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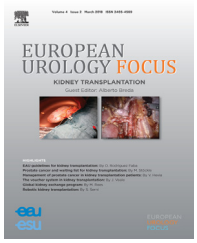

Guidelines

European Association of Urology Guidelines on Urethral Stricture Disease Part 3: Management of Strictures in Females and Transgender Patients

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Abstract

Context: Urethral stricture management guidelines are an important tool for guiding evidence-based clinical practice.
Objective: To present a summary of the 2021 version of the European Association of Urology (EAU) guidelines on management of urethral strictures in females and transgender patients.
Evidence acquisition: The panel performed a literature review on these topics covering a time frame between 2008 and 2018 and used predefined inclusion and exclusion criteria for study selection. Key papers beyond this time period could be included as per panel consensus. A strength rating for each recommendation was added based on the review of the available literature and after panel discussion.
Evidence synthesis: Management of urethral strictures in females and transgender patients has been described in a few case series in the literature. Endoluminal treatments can be used for short, nonobliterative strictures in the first line. Repetitive endoluminal treatments are not curative. Urethroplasty encompasses a multitude of techniques and adaptation of the technique to the local conditions of the stricture is crucial to obtain durable patency rates.
Conclusions: Management of urethral strictures in females and transgender patients is complex and a multitude of techniques are available. Selection of the appropriate technique is crucial and these guidelines provide relevant recommendations.
Patient summary: Although different techniques are available to manage narrowing of the urethra (called a stricture), not every technique is appropriate for every type of stricture. These guidelines, developed on the basis of an extensive literature review, aim

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to guide physicians in selecting the appropriate technique(s) to treat a specific type of urethral stricture in females and transgender patients.

Take Home Message: Although different techniques are available to manage urethral strictures, not every technique is appropriate for every type of stricture. Management of urethral strictures in females and transgender patients is complex and a multitude of techniques are available. Selection of the appropriate technique is crucial and these guidelines provide relevant recommendations.

1. Female urethral strictures

The management of female urethral stricture disease is summarised in Figure 1 and recommendations are provided in Table 1.

1.1. Definition and aetiology

A female urethral stricture (FUS) is defined as a "fixed anatomical narrowing" causing reduced urethral calibre, varying between <10 Fr and <20 Fr, with the majority of series defining <14 Fr as diagnostic, compared to a "normal" urethral calibre of 18–30 Fr [1].

True FUS occur in 0.08–5.4% of women with refractory lower urinary tract symptoms (LUTS), with a higher incidence among women older than 64 yr [2].

The aetiology of FUS is mainly idiopathic (48.5%), followed by iatrogenic (24.1%) and traumatic (16.4%) causes. In cases with iatrogenic aetiology, prior urethral dilations, difficult or traumatic catheterisation with subsequent fibrosis, and urethral surgery (mainly diverticulum surgery, fistula repair, and anti-incontinence procedures) are responsible for stricture development in the majority of patients [3–15].

1.2. Diagnosis

The symptoms of FUS are nonspecific and therefore generally nondiagnostic. They consist of mixed filling and voiding symptoms. It is important to exclude a urethral stricture in females with LUTS.

Assessment of the flow rate and postvoid residual volume is recommended as initial noninvasive screening tools and for simple monitoring of effect of treatment. Further examinations such as voiding cystourethrography, a voiding urodynamic study, cystourethroscopy, ultrasound, and magnetic resonance imaging can be performed when indicated [1,3,5,11,16,17].

1.3. Treatment

1.3.1. Minimally invasive treatments

Owing to its low complication rate, its minimally invasive nature, and the reasonable success rate, it is acceptable to start with urethral dilation as a first-line treatment for an uncomplicated FUS.

There are no papers detailing the use and outcomes of internal urethrotomy specifically for the management of FUS. If utilised, urethrotomy in the female urethra involves incisions at the 3 o'clock, 9 o'clock, and occasionally 12 o'clock positions [18].

