# EAU Guidelines on Urethral Strictures

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# 1. INTRODUCTION

# 1.1 Aims and scope

The European Association of Urology (EAU) Urethral Strictures Guidelines aim to provide a comprehensive overview of urethral strictures in male, female, and transgender patients. The Panel is aware of the geographical variations in healthcare provision.

It must be emphasised that guidelines present the best evidence available to the experts; however, following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account. Guidelines are not mandates and do not purport to be a legal standard of care.

# 1.2 Panel composition

The EAU Urethral Strictures Guidelines panel consists of an international multidisciplinary group of clinicians with particular expertise in this area. All experts involved in the production of this document have submitted potential conflict of interest statements which can be viewed on the EAU website: <u>http://www.uroweb.org/guideline/urethral-strictures/</u>.

# 1.3 Available publications

Alongside the full text version, a quick reference document (Pocket Guidelines) is available in print and as an app for iOS and Android devices. These are abridged versions which may require consultation together with the full text version. All documents can be viewed through the EAU website: <u>http://www.uroweb.org/guideline/urethral-strictures/</u>. A list of supplementary tables supporting this text can also be found online, along with an appendix of abbreviations specific to this text: <u>https://uroweb.org/guideline/urethralstrictures/?type=appendices-publications</u>.

# 1.4 Publication history

This document is a new Guideline first published in 2021. Additional information can be found in the general Methodology section of this print, and online at the EAU website: <u>http://www.uroweb.org/guideline/</u>. A list of associations endorsing the EAU Guidelines can also be viewed online at the above address.

# 1.5 Summary of Changes

This 2022 guideline represents a limited updated of the original 2021 text. References have been updated and now refer the reader to the final versions of the Panel's summary and systematic review papers. Minor grammatical and formatting issues have also been addressed.

# 2. METHODOLOGY

# 2.1 Methods

For the 2021 Urethral Strictures Guidelines, new and relevant evidence was identified, collated, and appraised through a structured assessment of the literature. A broad and comprehensive literature search, covering all sections of the Guidelines was performed. Databases searched included Medline, EMBASE, and the Cochrane Libraries, covering a time frame between 2008 and 2019 and restricted to English language publications. The panel defined by consensus inclusion and exclusion criteria for each topic before the scope search. Detailed search strategies are available online: <u>https://uroweb.org/guideline/urethral-strictures/</u>.

Relevant literature prior to the 2008 scope search cut-off was allowed if it was estimated to be of exceptional value by the panel. Relevant literature after the 2019 scope search cut-off was searched for by the panel member dedicated to a specific topic.

For each recommendation within the guidelines there is an accompanying online strength rating form, the basis of which is a modified GRADE methodology [1, 2]. Each strength rating form addresses a number of key elements namely:

- 1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence [3];
- 2. the magnitude of the effect (individual or combined effects);

- the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors);
- 4. the balance between desirable and undesirable outcomes;
- 5. the impact of patient values and preferences on the intervention;
- 6. the certainty of those patient values and preferences.

These key elements are the basis which panels use to define the strength rating of each recommendation. The strength of each recommendation is represented by the words 'strong' or 'weak' [4]. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternatives.

The Panel wants to highlight that "success" in urethral stricture treatment is poorly defined and subjective. "Success" is usually defined as urethral patency, either subjective by the absence of voiding symptoms or objective by imaging or urethral calibration. Despite urethral patency, the patient themselves might not consider the treatment as successful because of functional consequences (e.g., post-void dribbling, erectile/ejaculatory dysfunction, altered genital appearance). In this Guideline, the Panel agreed to avoid the term "success". Instead, the term "patency rate" or "stricture recurrence rate" will be used to clarify that only stricture recurrence was taken into consideration (as assessed by the authors).

The Panel would like to stress that patency after urethral surgery is dependent on the general principles of wound healing. These principles have stood the test of time and need to be respected [5]. Some examples:

- An anastomosis should be made between healthy urethral ends and without any tension.
- A graft requires a well-vascularised graft bed with a close contact between the graft and graft bed to promote imbibition and inosculation.
- If the full circumference of the urethral mucosa is destroyed, spontaneous regeneration will not take place.
- Contraction and fibrosis in a wound only stops after it is covered by its epithelium.

The Panel conducted two systematic reviews (SR) to support guideline recommendations, which were published in 2021:

- What is the role of single-stage oral mucosa graft urethroplasty in the surgical management of Lichen Sclerosus-related stricture disease in men? A systematic review [6];
- Free Graft Augmentation Urethroplasty for Bulbar Urethral Strictures: Which Technique Is Best? A Systematic Review [7].

The results of these reviews are included in the 2022 Urethral stricture guidelines.

