



# Surgical interventions in female urethral strictures: a comprehensive literature review

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Received: 30 December 2020 / Accepted: 4 June 2021 / Published online: 29 June 2021  
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## Abstract

**Introduction and hypothesis** Female urethral stricture (FUS) is an uncommon entity. Although there is no clinical consensus on the best modality of treatment, several studies have been published describing different techniques of FUS management. We carried out a literature review of the different surgical techniques used in the management of FUS and their results.

**Methods** We performed a systematic search of the PubMed and EMBASE databases and several cross-references. We grouped the data available from the studies into four general treatment categories.

**Results** We reported 35 studies (488 patients) with outcome measures; 53.48% of cases were presumably idiopathic in origin. A history of prior intervention was described in 91.29% of cases. As a surgical intervention, urethral dilatation (UD) had the lowest success rate of only 41.25%. In contrast, local flaps performed better (92.54% success rate) than local or oral grafts (87.30% and 89.94%, respectively). Only 9.43% of patients experienced mild to moderate post-surgery de novo incontinence; most of them recovered with pelvic floor exercises.

**Conclusion** In practice, UD is tried first for FUS, at least once, before urethroplasty. In case of failure or short recurrence following UD, urethroplasty should not be delayed. In experienced hands, urethroplasty has a better outcome.

**Keywords** Female urethral stricture · Urethral dilatation · Urethral stenosis · Urethroplasty · Dorsal onlay · Buccal mucosal graft

## Introduction

Bladder outlet obstruction (BOO) is an uncommon entity in women, the incidence being only 2.7–8% of women referred for voiding symptoms [1]. Female urethral stricture (FUS) is a more distinctive subgroup of female BOO and accounts for 4–13% cases of female BOO presenting with lower urinary tract symptoms (LUTS) [2]. The lower incidence compared to male strictures is attributed to the shorter length, straighter course and

greater anatomical mobility of the female urethra and the protection provided by the bony symphysis over its entire length [3]. Although true FUS is a rare subset of BOO, the incidence was 4% in the Nitti et al. series [4]. Urethral dilatation, often as an office ambulatory procedure, has been practiced for a long for a variety of nonspecific female voiding complaints [5]. However, various urethroplasty techniques have gradually gain ground in recent years for treating women with true FUS [6]. We aimed to report all the surgical interventions and their effectiveness in treating FUS in the literature to date. The primary outcome was to report the different interventional techniques reported in the literature for treating FUS. The secondary outcomes were the success rates and complications of the various techniques described.

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## Methods

## Sources

All retrospective and few prospective case series are included in this review, which followed the PRISMA statement

(Preferred Reporting Items for Systematic Reviews and Meta-analysis) [7]. We carried out an extensive electronic search through the PubMed and EMBASE databases. Search terms used were 'female or women' combined with the terms 'urethral stricture or urethral stenosis' or 'urethral dilatation' or 'urethrotomy' or 'urethroplasty' on January 2021. Filters used were 'humans, female, age more than 19 years and the English language'.

## Study Selection

Retrospective or prospective case series of women with FUS who underwent surgical intervention were included. For inclusion, we define the female urethral stricture as '*A fixed anatomical narrowing of the female urethra diagnosed by radiological evidence, urethral calibration or direct endoscopic visualization causing symptomatic voiding symptoms and dysuria*'. Papers not conforming to our inclusion criteria of 'female urethral stricture' such as urethral fistulas, diverticulum repair, congenital urethral abnormalities and post-pelvic fracture urethral loss were excluded. Also, full-text articles not providing the outcome data separately and citations from conference proceedings were excluded. Cross-references from the selected articles were scanned and hand-searched to identify any missed article. A pro forma was made in duplicate to record the extracted data from each of the selected full-text articles and checked by two of the authors (JC and NV).

**Participants** Women with idiopathic urethral strictures.

**Intervention** Surgical intervention grouped into two main categories (urethral dilatation and augmentation urethroplasty with local flap, local graft or oral graft).

**Comparison** Success rates among the different intervention techniques.

**Outcome measures** Stricture-free rate, improvement of flow rate (Qmax) and complications.

## Data extraction and quality assessment

Two of the authors (JC and NV) independently performed the abstracting, followed by the screening of full-text articles for quality assessment and results. Data include participant characteristics, intervention, outcome assessment tools and the results. Any dispute regarding the quality of the studies was resolved by the senior author, AC. Success was defined as 'No requirement of further intervention or surgery after the primary intervention'. We assessed the risk of bias in the included studies by using the Oxford (Centre for Evidence-based medicine, 2009) levels of evidence [8] as well as the JBI (Joanna Briggs Institute) assessment protocol for case

series [9]. Most of the selected studies were retrospective case series (Oxford level 4 evidence) with selection bias.

## Evidence synthesis

Electronic search identified 106 abstracts which, after removing the case reports and conference citations, reduced to 64 abstracts. Subsequent hand-searching led to four more full-text articles. A total of 68 full-text articles were identified from years unspecified to up till now. Thirty-three papers were rejected because of duplicate data and inadequate outcome reporting. All in all, 34 articles were ultimately included for the review. From 34 studies, 488 individual patients were reported with outcome measures after undergoing intervention for urethral stricture disease (Fig. 1).

## Results

### Methodological quality

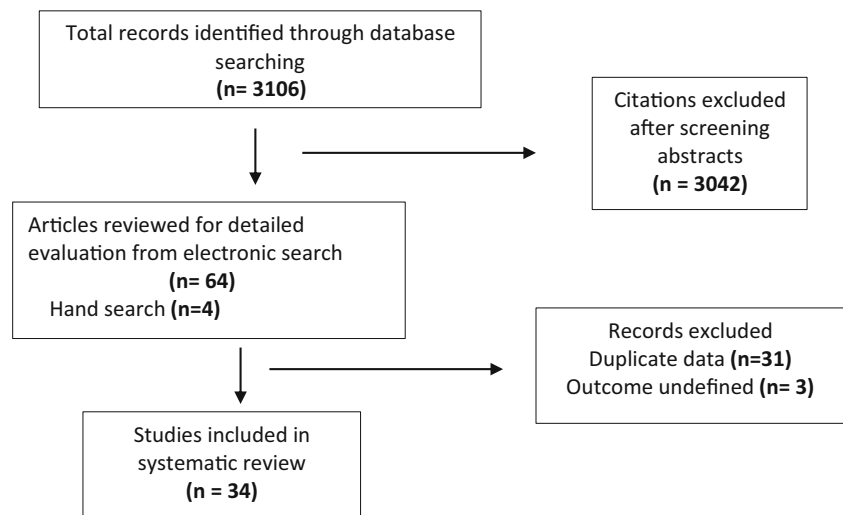
There were consecutive recruitments of cases in five series only [22, 27, 28, 40, 41]. All of the studies were retrospective case series, except one that was prospective [30]. Although most of the series had a well-described follow-up of > 1 year, some had only < 9 months follow-up [30, 32]. The confirmation of diagnosis was made clinically and other methods such as VCUG, cystourethroscopy, urethral calibration and UDS or a combination of these modalities (Table 1). The outcomes were assessed both subjectively and objectively in all the studies by using valid instruments. Most of the studies had an adequate number of cases, except a few [14, 24, 28, 32, 35] with fewer than five cases each (included because of their pioneering works).

### Outcomes in definitions, diagnostic tests and aetiology of FUS

*Female urethral stricture disease* does not have any standardised definition or strict diagnostic criteria. Inclusion criteria widely vary in several of the available studies. The definition followed by Smith et al. [10] was '*any fixed anatomical narrowing between the bladder neck and distal urethra of < 14 F preventing catheterisation and confirmed by urethrography or cystourethroscopy*'.

