)	11 (65)	0.80
Using systemic hormone replacement, number of patients (%)	3 (23)	2 (12)	0.46
Duration of symptoms, years (range)	4 (0.5–14)	12.8 (1–30)	0.03
Previous UD, number of patients (%)	3 (23)	7 (41)	0.30
Use of Heyman dilators, number of patients (%)	3 (10)	8 (47)	0.18
Home with catheter, number of patients (%)	5 (38)	9 (53)	0.48
Catheter duration (days)	13.5 (2–40)	10.5 (2–28)	0.77
Post-operative incontinence, number of patients (%)	4 (31)	1 (6)	0.11

Although counted as failures, a subgroup of a sixth of our patients had durable and satisfactory results after a second UD, an additional 2 patients were rescued with a third UD, and another two with a fourth UD. None of these patients required CIC for longer than 1 year after their last UD. Therefore, UD under general anesthesia can be safe and effective in the management of LUS. In contrast to male counterparts in whom each sequential dilation can result in a higher recurrence rate, this series in women suggests that repeat UD can ultimately produce satisfactory results.

The only significant difference between the success and failure groups was the duration of symptoms before presentation. However, the duration of symptoms does not account for the severity of symptoms; thus, it is possible that the success group suffered more severe symptoms and therefore presented earlier. Also, the fact that the rates of prior UD were higher among the failure group suggests that several women in the failure group had likely presented to other practitioners earlier.

We found no difference between the success and failure groups in the proportion of women who were menopausal but not using HRT, in contradiction to our hypothesis. However, as expected, rates of previous UD and use of Heyman dilators were higher in the failure group. Also, the duration of post-operative urethral catheter was longer in the success group. Not surprisingly, the follow-up was longer among women in the failure group as these patients required repeat UD procedures and closer monitoring. However, these differences were not statistically significant.

To our knowledge, few long-term studies on the use of dilation to manage LUS have been reported thus far. In Smith et al., 7 women were followed for a mean of 21 (range: 6–34) months [15]. These women underwent UD to 30-Fr in the office followed by long-term CIC [15]. According to our definition of success versus failure, 4 patients in the Smith et al. study would have been considered failures, requiring repeat UD or urethrotomy—in this context, the success rate would be 43 % [15]. Women in that study who were "failures" were initially noncompliant with CIC [15]. After compliance was ensured, patients did quite well, with reported improvement in symptoms [15]. As shown by Smith et al., the recurrence rate and need for repeat dilation was increased with patients discontinuing CIC [15]. However, we and other investigators have observed that many patients prefer repeat UD over ongoing CIC or more invasive surgical urethroplasty [13, 19].

Other studies currently available are not as directly comparable, as their inclusion criteria were broader and covered a variety of indications (voiding dysfunction, overactive bladder, meatal stenosis, bladder neck stricture) and a large range of interventions, some more invasive (urethrotomy, urethroplasty, mucosal graft, etc.) [3, 12, 13, 18]. Nonetheless, success rates in these studies range from 6 to 47 %, a finding not dissimilar from our success rate in this series [3, 12, 13, 18].

Strengths of our study include that the same diagnostic and interventional procedure (UD) was performed by the same surgical team. Specifically, each UD was carried out using progressively larger "sounds" up to the same size range and until the LUS was completely disrupted based on the ease of "sound" insertion. In addition, our longer follow-up and attempt to minimize the "lost to follow-up" bias by contacting all patients with less than 6 months' follow-up strengthened the study findings. Variables for success that were studied revealed the importance of early detection to ensure prompt management and better outcomes.

Limitations of our study include its retrospective nature and 2 patients remaining lost to follow-up. In addition, there was a lack of routine questionnaire usage to quantify the severity of the obstructive LUS symptomatology; thus, symptom reporting was subject to patient reporting. For example, patients in the success group often described frequency as urinating every 4–5 h whereas patients in the failure group described frequency as urinating every 1–2 h. There is no standard evaluation of female patients who present with obstructive urinary symptoms [18]. In addition, there is no consensus on the diagnostic urodynamic criteria for BOO in women and no widely-used validated symptom questionnaires to assess obstructive symptoms in women [18, 20]. Therefore, assessment involves a combination of patient-reported symptoms and imaging/urodynamic studies.

Another limitation is that only one intervention was used (UD under anesthesia). In addition, despite the fact that risk factors for success versus failure covered a wide range of variables, others, such as degree of urethral fibrosis, were beyond the scope of this study.

Conclusion

This long-term retrospective data analysis on LUS treated with urethral dilation under anesthesia suggests durable efficacy at a mean follow-up of 5 years in 43 % of patients. Another 30 % of our patients who underwent a second, third, and sometimes even a fourth UD, benefitted in the long term as well, with no need for CIC 1 year after their last UD. The most significant variable related to success was duration of symptoms before presentation for treatment, underlining the importance of the early recognition of LUS.

Compliance with ethical standards

Conflicts of interest None.

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