In addition, the panel drafted three summary papers of the guidelines which were published in European Urology and European Urology Focus:

- EAU guidelines on urethral stricture disease (part 1): management of male urethral stricture disease [8];
- EAU Guidelines on urethral stricture disease (part 2): diagnosis, perioperative management, and follow-up in males [9];
- EAU guidelines on urethral stricture disease (part 3): management of strictures in females and transgender patients [10].

# 2.2 Review

The Urethral Strictures Guidelines were peer reviewed prior to initial publication in 2021.

# 2.3 Future goals

A further SR was conducted in 2021 and will see publication in 2022:

- Is a course of intermittent self-dilatation (ISD) with topical corticosteroids superior at stabilising urethral stricture disease in men and improving functional outcomes over a course of ISD alone?

An update of the strictures guideline will be conducted when deemed necessary, but at latest after five years. Further SRs will be conducted after approval of the Guidelines Office.

# 3. DEFINITION, EPIDEMIOLOGY, AETIOLOGY AND PREVENTION

# 3.1 Definitions

In males, a urethral stricture refers to a narrowed segment of the anterior urethra due to a process of fibrosis and cicatrisation of the urethral mucosa and surrounding spongiosus tissue ("spongiofibrosis") [11, 12]. In the male posterior urethra, there is no spongiosus tissue and at this location the terms stenosis is preferred [11, 12]. The definition of meatal stenosis is generally accepted as a short distal narrowing at the meatus, without involvement of the fossa navicularis [12].

There is no universal definition for what constitutes a female urethral stricture (FUS). Female urethral stricture is defined by most authors as a 'fixed anatomical narrowing' causing reduced urethral calibre [13, 14]. This reduced urethral calibre is variously defined as between < 10 Fr to < 20 Fr [15, 16] with the majority of series defining < 14 Fr as diagnostic, compared with a 'normal' urethral calibre of 18-30 Fr.

In transgender patients, the term stricture is also used to define a narrowing of the reconstructed urethra despite the absence of surrounding spongious tissue.

# 3.2 Epidemiology

In males, a sharp increase in incidence is observed after the age of 55 years, with a mean age of 45.1 [17, 18]. Overall, the incidence is estimated to be 229-627 per 100,000 males [17]. The anterior urethra is most frequently affected (92.2%), in particular the bulbar urethra (46.9%) [18].

In females, 2-29% of patients presenting with refractory lower urinary tract symptoms (LUTS) have bladder outflow obstruction (BOO) [19-22] of whom 4-20% will have a urethral stricture [21-23]. True FUS therefore occurs in 0.08-5.4% of women with refractory LUTS. There is a markedly increased incidence in women over 64 years of age [24].

In children, most strictures are traumatic: related to iatrogenic causes in 27.8-48% and external trauma in 34-72% [25]. Less frequent congenital (13%), inflammatory (4%), or post-infectious strictures (1%) are seen. The bulbar urethra is the most frequently affected part of the urethra [25].

After hypospadias repair, meatal stenosis and urethral strictures are reported in 1.3-20% of cases, depending on the severity of the hypospadias and the technique used [26]. There is a significantly higher incidence of this type of strictures in well-resourced countries due to a higher surgical repair rate [27].

Up to 18% of all urethral strictures have been reported to involve the meatus or fossa navicularis, usually due to failed hypospadias repair (FHR), lichen sclerosus (LS), trauma/instrumentation or idiopathic causes [28-31].

Meatal stenosis post-circumcision has been reported in less than 0.2% of children undergoing circumcision as neonates [17].

In female-to-male (FtM) transgender patients ("trans men"), approximately 51% will suffer a urethral stricture [32]. Strictures almost exclusively arise at the neomeatus in male-to-female (MtF) transgender patients ("trans women") and occur in 14.4% of cases [33].

# 3.3 Aetiology and prevention

Stricture aetiology differs significantly throughout different regions in the world, due to differences in healthcare quality and environmental and practice patterns [27]. Regardless of geography, urethral stricture disease adversely impacts physical health and quality of life (QoL) [34, 35], notwithstanding costs associated with the treatment of primary and recurrent disease [36, 37]. The rationale for preventing urethral strictures is to avoid morbidity to the individual and costs to society. Prevention of urethral strictures encompasses reducing the causes of stricture (e.g., infection, trauma, iatrogenic injury) and where this is not possible, mitigating the risk.