*In the majority of the studies, the authors used a combination of various diagnostic tests along with symptomatic assessment.* The common among them was post-void residual (PVR), voiding cystourethrography (VCUG), uroflowmetry, urethroscopy and office urethral calibration. The video-urodynamic study (VUDS), transvaginal ultrasound (TV-US) and MRI were used more selectively. Urethral calibre < 14 F (measured in the office set-up) was regarded as

Fig. 1 PRISMA flow chart



diagnostic in some studies [10, 17, 19, 29], whereas in others, a lumen < 10 F [26], 12 F [39, 43], 16 F [31] or 17 F [11] was set as the calibre threshold. Maximal flow rate (Qmax) was regarded as a common criterion to diagnose and quantify the severity of stricture. A Qmax < 12 ml/s was set as the cutoff level in several studies [17, 19, 29, 30, 31, 32], whereas a value of 10 ml/s and 20 ml/s was the lower limit in two studies [26, 30], respectively. Voiding cystourethrography (VCUG) was used in most of the studies to confirm the diagnosis and stricture location radiologically as a 'fixed anatomical narrowing between the bladder neck and distal urethra with ballooning of the proximal urethra above the stricture during voiding'. Postvoid residual urine (PVR) threshold value varies in several studies from 60 ml to 90 ml, or even 100 ml. Several studies used video-urodynamics (VUDS) or urodynamics (UDS) selectively, especially when there was high PVR, history of retention or high Qmax. Several authors used a Pdet Qmax value > 20 cm. H<sub>2</sub>O as the lower limit to define BOO, whereas others set it as 30 cm or even 50 cmH<sub>2</sub>O. In addition to Pdet Qmax, nomograms such as the AG nomogram, Schafaeer linPURR diagram [15], Solomon-Greenwell pressure-flow nomogram [21] or Blaivas-Groutz nomogram [11, 36] were also used to diagnose female BOO. Urethroscopy was used in 25 studies to diagnose and evaluate the length or site of the stricture. MRI or transvaginal ultrasound (TV-USG) was used only occasionally (only in 5 series) for assessing the stricture (fibrosis and extent) or any local pathology. The diagnostic tests used to make the diagnosis are shown in Table 2.

The exact aetiology of FUS is believed to be multifactorial and mostly idiopathic. The presumed aetiological factors were mentioned in 229 (46.92%) women out of a total of 488 cases. Of these, 214 (43.85%) women were presumed to have an iatrogenic stricture (prolonged catheterisation, traumatic vaginal delivery, gynaecological surgery), 10 (2.04%) post-traumatic strictures and 5 (1.02%) inflammatory strictures.

The idiopathic variety constituted 50.20% (245 patients), whereas 14 (2.86%) patients were of unknown category.

Three hundred fifty-five patients had a history of prior intervention for urethral stricture disease. Of these, 347 (97.74%) women had a history of repeated urethral dilatation with or without urethrotomy, and 4 (1.12%) women had a history of prior urethroplasty. Among those patients with previous dilatation, two patients also had a cystostomy tube in place before the urethroplasty procedure. Two women (0.56%) had a prior history of urethral sling surgery.

### Outcomes of surgical intervention for FUS

*Urethral dilatation* (with or without urethrotomy) and *augmentation urethroplasty* are the two main techniques described in FUS treatment. Augmentation is usually done by utilizing tissues from either the local area (vaginal or labial tissue as a flap or free graft) or distant site (oral mucosal free graft). The augmentation is done by putting the flap or graft either *dorsally* (12 o'clock position) or *ventrally* (6 o'clock position) in the urethra. The studies used different parameters, both subjective and objective, to assess the outcome. Subjective parameters were the symptoms, and the degree was measured by various quantification methods (PGI/S scale, AUA score, Likert scale, sexual function questionnaires). Objective parameters measured were uroflowmetry, PVR, urethral calibre size, cystourethroscopic findings, UDS and VCUG. Table 3 shows the 34 studies with different intervention techniques and their outcomes.

### Outcomes of dilatation

The primary form of treatment in four studies was *urethral dilatation* [10–13] (Table 4). The urethra was dilated up to 30 F in 7 patients, 41 F in 93 patients and 39–43 F in 30 patients (a total of 130 patients), whereas in 7 women, it was

**Table 1** Case series (34 studies) on FUS with effectiveness of different interventions and their outcomes

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
1	Smith et al., 2006 [10] N=7 Location: UC	Catheterisation: 4 Cystoscopy: 3	Symptom assessment: All VCUG or video UDS: All Calibration: All	Retrospective design Inclusion criteria: Fixed anatomical narrowing between the bl. neck and distal urethra of < 14 F preventing catheterisation Exclusion criteria: Post-radiotherapy, gynaecological/pelvic malignancy Method: UD up to 30 F. Urethroscopy after each UD Mean follow-up: 21 months	Oxford Level 4 JBI criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics UC Appropriate statistical analysis UC	All women had to undergo daily CISC for initial 6 months Monitored every 3–6 months while on CISC No recurrence while on CISC AUA score improved by 10.7 points No complications of CISC No de novo SUI 57% stricture-free rate Compliance with CISC is a must
2	Blaivas et al., 2012 [11] (10 patients) N=17 Location: 8 Proximal: 8 Mid: 3 Distal: 5 Panurethral: 1	Idiopathic 8 Iatrogenic 6 Traumatic 2 Diverticulum 1	Symptom assessment: All Uroflowmetry: All VUDS with stress cystogram: 14 (Blaivas-Groutz nomogram was used) Cystourethroscopy: All	Retrospective design Inclusion criteria: Clinical diagnosis, confirmed stricture on cystoscopy, urethral obstruction on video UDS, urethral calibre < 17 F Exclusion criteria: UC Method: UD: 7 Vaginal flap urethroplasty: 9 (Martius flap used in 4 cases) BMG urethroplasty: 1 Mean follow-up: 5 years for urethroplasty, 2 years for UD	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Stress cystogram was mandatory No use of routine post-operative CISC Recurrence defined by pre-operative criteria Vaginal flap and BMG urethroplasty have high success rate 100% at 1 year and 78% at 5 years UD had only 6% success rate Urethroplasty had 100% success rate
3	Romman et al., 2012 [12] N=93 Location: UC	Previous UD: 28 Hysterectomy: 44 Other Gynaecological surgery: 11 Idiopathic: 10	Symptom assessment: All Qmax: All PVR: All Lateral VCUG: All Cystourethroscopy: All	Retrospective design UD under GA Inclusion criteria: Bothersome LUTS with distal urethral	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y	History of UD is more common in the failure group Success defined as complete or major LUTS resolution at a minimum of

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
4	Popat et al., 2016 [13] N=30 Location: UC	Idiopathic: 19 Dilatation: 10 Urethrotomy: 1	Symptom assessment: All Urethroscopy: all VCUG:24 UDS: 15 MRI: 10	narrowing and proximal ballooning on lateral VCUG Exclusion criteria: Women with extramural, intramural or non-distal urethral pathology or NGB Method: UD: 26 women (Prait dilators up to 41 F) Mean follow-up: 46 months	Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics UC Appropriate statistical analysis Y	6 months after a single session of UD Failure: any patient needing additional intervention/CISC/recurrence during the follow-up Tearing at the meatal margin requiring stitch is a good indication of success Success: 47 patients (51%) Failure: 46 (49%) Outcome measures: No. of UD procedures after operation + duration and frequency of CIC. Qmax improves, reduction in PVR Success: Ability to void after 1st UD without the need for another UD/CIC Failure: Recurrent LUTS requiring repeat UD/chr. CIC/urinary diversion Duration of symptoms most important in failure; 12.8 years(failure group) vs. 4 years (success group) De novo urge incontinence: 5 (one required surgery) No other post-op complications
5	Tanello et al., 2002 [14] N=2 Location: Mid and distal urethra: All	Trauma 1 Inflammatory 1	Symptoms: All Qmax: all PVR: all Cystourethroscopy: All Calibration: All	Retrospective design Inclusion criteria: FUC evidenced by VCUG, low Qmax and high PVR Exclusion criteria: Pelvic malignancy, pelvic trauma, NGB Method: Labia minora pedicled flap urethroplasty (ventral approach)	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Appropriate statistical analysis Y	Outcome measured by improvement in subjective symptoms, Qmax, PVR and calibration size Success rate: 100% De novo SUI: 1