Patency after dilation ranges from 7.5% to 51% [3,9,17,19]. When dilation was continued with intermittent self-dilation, stabilisation of the stricture with "patency" was obtained in 37.3–100% of cases at 12–21 mo of follow-up [13,14,20,21].

There is no specific treatment regimen available for the timing and frequency of intermittent dilation.

The patency rate of meatoplasty at 12 mo reported in a small case series was excellent (97%). For short meatal strictures, meatoplasty is a first-line treatment option [22].

1.3.2. Urethroplasty

Urethroplasty for FUS provides good patency rates with low complication rates. The literature consists of small retrospective case series. Thus, comparison between different techniques is not possible and no particular type of urethroplasty is found to be superior to another. The technique of choice should be determined by the surgeon's experience, the availability and quality of graft/flap material, and the quality of the ventral versus dorsal urethra.

Patency rates of 73–100% were reported after follow-up of 22–27 mo among women who underwent vaginal graft augmentation urethroplasty performed via a dorsal approach [23–26].

Techniques described for vaginal flap urethroplasty consist of an inverted vaginal U-flap, a lateral vaginal C-flap, and a vaginal island flap, all via a ventral approach. Patency rates of 67–100% after follow-up of 30–80.7 mo were reported. Potential complications include urinary incontinence, urinary tract infections, and intravaginal direction of the urinary stream [3,4,6,10,12,13,27,28].

Dorsal or ventral augmentation urethroplasty using a labial or vestibular graft also results in high patency rates (75–100%) at follow-up of 6–24 mo. No long-term complications were reported [7,14,29,30].

In labial or vestibular flap urethroplasty, patency rates of 88–100% and no adverse effects were observed [31,32].

With the use of buccal and lingual mucosal grafts, comparable patency rates between 50% and 100% were observed for dorsal and ventral onlay augmentation urethroplasty. Only low-grade short-term adverse effects were reported [3–6,8,11,26,31,33–36].

Anastomotic urethroplasty has only been described in two cases in the literature, both in women with a very short mid-urethral stricture and both of whom were stricture-free at 4- and 24-mo follow-up, respectively. Neither woman suffered from urinary incontinence postoperatively [6,37]. Further information is available in Supplementary Table 1.