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
6	Montorsi et al., 2002 [15] N=17 Location: Distal urethra + urethral meatus: All	Idiopathic: All	Symptom assessment (AUA score): All Uroflowmetry: All PVR: All VCUG: All UDS with nomograms: All	Mean follow-up: 24 months  Retrospective design Inclusion criteria: AUA score < 20, BOO on UDS (Abraham-Griffiths nomogram and the Schaefer linPURR diagram), urethral calibre < 20, FUS on VCUG Exclusion criteria: Pelvic malignancy, pelvic trauma, NGB Method: Vaginal vestibular Y-pedicle flap (ventral) inlay urethroplasty Mean follow-up: 12 months	Complete inclusion UC Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis N Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome assessed by improvement in Qmax, PVR, no BOO on UDS and urethral calibration No complications Success: Improvement in AUA score, Qmax, PVR, unobstructed pattern on UDS and nomograms, calibration size > 28 F and normal lumen on VCUG Failure: Inability to attain improvement with recurrence Success rate: 88%
7	Schwender et al., 2006 [16] N=8 Location: UC	Traumatic urethral dilations: All	Symptom assessment: All Urethral calibration: All UDS: 4 No UFM or PVR estimation done	Retrospective design Inclusion criteria: Symptoms of urgency and frequency with inability to pass a catheter in office, raised PVR Exclusion criteria: Pelvic malignancy, pelvic trauma, NGB Method: Vaginal vestibular inlay flap (anterior approach) (2 patients had concomitant PV sling, 6 underwent BN collagen injection) Mean follow-up: 2.5 years	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics UC Clear reporting of clinical information UC	Outcome assessed by improvement in symptoms and urethral calibre. Post-operative daily CISC after catheter removal (14 F catheter); however the duration: UC Dilatation only for one patient at 6 weeks No de novo incontinence Success rate: 100% De novo SUI (2) and UI (2)

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
8	Simonato et al., 2010 [17] N=6 Location: Mid+Distal stricture: 5 Panurethral stricture: 1 Mean stricture length: 2.4 cm	Infective: 2 Idiopathic: 4 Two patients had associated cystocele.	Flexible cystoscopy: All Uroflowmetry: All PVR: All VCUG: All UDS: 3	Retrospective design Inclusion criteria: Fixed anatomical narrowing < 14 F between bladder neck and meatus that prevents instrumentation with Qmax < 12 ml/s Exclusion criteria: Pelvic malignancy, pelvic trauma, NGB Method: Vaginal flap (C-shaped) and lateral vestibular pedicle Mean follow-up: 70.8 (25–100) months	Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis	Outcome assessed by improvement in symptoms, Qmax, PVR by catheter insertion. One patient needed CISC due to PVR and cystocele (no recurrence) Success: Improvement in Qmax, PVR and no recurrence in Qmax, Failure: Recurrence No use of routine CISC
9	Gormley et al., 2010 [18] N=12 Location: Distal urethra: All	Traumatic/difficult catheterisation: All	Symptoms assessment: All Cystourethroscopy: all VCUG: All PVR: All Uroflowmetry: All Calibration: All	Retrospective design Inclusion criteria: Women with FUS with a history of at least one UD or urethrotomy and difficult/failed catheter placement Exclusion criteria: Pelvic malignancy, pelvic trauma, NGB Method: Vaginal inlay flap urethroplasty (2 patients with concomitant PV sling) Mean follow-up: (3 months –9 years) 30 months	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Success: subjective relief of symptoms and able to catheterize with a 16 F catheter Post-operatively CISC: all Recurrent UTI: 2 UI:1 83% stricture-free rate

Table 1 (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
10	Önol et al., 2011 [19] N=17 Location: Mid+Distal: 10 Mid: 3 Distal: 4	Idiopathic: 9 Idiopathic: 8	AUA symptom score: All Uroflowmetry: All VCUG: All Cystourethroscopy: All UDS: All	Retrospective design Inclusion criteria: FUS with urethral calibre < 14 F, Qmax < 1.2 ml/s and Pdet Qmax > 20 cmH <sub>2</sub> O Exclusion criteria: Pelvic malignancy, pelvic trauma, NGB Method: Vaginal flap (reverse U-shaped anterior flap) inlay: 10 Urethral mucosal flap: 1 BMG(ventral onlay)+Martius flap: 2 BMG(dorsal onlay): 2 Circular BMG reconstruction: 2 Mean follow-up: 24 (6–78) months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Outcome measured by post-op AUA score, Qmax, PVR Success: Significant amelioration of symptoms, improvement of AUA score without any de novo incontinence Failure: Recurrence of stricture by a need for additional CISC/dilatation because of obstructive voiding and calibre < 14 F in last follow-up visit Routine post-op CISC not used No de novo incontinence 100% success rate
11	Kowalik et al., 2014 [20] N=10 Mid: 6 Distal: 4 Average stricture length: 1.25 cm	Idiopathic: 9 Traumatic: 1	Symptom assessment Uroflowmetry: All PVR: All VCUG: All Urethroscopy: All UDS: All	Retrospective design Inclusion criteria: Evidence of FUS on cystoscopy and/or UDS indicating BOO Exclusion criteria: NGB, abnormal focal neurological symptoms, malignancy Method: Vaginal flap: 6 (U-shaped vaginal inlay ventral approach) BMG graft: 4 Mean follow-up: 34 months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Outcome measured in terms of Qmax improvement and reduction of PVR Follow-up included calibration (> 16 F), symptom assessment, VCUG, cystoscopy when voiding difficulty Success: Improvement of symptoms, Qmax, PVR Failure: Recurrence of stricture Success rate: vaginal flap: 66%, BMG: 100% Recurrence in two patients with vaginal flap urethroplasty No de novo SUI or UI
12	Spilortos et al., 2017 [21] N=26 Location of stricture: UC	Idiopathic: 11 Traumatic Urethral catheterisation: 11	Symptom assessment: All Uroflowmetry: All VCUG: All	Retrospective design Inclusion criteria: VCUG evidence of ballooning of ur. proximal	Appropriate statistical analysis Y Oxford Level 4 JBI criteria:	Success: Resolution of BOO as shown by improvement of symptoms, no requirement of UD



**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
13	Romero-Maroto et al., 2018 [22] N=9 Location: Mid-distal: 5 Distal: 1 Panurethral: 3	NVD trauma: 4  Unknown: 4 Catheterisation: 4 NVD: 1	PVR: All Urethroscopy: All VCMG: 22 MRI: 14  Uroflowmetry: All VCUG: All PVR: All Urime CS: All UDS and cystoscopy: when calibre > 14 F	to a segment of a narrow urethra + Pdet Qmax > 2 Qmax (Solomon-Greenwell pressure-flow nomogram)+ cystoscopic evidence of anatomical stricture Exclusion criteria: Pelvic trauma, pelvic malignancy, NGB Methods: BMG urethroplasty: 14 Vaginal flap urethroplasty: 2 UD: 8 Urethrotomy: 1 Meatoplasty: 1 Mean follow-up: 36 months	Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion Y Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion Y Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y	or CISC, Qmax and PVR, UDS when possible Failure: Recurrence of stricture Urethroplasty had highest success rate of 93%, mild de novo incontinence in 2 patients (not requiring treatment, only PFMT) and no other complications. All patients with UD recurred 93% success rate for BMG urethroplasty 0% for UD  Outcome measured by improvement in symptoms scores (PG-I), PVR, Qmax No complications or UI reported Safe alternative compared to Blandy's technique (retrusive meatus) provides an orthotopic meatus
14	Hajebrahimi et al., 2019 [23] N=14 Location: Mid+distal stricture: 12 Proximal: 2	Not clear: Some had trauma, infection, atrophic urethritis. History of UD: all (long-standing)	Subjective symptoms with scoring scale: All Cystourethroscopy: All UDS: Selective VCUG: All	Retrospective design Inclusion criteria: Urethroscopy, PVR > 100 ml, age > 18 years, diagnosed urethral stricture on imaging, UDS, retention or severe voiding dysfunction and failed conservative treatment	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y	Outcome measure: Improvement in Qmax, reduction in PVR, improvement in subjective symptoms score (PG-I, AUA) De novo UI: 3 patients (botulinum given)