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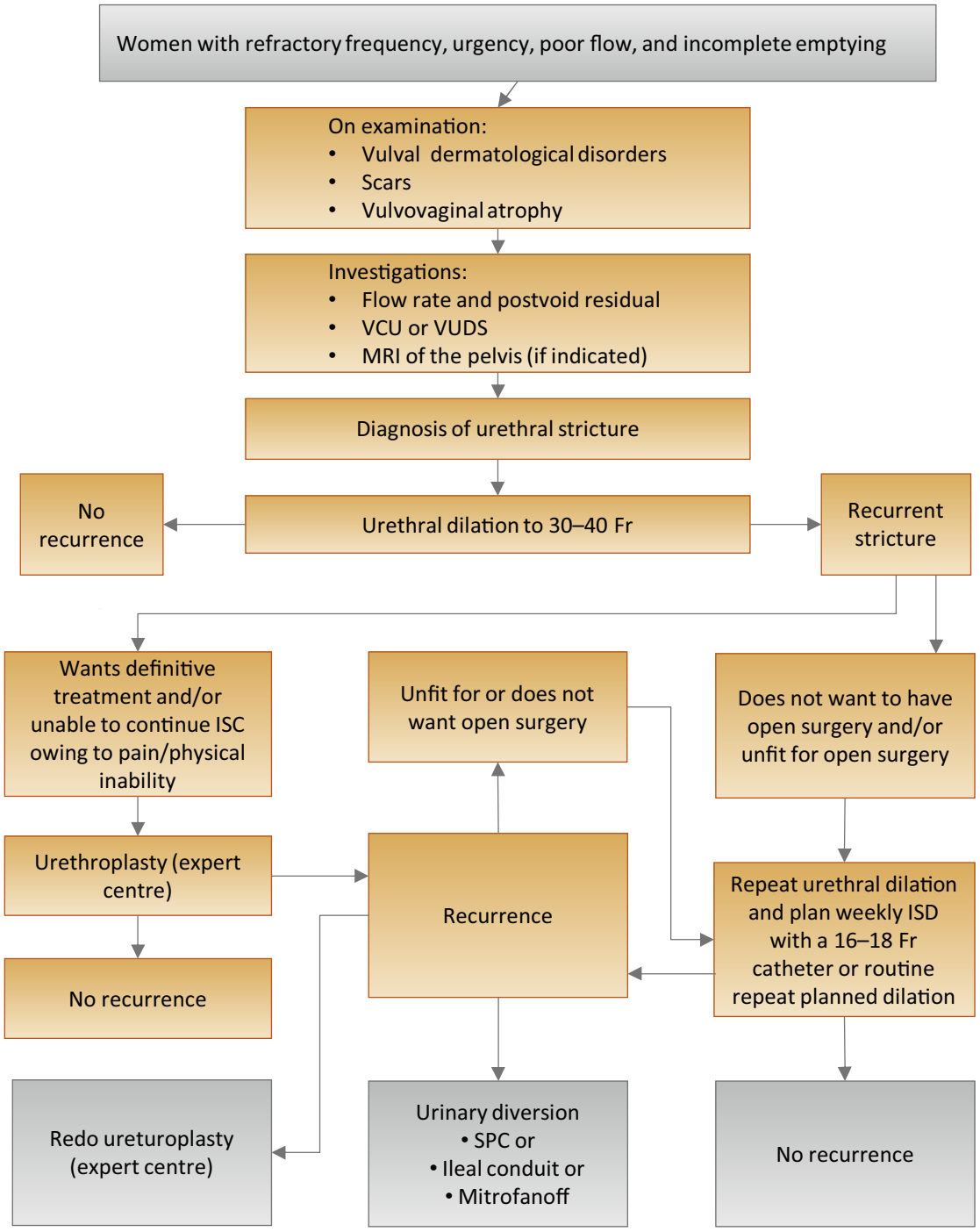

Fig. 1 – Women with refractory frequency, urgency, poor flow and incomplete emptying. ISC = intermittent self-catheterisation; MRI = magnetic resonance imaging; VCU = voiding cystourethrography; VUDS = video urodynamics; ISD = intermittent self-dilation; SPC = suprapubic catheter.

2. Strictures in transmen

2.1. Prevention

In transmen, strictures most often occur at the neomeatus and the anastomotic site, at both ends of the neophalloplasty flap. Hypoperfusion of the flap in the early postoperative period should be avoided [38]. Effective measures to decrease the stricture rate include providing a well-vascularised support to the fixed part of the urethra and creating the anastomosis via coverage with bulbospongiosus muscle [39] and with local tissue flaps. These flaps include paravaginal tissue flaps and labia minora flaps. Prefabrication of the neophallic urethra with a vaginal mucosa graft harvested during the vaginectomy procedure resulted in a remarkably low stricture rate (4.5%) [40]. By contrast,

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Table 1 – Recommendations for the management of ureth strictures in females

Recommendation	Strength rating
Measure the flow rate and postvoid residual and perform voiding cystourethrography or vide -urodynamics in all women with refractory lower urinary tract symptoms.	Strong
Perform urethral dilatation to 30–41 Fr as the initial treatment for FUS	Weak
Perform repeat urethral dilatation and start planned weekly intermittent ISD with a 16–18 Fr catheter for the first recurrence of FUS	Weak
Perform urethroplasty in women with a second recurrence of FUS and who cannot perform ISD or want definitive treatment. The technique for urethroplasty should be determined by the surgeon's experience, the availability and quality of graft/flap material. and the quality of the ventral versus dorsal urethra.	Strong
Treat meatal strictures with meatotomy/ meatoplasty.	Weak

FUS = female urethral stricture; ISD = intermittent self-dilation.

prefabrication of the neophallic urethra with a skin graft led to a high stricture rate (87.5%) [41]. Therefore, the preventive effect of prefabrication on stricture formation remains questionable and might be confounded by different graft materials.