Table 1 (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
19	Gozzi et al., 2011 [28] N=4 Location: UC	Idiopathic: All	Symptom assessment: All VCUG: All Cystoscopy: All Urethral calibration: All Uroflowmetry: All	Retrospective design Inclusion criteria: FUS evidenced by VCUG, low flow rate and cystoscopic visualization of scarred tissue Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Method: Labia minora epidermal (ventral placement at 6 o'clock) graft urethroplasty Mean follow-up: 15 months	Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion Y Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Outcome assessed by Qmax and VCUG No post-op CI/SC No de novo incontinence No other complications 100% success rate
20	Rehder et al., 2010 [29] N=8 Location: Proximal or mid-urethral: All Mean stricture length: 16 mm	Idiopathic: All	Symptom assessment: All TV-USG: All Cystourethroscopy: All UDS: All VCUG: All Uroflowmetry: All Calibration: All	Retrospective design Inclusion criteria: Qmax < 12 ml/s, Pdet Qmax. 30 cmH <sub>2</sub> O, urethral lumen < 14 F, FUS on VCUG, urethral narrowing on cystoscopy Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Method: Dorsal urethroplasty (6 o'clock in this study) using the labia minora skin graft Follow-up: 24 months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics UC Clear reporting of clinical information UC Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Outcome measured by symptomatic improvement, Qmax, UDS parameters, cystourethroscopy (at 6 months) Failure: Stricture-free for a minimum of 1 year No de novo incontinence No other complications No post-op CI/SC One patient developed meatal stenosis Re-structure: 2 75% success rate

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
21	Manasa et al., 2019 [30] N=13 Location: Mid: 11 Distal: 2	Idiopathic or dilatation trauma: All	Symptom assessment and IPSS score: All FSFI score: All Uroflowmetry: All PVR: All Cystourethroscopy: All UDS: All	Prospective design Inclusion criteria: FUS evidenced by visual demonstration of narrowing on cystoscopy, IPSS. 7, Qmax < 20 ml/s Exclusion criteria: NGB, prior urethral surgery, pelvic fracture, genitourinary malignancy Method: Dorsal onlay vaginal graft urethroplasty Mean follow-up: 8.5 months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome assessed by improvement in IPSS, IFSI score and Qmax, PVR Also evaluates sexual and functional results Re-do urethroplasty needed in 1 patient No de novo incontinence 76.92% success rate
22	Chakraborty et al., 2021 [31] N=24 Location: Mid: 18 Mid+distal: 6 Length: 1.32 cm	Idiopathic: All	Symptom assessment scoring (PGI): All Uroflowmetry: All PVR: All VCUG: 18 Urethral calibration: All	Retrospective design Inclusion criteria: FUS evidenced by low Qmax, 12 ml/s, high PVR, > 50 ml, urethral calibre < 16 F and cystourethroscopic finding of FUS Exclusion criteria: NGB, cystocele, genital prolapse, primary BN obstruction, pelvic malignancy or pelvic fracture trauma Method: Dorsal vaginal onlay graft urethroplasty Mean follow-up: 20.30 months	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome measured by improvement in symptom score, Qmax, PVR and calibration size Success: No return of symptoms with adequate Qmax, PVR and calibration size > 18 F Failure: need for UD or CISC Success rate: 87.30% No de novo incontinence No other complications

Table 1 (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
23	Migliari et al. <sup>9</sup> , 2006 [32] N=3 Location: UC	Idiopathic: 1 Iatrogenic trauma: 2	Symptom assessment: All VCUG: All Uroflowmetry: All PVR: All UDS: All	Retrospective design Inclusion criteria: Urodynamically proven BOO with Qmax < 12 ml/s, Pdet Qmax > 20 cmH <sub>2</sub> O, PVR (90–200 ml) Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Dorsal BMG urethroplasty Mean follow-up: 6 months	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome assessed by UDS(Blaiva-Groutz nomogram), Qmax and Pdet Qmax and symptom assessment Post-op CISC: 1 patient for 3 months No de novo incontinence No other complications 100% success rate
24	Berglund et al., 2006 [33] N=2 Location: UC	Idiopathic: All	Symptom assessment: All VCUG: All Cystoscopy: All Uroflowmetry: All PVR: All Calibration: All	Retrospective design Inclusion criteria: FUC evidenced by VCUG and urethroscopy Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Method: Ventral BMG inlay urethroplasty Mean follow-up: 24 months	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion UC Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome measured by Uroflowmetry, PVR, calibration, VCUG Success: Improvement of symptoms, Qmax and PVR without recurrence Failure: Recurrence of stricture No de novo incontinence No complications Success rate: 50%
25	Sharma et al. <sup>29</sup> , 2009 [34] N=15 Location: UC Length: 2.45 cm	Idiopathic: 9 Catheterisation: 3 Obstetric trauma: 1 Prior caruncle excision: 1	Symptom assessment: All USG-KUB: All PVR: All VCUG: All UDS: Selective	Retrospective design Inclusion criteria: patients with urethral, bladder or pelvic malignancy, NGB,	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y	Outcome measured by symptom assessment, uroflowmetry, VCUG, cystourethroscopy (if required)

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
26	Castillo et al., 2011 [35] N=2 Location: UC	Idiopathic: All	Symptom assessment: All Uroflowmetry: All PVR: All VCUG: All Cystourethroscopy: All	oral pathology, history of anti-incontinence surgery, primary BN obstruction Method: Dorsal onlay LMG urethroplasty Mean follow-up: 12 months	Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Success: Improvement in flow rate > 15 ml/s and PVR without instrumentation-requirement and normal image on VCUG Failure: Restenosis No de novo incontinence One patient had initial wound infection One patient needed UD, settled at 1 year
27	Goel et al., 2014 [36] N=8 Location: Mid and distal: All	Idiopathic: All	AUA symptom score: All Uroflowmetry: All PVR: All Calibration with 14 F catheter VCUG: All UDS: All	Retrospective design Inclusion criteria: Moderate to bothersome LUTS with evidence of low flow and stricture on VCUG and BOO on UDS Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Method: Dorsal BMG urethroplasty Mean follow-up: 14.8 months	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Appropriate statistical analysis Y	Outcome measured by improvements in AUA score, Qmax, PVR and urethral calibration at 3-, 6-, 12-month intervals No CISc Success: Qmax < 12 ml/s Failure: Inability to calibrate with 18 F catheter

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
28	Powell et al., 2017 [37] N=6 Location: UC Length: 1.2+4 cm	Idiopathic: 3 Iatrogenic trauma: 3	Symptom-score assessment(Likert scale): All Pelvic-exam and supine stress test: All VCUG: All Uroflowmetry: All PVR: All Cystoscopy: All	Retrospective design Inclusion criteria: FUS proven by VCUG, low flow, high PVR and cystourethroscopy Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Method: Dorsal onlay BMG urethroplasty Mean follow-up: 18.6 months	Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4	Two recurrences of stricture No de novo incontinence 62.5% success rate
29	Mukhtar et al., 2017 [38] N=22 Location: Proximal: 6 Mid: 11 Distal: 5 Length: 2 (0.5–3.5) cm	Idiopathic: 14 Iatrogenic trauma: 8	Symptom assessment: All Uroflowmetry: All PVR: All VCUG: All UDS: All MRI pelvis: All	Retrospective design Inclusion criteria: Urodynamically proven BOO on UDS with VCUG evidence of FUS Exclusion criteria: Pelvic malignancy, urethral trauma, NGB Method: BMG ventral onlay urethroplasty Martius flap: All cases Mean follow-up: 21.5 months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes measured by improvement in symptoms, Qmax, PVR, development of any de novo SUI Cystoscopy on patients not meeting the 'success' criteria Success: Absence of recurrence defined by normalization of flow rate (> 12 ml/s), PVR (< 100 ml) and symptom resolution Failure: No CD 2/3 complications. CD grade in 1 patient only De novo SUI: 1 No post-operative CISC	Outcome measured by improvement in symptoms, Qmax, PVR, development of any de novo SUI Cystoscopy on patients not meeting the 'success' criteria Success: Absence of recurrence defined by normalization of flow rate (> 12 ml/s), PVR (< 100 ml) and symptom resolution Failure: No CD 2/3 complications. CD grade in 1 patient only De novo SUI: 1 No post-operative CISC



**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
30	Nayak et al., 2019 [39] N=12 Location: UC	Idiopathic: 9 Iatrogenic trauma: 3	Symptom assessment with AUA score: All VCUG: All Uroflowmetry: All PVR: All Calibration with 12F catheter: All	Retrospective design Inclusion criteria: AUA score > 7, Qmax < 12 ml/s, urethral calibre < 12 F, thick-walled trabeculated bladder on USG with PVR > 100 ml Exclusion criteria: NGB, abnormal focal neurological symptoms Method: Ventral inlay BMG urethroplasty Follow-up: 18 months	Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Success rate: 95%  Outcome measured by Qmax, PVR and AUA score improvement and urethral calibration Success: Improvement in Qmax, PVR without intervention and no recurrence Failure: Increase in AUA score, Qmax < 12 ml/s, failure to calibrate with 18-F catheter No routine CHSC post-operatively No de novo incontinence Success rate: 92%
31	Ozluherden Y et al., 2020 [40] N=7 Location: UC Length: 3.1 (2–4) cm	Idiopathic: 5 Lichen sclerosis: 2	Symptom assessment: All Uroflowmetry: All VCUG: All PVR: All	Retrospective design Inclusion criteria: FUS evidenced by VCUG, low flow rate and raised PVR Exclusion criteria: pelvic trauma, malignancy, NGB Method: BMG ventral onlay urethroplasty Mean follow-up: 23 (7–48) months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Outcome measured by improvement in symptoms, Qmax, PVR, donor site morbidity and sexual questionnaires Success: Improvement of symptoms, flow rate and PVR without recurrence in the follow-up period Failure: Any instrumentation (UD or surgery) after stricture surgery No de novo incontinence or other complications 100% success rate

Table 1 (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
32	Hampson LA et al., 2019 [41] N=39 Location: Distal: 6 Mid: 15 Proximal-mid: 5 Panurethral: 5 Length: 2.1 (0.1–5) cm	Idiopathic: 19 Iatrogenic: 14 Trauma: 6	Assessment of symptoms: All Uroflowmetry: All PVR: All VCUG: All Calibration: All Cystoscopy: All	Retrospective design Inclusion criteria: At least 12 months of follow-up after repair and a post-urethroplasty cystoscopy Exclusion criteria: NGB, pelvic trauma, malignancy Methods: Dorsal BMG urethroplasty One patient had concomitant anti-incontinence surgery Mean follow-up: 33 (7–106) months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion Y Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y	Outcome measured by symptomatic improvement, VCUG, Qmax, PVR and calibration 77% success rate Success: Symptomatic improvement, calibration with cystoscope > 17 F Failure: Inability to pass a 17-F cystoscope No de novo incontinence Mean time to recurrence 14 (2–38) months. Recurrence managed by UD/urethrotomy and CISC (7), re-do urethroplasty (1), simple cystectomy (1)
33	Gomez et al., 2019 [42] N=17 Location: Mid-distal: All	Idiopathic: All	Symptom assessment: All Uroflowmetry: All VCUG: All Cystourethroscopy: All PVR: All UDS: Selective	Retrospective design Inclusion criteria: FUS evidenced by VCUG, reduced flow, UDS and cystourethroscopy Exclusion criteria: NGB, pelvic trauma, malignancy Method: Dorsal onlay BMG urethroplasty Mean follow-up: 15 months	Appropriate statistical analysis Y Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome measured by uroflowmetry, PVR, symptomatic improvement No routine use of CISC 87% success rate One patient needed transfusion No de novo incontinence No other complications

**Table 1** (continued)

No.	Author, publication date, location and no. of participants	Aetiology	Investigations	Methods and duration of follow-up	Oxford level of study JBI Overall appraisal	Outcome measures, effectiveness and comments
34	Coguplugil et al. <sup>63</sup> , 2021 [43] N=8 Location: Distal: 4 Mid: 2 Mid-distal: 2 Mean length: 1.62 cm	Idiopathic: 5 Iatrogenic: 3	Symptom assessment: All Uroflowmetry: All PVR: All VCUG Video-UDS Cystourethroscopy	Retrospective review Inclusion criteria: UDS evidence of FUS with Qmax < 12 ml/s and Pdet Qmax > 20 cmH <sub>2</sub> O Exclusion criteria: UC Method: Dorsal onlay BMG urethroplasty Mean follow-up: 16.37 months	Oxford Level 4 JBI criteria: Clear criteria for inclusion/exclusion Y Conditions measured in a standard way Y Valid methods for identification used Y Consecutive inclusion N Complete inclusion Y Clear reporting of demographics Y Clear reporting of clinical information Y Outcomes/follow-up results reported Y Clear reporting of presenting sites/clinics Y Appropriate statistical analysis Y	Outcome assessed by uroflowmetry, PVR, VCUG and calibration Success: Improvement in Qmax, PVR and symptoms without any restenosis Failure: Requirement of intervention or recurrence 100% success rate No de novo incontinence No other complications, except one patient experienced dyspareunia No post-operative routine CIS

Abbreviations: Y: yes, N: no, UC: unclear, BMG: buccal mucosal graft, LMG: lingual mucosal graft, FSFI: Female Sexual Function Inventory, AUA: American Urological Association, IPSS: International Prostate Symptom Score, PGI and PGI-S: patient self-grading of symptoms improvement and severity score P, VCUG: voiding cystometrograph, UDS: urodynamic study, dorsal: 12 o'clock position, ventral: 6 o'clock position, Qmax: peak flow rate, Pdet Qmax: detrusor pressure at peak flow, JBI: Jonna-Briggs Institute, BN: bladder neck, NGB: neurogenic bladder, UI: urgency incontinence, SUJ: stress urinary incontinence

**Table 2** Diagnostic tests

Investigation	Number of studies
Uroflowmetry and Qmax	31
PVR estimation	28
Voiding cystourethrography	29
Urethroscopy	24
Urethral calibration (office)	10
Urodynamic study	21
MRI	4
TV-USG	1
USG-KUB	1

Abbreviations: Qmax: peak flow rate, PVR: postvoid residual, TV-USG: transvaginal ultrasonography, USG-KUB: ultrasonography of kidney, ureter, bladder area

unclear to what extent the dilatation was carried out. Fifty-three women had a history of prior urethral dilatation, whereas one had prior urethrotomy.

In the series by Smith et al., all patients were advised to carry out daily CISC (intermittent self-catheterisation) [10]. Three of these seven patients did require further dilatation over and above CISC (in this context, the success rate would be much lower, only 43%). Romman et al. had a success rate of 51% (in the failure group, 39% had a history of previous dilatation compared to only 17% in the success group). Tearing of the meatus requiring hemostatic suture placement to the adjacent vaginal wall was associated with a better outcome as happened in 81% of the success group compared to 71% in the failure group [12]. The mean time to failure was 12 months. Duration of symptoms before presentation was found to be a significant factor [13]. There were no de novo incontinence reports or other significant complications in the dilatation series, except in the Popat et al. series [13], which reported a 17% incidence of urge incontinence after dilatation.

Overall, urethral dilatation's success rate was 41.2% at a mean follow-up of 34.75 months. The success rate varies according to the number of previous dilatation sessions, as evident from the fact that the success rate comes down from 55.4% in women without prior dilatation to 14.9% with multiple previous dilatations (Table 4).