2.2. Diagnosis

Diagnostic modalities should give information about the stricture location, stricture length, concomitant fistulas, concomitant diverticula, and communication with the vaginal remnant. Retrograde urethrography is the standard diagnostic modality, with urethroscopy in the case of equivocal findings. In the case of complete obliteration, voiding cystourethrography should be performed to obtain information about the proximal part of the urethra. If necessary, this can be correlated with flexible cystoscopy through the suprapubic tract [42].

2.3. Treatment

The treatment depends on the time after neophallic reconstruction, the stricture location and length, and the quality of local tissues [42].

2.3.1. Strictures early after neophallic reconstruction

Urethral surgery on tissues in the acute phase of inflammation and wound healing is not indicated and should be postponed until any healing problems of the neophallus have been resolved and scar tissue formation in the urethra has been stabilised. This usually takes 6 mo. Endoscopic incision for short (<3 cm) urethral strictures has been performed, mainly at the anastomotic site, with a stricture-free rate of only 16.7% when performed within 6 mo after neophallic reconstruction. Insertion of a suprapubic catheter is the first-line treatment in cases of obstructive symptoms severely affecting the patient's quality of life, recurrent urinary tract infection, or retention. This is a nonspecialist intervention and can be performed by any urologist. An alternative is to create a perineostomy, which is a specialist procedure and should only be performed by a urologist familiar with transgender urethral anatomy. The perineostomy may be closed at the time of formal urethral reconstruction [43].

2.3.2. Meatal strictures

Intermittent urethral dilation is an option for low-grade meatal strictures, with the dilation interval depending on the stricture recurrence interval. Intermittent urethral dilation is only a palliative treatment. Patients with high-grade meatal strictures, those who refuse intermittent urethral dilation, and those who want a durable solution should be offered simple meatotomy. Patency is 75% (mean follow-up 39 mo) but the drawback is that the meatus will be in a hypospadic position [43]. If a hypospadic meatus is not acceptable, a staged urethroplasty can be offered with retubularisation of the urethra after at least 3 mo and when the tissues have healed [43].

2.3.3. Strictures at the neophallic urethra

Endoscopic incision of a short stricture at the neophallic urethra has been reported but evidence is very scarce and the long-term results seem to be disappointing (66% failure rate after median follow-up of 51 mo).

Because of the absence of the corpus spongiosum, it is difficult to find a suitable graft bed for graft urethroplasty. One-stage graft urethroplasty is thus only possible if the graft can be supported and covered by healthy fatty tissue surrounding the neophallus. Experience is very limited and the stricture-free rate reported was 50% after mean follow-up of 102 mo [43].

The standard treatment for these strictures is staged urethroplasty with marsupialisation of the urethra in the first stage and retubularisation during the last stage [42,43]. In cases with poor quality of the urethral plate, the plate can be augmented by a graft (buccal mucosa or full-thickness skin graft) [43,44]. A stricture-free rate of 69.7% has been reported for this technique (mean follow-up 25 mo) [43].

For complex (eg, fully obliterated) or recurrent strictures at the neophallic urethra, complete urethral substitution of this part needs to be performed. Different suitable flaps have been described (radial forearm free flap, superficial circumflex iliac-artery free flap, pedicled groin flap). Double-face grafts with the ventral graft supported by rotating part of the neoscrotum or by a gracilis flap have been successfully reported for a very limited number of patients [42].

2.3.4. Strictures at the anastomosis of the neophallic urethra-fixed part of the urethra

Strictures at the junction between the neophallic part of the urethra (skin) and the fixed part of the urethra (mucosa) are usually short.

Short, nonobliterative strictures can be treated with endoscopic incision. The stricture-free rate for a first

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endoscopic incision was 45.5%, but this dropped to 0% in the case of three or more attempts (median follow-up 51 mo) [45]. Therefore, repetitive endoscopic incisions should be discouraged unless with palliative intent.

For very short (<1 cm) low-grade strictures, Heineke-Mikulicz urethroplasty is an option, for which a stricture-free rate of 57.9% after mean follow-up of 44 mo was reported [43].

If endoscopic incision fails or if the stricture is nearly or completely obliterative, the options are excision and primary anastomosis or free-graft urethroplasty. In the case of short (<2–3 cm) strictures, excision of the scarred part of the anastomosis with end-to-end anastomosis led to a stricture-free rate of 57.1% (mean follow-up 35 mo) [43,44]. If a tension-free anastomosis is not possible, usually for strictures longer than 2 cm, urethroplasty with a ventral onlay buccal mucosa graft resulted in a stricture-free rate of 50% (median follow-up 9.5 mo) [46]. In cases of insufficient ventral tissue during graft urethroplasty, the graft should be supported by a local fasciocutaneous flap [47]. An alternative (especially after failure of the previous techniques) could be to use a staged approach, but no data are currently available [46].

2.3.5. *Strictures at the fixed part of the urethra*

The fixed part of the urethra has a more reliable blood supply and the dorsal part of the urethra is supported by the corporal bodies of the clitoris. Therefore, one-stage dorsal inlay graft urethroplasty is possible for strictures at this site. However, experience is very limited [42,43]. A staged repair with or without a dorsal graft is a reliable treatment for these rare strictures [43].

2.3.6. *Definitive perineostomy*

The vast majority of transmen have a strong desire to void in a standing position [42]. Therefore, definitive perineostomy should only be offered to those with refractory strictures or patients with strictures who do not want to undergo complex reconstructive surgery [43,44].

2.4. *Perioperative care*

Anecdotally, after endoscopic incision and urethroplasty the urethral catheter is maintained for 2–3 wk [45,46]. Pericatheter urethrography before catheter removal is recommended, as it might be challenging to reinsert the urethral catheter in cases of urinary extravasation [46].

3. Strictures in transwomen

3.1. *Prevention*

Neomeatal stenosis is usually a sign of tissue healing complications and appears to be related to wound infection. Therefore, any effort to reduce wound infection might prevent stenosis at the neomeatus. In addition, excessive urethral mobilisation and consequential devascularisation should be avoided to minimise distal urethral ischaemia [48].

Table 2 – Recommendations for the management of urethral strictures in transgender patients

Recommendation	Strength rating
Do not perform endoscopic incision or urethroplasty within 6 mo after neophalloplasty.	Strong
Do not perform more than two endoscopic incisions for strictures in transmen unless with palliative intent.	Strong
Perform staged urethroplasty for strictures at the neophallic urethra if open reconstruction is indicated.	Weak

3.2. *Treatment*

It is acceptable to start with dilation of a short and non-obliterative stricture in transwomen, although no long-term data on effectiveness are available [48,49]. If this is not possible or if it fails, a short (<1 cm) meatal stricture can be treated with YVY meatoplasty, which has a stricture-free rate of 85% [50]. Somewhat longer (1–2 cm) meatal strictures can be treated with a neovaginal advancement flap (inverted U-flap or 7-flap), with no recurrence observed after median follow-up of 37 mo [51].

Recommendations for the management of urethral strictures in transgender patients are provided in Table 2.

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Study concept and design: Campos-Juanatey, Osman, Greenwell, Martins, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos, Lumen.
Acquisition of data: Lumen, Campos-Juanatey, Greenwell, Martins, Osman, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos.
Analysis and interpretation of data: Lumen, Campos-Juanatey, Greenwell, Martins, Osman, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos.
Drafting of the manuscript: Riechardt, Waterloos.
Critical revision of the manuscript for important intellectual content: Campos-Juanatey, Osman, Greenwell, Martins, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos, Lumen.
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Appendix A. Supplementary data

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