## Outcomes of augmentation urethroplasty

Thirty-two studies reported outcomes after using various methods of *augmentation urethroplasty* totalling 351 patients. *Vaginal or labial flaps* were used in 11 studies (97 women) [11, 14–29]. Twenty-one studies reported the use of free grafts. Of these, 8 studies used *local vaginal or labial grafts* (85 women) [24–31], and 17 studies used oral graft (*lingual or buccal mucosal*), totalling 169 women [11, 19, 21, 24, 32–43]. The surgical approach was explained for each of the categories with graft placement location in the urethra (either *ventrally* at 6 o'clock or *dorsally* at 12 o'clock position).

## Outcomes of vaginal or labial flaps

*Vaginal or labial flaps* have been used in 11 studies (97 women), as shown in Table 5. Ten studies (95 patients) described the use of vaginal flaps, whereas only one study (2 patients) described the labial flap method. Seventy of the 97 women had a history of UD or urethrotomy before urethroplasty. Tanello et al. reported using *labia minora pedicled skin flap* placed ventrally in the urethra in two patients with 100% success [14]. The rest of the studies used various types of *vaginal inlay flap in U-, Y- or C-shaped fashion*. Reversed U-shaped vaginal flap was used in 7 studies (63 women) [11, 16, 18, 19, 20, 21, 23]. The basic principle was the same: raising a *reversed U-shaped vaginal flap* anteriorly and placing this to the opened urethrotomy incision (inlay flap) at the 6 o'clock position. *The lateral-based vaginal flap* was used in two studies [14, 22]. Romero-Maroto et al. used the lateral-based flap based on Orandi's male urethral stricture surgery [22]. *The Y-shaped ventral vaginal flap* was used in one study with a dorsal inlay (12 o'clock) approach [15]. In the same study, an upper urethral mucosal flap was used in one case. In this particular case, a mucosal flap from the proximally dilated urethra was utilized to augment the urethra ventrally (*urethral mucosal flap urethroplasty*). *The C-shaped ventral vaginal flap* was used in one study with a ventral inlay approach [17]. Seven patients underwent concomitant pubovaginal sling operation, four Martius flaps, one bladder neck collagen injection and diverticulectomy. De novo urge incontinence was reported in four patients (one received botulinum toxin injection), whereas stress incontinence was found in

**Table 3** Comparison and the outcomes and follow-up of the different techniques used in FUS management

Technique used	No. of studies	No. of interventions	Mean success rate in %	Mean follow-up in months
Urethral dilatation	4	137	41.25	34.75
Local flap urethroplasty	11	97	92.54	37.13
Local graft urethroplasty	8	85	87.30	20.35
Oral graft urethroplasty	17	169	89.94	21.54

**Table 4** Female urethral dilatation series

Study	No. of patients	Previous intervention	Technique	Concomitant procedure	Postop ISC	Stricture-free %	Mean follow-up (months)	De novo incontinence	Other complications
Smith et al. [10], 2006	7	No	30 F/sounds	No	Yes	57	21	No	No
Blaivas et al. [11], 2012	7	All	Not defined	No	No	14	29	No	No
Romman et al. [12], 2012	93	Dilatation (26)	41 F/Pratt dilators	Plication of ext. meatus if bleeding	No	51	46	No	No
Popat et al. [13], 2016	30	Dilatation (10) Urethrotomy (1)	39–43 F/Heyman dilators in 8	No	Yes	43	59	Urgency incontinence (5)	No
Pooled data of 4 studies	137	44	–	–	–	41.25 # 14.9 * 55.4	34.75	–	–

# Success rate with prior UD, \* success rate without prior UD

only two cases (one received trans-obturator tape). Recurrent UTI and inward urinary stream were reported in four cases.

Overall, the mean success rate in these 11 studies (97 women) was found to be 92.54%, with a mean follow-up of 37.28 months. The definition of a successful outcome was different in several of the studies, and post-operative ISC (although not conforming to our definition) was done as a routine for some time during the follow-up period. Twenty of the 97 women were instructed to perform daily CISC post-operatively.

### Outcomes of vaginal grafts

Table 6 shows the eight studies (85 patients) that reported the use of *local tissue grafts (vaginal or labial)* [24–31]. *Dorsal onlay VG urethroplasty* was done in five studies (66 women) [24–26, 30, 31], whereas *labia minora graft (LMG)* augmentation was done in three studies (19 women) [27–29]. In all VG studies, the graft was placed *dorsally* (12 o'clock position), whereas, in the LMG studies, it was placed *ventrally* (6 o'clock position). Repeated urethral dilatation was done in all 85 women (with additional urethrotomy in 10 and meatoplasty in 1 patient). Two patients had cystostomy pre-operatively. There was no incidence of de novo incontinence or the use of routine post-operative CISC. The reported successful outcome was 87.30% at a mean follow-up of 20.35 months.

### Outcomes of oral grafts

Table 7 shows the 17 studies (169 patients) where tissues from the oral cavity were used in augmenting the stricture [11, 19–21, 24, 32–43]. Most of the patients (165) had a prior history of UD or urethrotomy. *BMG* harvested from the inner cheek was used in 16 studies, although the graft application method was different. While 12 studies (82 women) used the *dorsal onlay* approach (12 o'clock), four studies (33 patients) used the *ventral onlay* (6 o'clock position) technique. In 22 patients with the ventral onlay technique, a concomitant Martius flap was used. In one study, an innovative *ventral inlay approach* was used [39]. According to the authors, 'onlay' means placing and quilting the BMG in the urethrotomy gap after fully mobilizing the urethra with a full-thickness U-shaped or circumferential perimeatal incision. 'Inlay', on the other hand, means placing the BMG in the gap produced by an intra-meatal longitudinal incision without fully mobilizing the full thickness circumferentially [39]. *Circumferential BMG (tube graft)* was used in one study (two patients) [19]. *Dorsal lingual onlay graft* was used in one study only [34] with 15 women. There was no incidence of de novo incontinence or significant complications. Routine post-operative CISC was not used.

**Table 5** Female urethroplasty (vaginal and labial flap) series

Study	No. of patients	Previous intervention	Technique	Concomitant procedure	Postop ISC	Stricture-free %	Mean follow-up (months)	De novo incontinence	Other complications
Tanello et al.[14], 2002	2	Dilatation (all)	Labial flap inlay Lateral based Ventral approach	No	No	100	24	Stress incontinence (1)	No
Montorsi et al.[15], 2002	17	No	Vesitubular flap inlay Y-shaped flap	No	No	88	12	No	No
Schwender et al.[16], 2006	8	Dilatation (6) Urethrotoomy (2)	Dorsal approach Vaginal inlay U-shaped flap	Pubovaginal sling (2) Collagen injection (1)	No	100	30	No	No
Simonato et al.[17], 2010	6	Urethrotoomy (all)	Ventral approach Vaginal flap inlay C-shaped flap	No	No	100	58.5	No	No
Gomley et al.[18], 2010	12	Dilatation/ urethrotoomy (all)	Ventral approach Vaginal flap inlay U-shaped flap	Pubovaginal sling (2)	Yes	83	30	Urgency incontinence(1)	Recurrent UTI (2)
Önol et al.[19], 2011	11	Dilatation (5) Urethrotoomy (3)	Ventral approach Vaginal inlay U-shaped flap Ventral approach (10) Urethral mucosal inlay Ventral approach (1)	No	No	100	36	No	Inward urinary stream (2)
Blaivas et al.[11], 2012	10	Dilatation (all)	Vaginal flap inlay U-shaped flap	Pubovaginal sling (5) Martius flap (4)	No	80	53	No	No
Kowalik et al.[20], 2014	6	Dilatation (all)	Ventral approach Vaginal flap inlay U-shaped flap	Diverticulectomy (1)	Yes	67	34	No	No
Spilotros et al.[21], 2017	2	Dilatation (all)	Ventral approach Vaginal flap U-shaped flap	No	Yes	100	34	No	No
Romero-Maroto et al. [22], 2018	9	Dilatation (7) Urethrotoomy (1)	Ventral approach Vaginal flap	No	No	100	81	No	No
Hajebrahimi et al.[23], 2019	14	Dilatation (12) Urethrotoomy (2)	Lateral based flap Ventral approach Vaginal inlay flap U-shaped flap Ventral approach	No	No	100	16	Stress incontinence (2) Urge incontinence (3)	
Pooled mean of 11 studies	97	–	–	–	–	92.54	37.13	–	–

**Table 6** Female urethroplasty (vaginal and labial graft) series

Study	No. of patients	Previous intervention	Technique	Concomitant procedure	Postop ISC	Stricture-free %	Mean follow-up (months)	De novo incontinence	Other complications
Tsvian & Sidi [24], 2006	2	Dilatation (all)	Vaginal graft	No	No	100	27	No	No
Petrou et al. [25], 2012	11	Dilatation (all)	Dorsal onlay Vaginal graft	No	No	73	23	Stress incontinence 5	No
Singh et al. [26], 2013	16	Dilatation (13) Urethrotomy (3)	Dorsal onlay Vaginal graft	No	No	100	24.5	No	No
Önol et al. [27], 2014	7	Dilatation+ urethrotomy (5)	Labia minora graft	No	No	86	18.2	No	No
Grozzi et al. [28], 2011	4	Cystostomy tubes (2) Dilatation (all)	Ventral Inlay Labial graft	No	No	100	15	No	No
Rehder et al. [29], 2010	8	Dilatation (all) Mentoplasty (1)	Ventral approach Labial graft	No	No	75	24	No	NO
Manasa et al. [30], 2019	13	Dilatation (all)	Vaginal graft	No	No	76.92	8.5	No	No
Chakraborty & Vyas. [31], 2021	24	Dilatation (22) Dilatation + urethrotomy (2)	Dorsal onlay Vaginal graft	No	No	87.5	22.62	No	No
Pooled data of 8 series	85	85	-	-	-	87.30	20.35	-	-

Most of the series reported a higher success rate (> 90%) [19, 24, 32, 34, 35, 39 40, 43]. However, interestingly, the most recent and largest retrospective series by Hampson (2019) reported only a 33% success rate with BMG [41]. The mean success rate was found to be 89.94% at a mean follow-up of 22.54 months.

**Outcome in terms of complications**

Incontinence, although uncommon, is the most common complication mentioned in all the urethroplasty series. Fifteen women (9.43%) experienced incontinence, of which 11 (73%) had stress and 4 (27%) urge incontinence. Most of the stress and urge incontinences were mild to moderate in nature and either stopped spontaneously or after pelvic floor exercise. Donor site morbidity was noticed in two cases of BMG urethroplasty. Other complications (transfusion, meatal stenosis or wound infection) were rare (incidence: one each). Recurrence or restenosis is considered a failure and is mentioned in Tables 3–7.

**Discussion**

In this comprehensive literature review, data for a total of 488 patients from 34 studies were available for analysis. All the studies on FUS have been published since 2000, indicating a growing interest in this uncommon entity. The principal findings are that the urethroplasty techniques have better outcomes (success rate: 87% to 92% at a mean follow-up of 26.34 months) than urethral dilatation (success rate: 41.25% at a mean follow-up of 34.75 months) that often results in rapid recurrence requiring further intervention in > 50% cases (Table 3).

Stricture aetiology was presumably identified in 47% women in our review (50% idiopathic, 44% iatrogenic, 2% trauma, 1% inflammatory). Although the idiopathic variety constitutes nearly 50% of cases [6, 10, 12], some recent series reported iatrogenic injury (instrumentation, surgery) as the most common cause followed by traumatic vaginal delivery [21, 41, 44]. The stricture site in women is usually the mid (mostly) and distal urethra [15, 30]. The symptoms of FUS are mixed irritative and obstructive [6]; the severity can be quantified by using the QOL score tools such as the PGI-S scale (Patient Global Impression of Symptom severity) [22, 23] or AUA score [15, 19, 27, 30, 36]. All the patients in our review had a long-term history of poor urinary flow and incomplete voiding.

A correct pre-operative diagnosis is a foundation for a correct operative approach and a successful outcome. However, the diagnostic criteria for FUS are still undefined. While Brannan et al. [45] suggested the pathological urethral calibre as ≤ 20 F, some others set the cutoff value as 12 F [23], 14 F

**Table 7** Summary of contemporary female urethroplasty (oral mucosal graft) series

Study	No. of patients	Previous intervention	Technique	Concomitant procedure	Postop ISC	Stricture-free %	Mean follow-up (months)	De novo incontinence	Other complications
Tsvivan & Sidi [24], 2006	1	Dilatation & urethrotomy	BMG Dorsal onlay	No	No	100	27	No	No
Migliari et al. [32], 2006	3	Dilatation & urethrotomy (2)	BMG Dorsal onlay	No	No	100	6	No	Storage LUTS for a short time
Berglund et al. [33], 2006	2	Urethroplasty (1) Dilatation	BMG Ventral onlay	No	No	50	24	No	No
Sharma et al. [34], 2010	15	Dilatation & Urethrotomy (all)	Lingual mucosal graft Dorsal onlay	No	No	93	12	No	No
Önol et al. [19], 2011	6	Dilatation (4) Sling (2)	BMG Dorsal onlay (2) BMG Ventral onlay (2) BMG circumferential tube (2)	Martius flap (2)	No	100	24	No	No
Castillo et al. [35], 2011	2	Dilatation (all)	BMG Dorsal onlay	No	No	100	18	No	Donor site haematoma (1)
Blaivas et al. [11], 2012	3	Dilatation (1) Flap urethroplasty (2)	BMG Dorsal onlay	No	No	100	25	No	No
Goel et al. [36], 2014	8	Dilatation (all)	BMG Dorsal onlay	No	No	75	14.8	No	No
Powell et al. [37], 2017	6	Dilatation (4) Urethrotomy (1) Urethroplasty (10)	BMG Dorsal onlay	No	No	67	18.6	Urge incontinence (1)	No
Mukhtar et al. [38], 2017	22	Dilatation (all)	BMG Ventral onlay	Martius flap (all)	No	95	21.5	Stress incontinence (1)	No
Kowalik et al. [20], 2014	4	Dilatation (all)	BMG Dorsal onlay	No	No	100	34	No	No
Nayak et al. [39], 2019	12	Dilatation (9)	BMG Ventral inlay	No	No	92	18	No	No
Spilotros et al. [21], 2017	14	Dilatation (8) Urethrotomy (1) Meatoplasty (1)	BMG Dorsal onlay	No	No	93	36	Stress incontinence (3)	No
Ozluherden Y et al. [40], 2020	7	Dilatation (all)	BMG ventral onlay 'AZ tech'	No	No	100	23	No	No
Hampson et al. [41], 2019	39	Dilatation (34)	Buccal mucosal Dorsal onlay	Anti-incontinence procedure (1)	No	77	33	No	7
Gomez et al. [42], 2019	17	Dilatation (16)	BMG Dorsal onlay	No	No	87	15	No	Transfusion (1)
Coguplugil et al. [43], 2021	8	Dilatation (all)	BMG ventral inlay	No	No	100	16.37	No	No
Pooled data of 16 series	169	–	–	–	–	89.94	21.54	–	–



[10, 19] or even 20 F [20, 25, 46]. Although urethral calibre seems to correlate with neither the severity of symptoms nor the surgical outcome, it may be valuable in assessing recurrence in a post-operative setting [47]. A low-flow, high-pressure pattern during voiding on UDS is suggestive of BOO. However, there are differences among authors regarding the cutoff values of  $P_{det} Q_{max}$  (cmH<sub>2</sub>O) and  $Q_{max}$  (ml/s), for example: '> 42, < 9' [4], '> 25, < 12' [48], '> 20, < 15' [49] or '> 35, < 15' [50]. Most of the authors prefer to use simple uroflowmetry, urethroscopy, PVR estimation and VCUG as diagnostic tests. UDS is more useful to rule out bladder dysfunction in selected cases to help predict post-urethroplasty failure. MRI or TV-US may be considered for assessing the degree of periurethral fibrosis, diverticulum or any other local pathology [6].

In the absence of any clear consensus on the definition of FUS, we have used the criteria as followed by Osman et al. [6]: "A symptomatic, anatomical narrowing of the urethra based on a failure of catheterisation, urethral calibration, visual inspection, or endoscopy or radiography". In this way, it is easier to decide upon the exclusion criteria such as meatal stenosis, primary bladder neck or a functional obstruction, neurogenic bladder, pelvic irradiation, urologic or gynecologic malignancy or trauma". Accordingly, 'success' was defined as the ability to void after the procedure without further urethral dilatation (UD), whereas 'failure' was defined as recurrent LUTS requiring repeat UD, chronic CISC, additional surgery or urinary diversion [51]. *In our opinion, an initial period of CISC after urethroplasty should not be regarded as a failure unless CISC is required on a regular or chronic basis to keep the urethral patency.*

Urethral dilatation (UD) is usually the most frequently chosen intervention, often indiscriminately, because of its simple and straightforward nature [5]. However, repeated UD has the potential for further fibrosis and earlier recurrence, as evidenced by a higher failure rate in patients with prior dilatation [6, 12]. The stricture-free rate in different series varies from 14% to 59% [10–13]. Osman et al.'s review quoted a success rate of 47% (27.2% in patients with prior dilatation vs. 58% without previous dilatation) [6]. The corresponding figures in our review are 41.25% (55.4% vs. 14.9%). Overall, attempting UD as a first-line intervention is still relevant in FUS.

Rosenbaum et al. [48] suggested using optical urethrotomy (at the 3 and 9 o'clock positions) to minimize stricture recurrence. However, its long-term efficacy is unverified [47]. Ackerman et al. [52] recommended a judicious use of UD and urethrotomy; with rapid recurrence after UD, an earlier urethroplasty is advisable.

Although the decision to perform urethroplasty is essentially driven by the patient who wants to get rid of CISC and periodic dilatation, proper counselling is essential before surgery. Urethroplasty can be done using *local vascularised flaps* or *free grafts* (local or distant). Important factors determining

the surgical approach depend on stricture length, site, length of the healthy proximal urethra, bladder neck integrity and surgeon's experience [52, 53].

Vaginal or labial flaps are the most commonly used substitution female urethroplasty techniques with a mean success rate of 91% [6]. Advantages of local flaps include good mobility with excellent vascularity and can be easily harvested with minimal morbidity.

Vaginal grafts (VG) are also popular because they are hair-free, elastic, easily accessible and naturally wet with infection resistance. Also, VG is cosmetically sound and can be done under spinal anaesthesia. The mean success rate of VG was 80% [6]. Complications of VGs are vaginal narrowing and dyspareunia. Also, in patients with vulvovaginal atrophy, local tissue quality suffers. Labia minora graft (LMG) is as promising as that of BMG in quality and graft take. It is thin and can be easily harvested with minimal donor site morbidity or cosmetic effect. LMG is usually used as a ventral inlay at the 6 o'clock position with a mean success rate of 86% [27, 28]. In our review, the overall success rates of local flaps and grafts are 92% and 87%, respectively.

Buccal mucosal graft (BMG) is the most widely used augmentation material in recent series [21, 39–42], including our review. Although El-Kasaby et al. are credited with the first use of BMG in male urethroplasty [54], Barbagli [55] popularized the technique. The advantages of BMG are being wet and hair-free and having a good vascular pattern and graft take, minimal contraction and easy harvestability with low donor site morbidity. Most of the series reported a > 90% success rate [19, 32, 36, 39, 40, 43]. However, interestingly, the most recent and largest retrospective series by Hampson et al. in 2019 [41] reported a mere 33% success rate. Most of the authors applied a buccal graft as a *dorsal onlay technique* [11, 21, 36] *instead of a ventral onlay* [40, 43]. Lingual mucosal graft (LMG) was first used by Simonato et al. [47] for male urethroplasty. The graft is of thin, smooth oral mucosa and easily harvestable with minimum donor site morbidity [29, 34]. Oral grafts are the most commonly used tissue for urethral augmentation in our review, with a mean success rate of 90%.

The main concerns related to dorsal urethrolisis are *the potential injury to the neurovascular bundle (NVB) and the striated sphincter. The potential advantages of the dorsal technique are decreased risk of incontinence, fistula or diverticular formation and meatal hypospadias*. In addition, there is a more physiological voiding with a reduced risk of ventral scarring, thus facilitating any future anti-incontinence surgery. However, the potential disadvantage is NVB injury [11, 24, 32]. The ventral approach, on the other hand, is more prone to give rise to stress incontinence unless a synchronous pubovaginal sling is placed [11].

Irrespective of the urethrolisis technique used, the potential surgical complications are haematoma, wound gaping or

infection. However, new-onset incontinence (mild to moderate) is the most common complication, which resolves spontaneously or with pelvic floor exercise and rarely needs corrective surgery.

In their review, Osman et al. [6] showed that UD had the lowest mean success rate of 47%, followed by a local flap rate of 91%, local graft rate of 80% and BMG rate of 94%. Similarly, Faiena et al. also reported the highest success rate with vaginal flap and BMG [56]. In our review, the corresponding figures are 41%, 92%, 87% and 90%, respectively. Therefore, all urethroplasty techniques had a higher mean success rate (80–94%) compared to UD (< 50%) (Tables 6 and 7).

All the studies included in this review are heterogeneous, with a small number of patients. All are short case series (level 4 evidence) of descriptive nature and varied criteria for inclusion, success and failure. There was a very low incidence of de novo stress incontinence in several of the studies [11, 10, 15, 26, 34, 41, 42]. It seems that some complications were underreported, or most of the strictures were located distally, which allowed treatment without sphincter injury. Follow-up periods were shorter in some of the studies. Also, any meaningful comparison of the results to stricture location and length is not possible because these were not routinely reported in most of the studies. Since a randomized controlled trial is not feasible for such an uncommon entity comparing UD and different urethroplasty techniques, the flaws mentioned above are expected to remain in such a review made from level 4 studies. Finally, it may be suggested that an international registry collect data prospectively for more robust and long-term evidence.

## Conclusion

UD has a mean success rate of only 41% at a mean follow-up of 35 months. Also, the success rate significantly decreases with repeated dilatations compared to the first dilatation. The mean time to failure is 12–15 months. Thus, it has the lowest success rate with minimum complications. In contrast, augmentation urethroplasty has the highest success rate of 90% at a mean follow-up of 27 months. The success rate of local flap augmentation is similar to that of free grafts (92.54% vs. 89.16%). Among free grafts, the BMG success rate is just marginally superior to that of local grafts (91% vs. 87%) at a follow-up of 22 and 20 months, respectively. Despite insufficient data and high-level evidence, it seems that local vaginal graft or BMG is a valuable technique concerning success rate and technical simplicity. It is our opinion that initially UD should be tried with a period of observation with CISC. Patients requiring more than two dilatations or early recurrence should be counselled about urethroplasty in a centre with the necessary expertise.

**Abbreviations** FUS, Female urethral stricture; UD, Urethral dilatation; BMG, Buccal mucosal graft; LMG, Lingual mucosal graft; VG, Vaginal graft; BOO, Bladder outlet obstruction; CISC, Clean intermittent self-catheterisation

**Author contribution** JNC: Data collection, manuscript writing and made a substantial contribution to the concept and design of the work with drafting, acquisition, analysis and interpretation of data.

AC: Analysis and interpretation of data, manuscript editing.

NV: Data collection, revision of the manuscript, critical analysis of the manuscript content.

All three authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content. All the authors have read and approved the manuscript.

## Declarations

**Conflict of interest** The authors declare no conflict of interests.

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