# 3.3.1 Aetiology and prevention in males

#### a. Sexually transmitted infection

Urethritis due to sexually transmitted infection (STI), in particular gonorrhoea, was previously a major cause of urethral strictures in well-resourced countries accounting for 40% of all cases [38]. The wide-scale promotion of safe sexual practices and easier access to sexual health services, resulting in timely treatment with

antimicrobials, is thought to have led to the considerable reduction in the problem [38]. Infective urethritis now accounts for 0.9% to 3.7% of cases in contemporary series from well-resourced countries [38, 39] but continues to be the major cause of strictures in low-resourced countries comprising 41.6% of all strictures [40].

Summary of evidence	LE
Access to investigation and treatment of STI is associated with a temporal decline in the incidence of	3
infective urethritis related strictures.	

Recommendation	Strength rating
Advise safe sexual practices, recognise symptoms of sexually transmitted infection, and	Strong
provide access to prompt investigation and treatment for men with urethritis.	

# b. Inflammation

Lichen sclerosus involves the urethra in 20% of cases [41] and is the most common cause of panurethral stricture disease (48.6%) [18]. The aetiology of LS has not been fully elucidated but is thought to have an autoimmune origin [42]. Lichen sclerosus may be associated with environmental factors and non-autoimmune comorbidities. Uncircumcised men are far more likely to suffer LS than circumcised men (age-adjusted odds ratio [OR] of 53.55; 95% confidence interval [CI]: 7.24-395.88) [43]. Lichen sclerosus is also associated with higher mean body mass index (BMI), diabetes mellitus, coronary artery disease, tobacco usage, hyperlipidaemia, and hypertension [44-46].

#### c. External urethral trauma

External trauma to the urethra is the second most common cause of stricture formation in adults [38]. The urethra is vulnerable to trauma during certain activities including sport, driving a vehicle, sexual intercourse and during combat. The bulbar urethra is the site most frequently affected by blunt trauma [12], usually as a result of straddle injuries or kicks to the perineum. Penile fracture is associated with a urethral injury in 15% of cases [47]. Motor vehicle accidents are the main cause of blunt injuries to the posterior urethra associated with pelvic fractures [48]. Penetrating injuries of the urethra are uncommon during non-combat situations [49].

#### d. latrogenic urethral injury

latrogenic injury to the urethra is one of the most common causes of strictures in well-resourced countries [18, 38] accounting for 32-79% of all strictures [38, 50]. In children, specifically iatrogenic causes were identified in 6.7-25% of cases [51]. Preventing iatrogenic urethral injury represents the main way in which urologists can prevent urethral strictures. latrogenic urethral injury most commonly results from urethral instrumentation (e.g., catheterisation, cystoscopy), surgery for benign prostatic obstruction (BPO), surgery for prostate cancer, or radiotherapy [39].

#### d.1 Urethral catheterisation

Urethral strictures are a recognised complication of urethral catheterisation accounting for 11.2-16.3% of all strictures [18, 38]. In a meta-analysis by Hollingsworth *et al.*, the pooled percentage of patients who developed urethral stricture or erosion after short-term catheterisation (< 3 weeks) in higher-quality studies was 3.4% (Cl: 1-7%) [52]. In studies comprised mainly of men with spinal cord injury with indwelling urethral catheters, the pooled estimate of urethral stricture or erosion was 8.7% (Cl: 0.0-18.7%) [52].

Urethral strictures following catheterisation may arise as a consequence of injury during attempts at insertion or during the period a catheter remains *in situ*. During insertion, the urethra may be injured by formation of a false passage by the catheter tip (29.7%) or inflation of the balloon within its lumen (70.3%) [53]. The rate of urethral injuries due to catheterisation was found to be 3.2 per 1,000 inpatients [54]. A six-month prospective multicentre study found that of 37 patients with catheter-related urethral trauma referred to urologists, 24% continued to perform ISD once weekly and 11% required at least one urethral dilation for urethral stricture [55]. In another follow-up study of 37 patients with catheter-related urethral trauma, 78% of patients developed urethral stricture [53]. The most common locations of trauma are the bulbar and posterior urethra [56].

Catheter-related trauma can be prevented through several measures [57]. Studies have indicated around 25% of all indwelling catheterisations in hospitals were unnecessary and inappropriate [58, 59]. Implementation of guidelines [60, 61] and specific criteria [62] have been shown to reduce catheterisation rates. Several studies have identified deficits in the knowledge of urethral catheterisation amongst resident doctors [63, 64]. This is postulated to be a factor in catheter-related trauma [64]. A targeted training program on urethral catheterisation

for nursing staff was shown to be effective in reducing iatrogenic urethral injuries in a prospective single institution study [54].

In addition to guidance and education, another approach to safer catheterisation is modification of the standard Foley catheter. A novel catheter balloon pressure valve safety system was developed to prevent balloon inflation injury though this has not been assessed in comparative studies [65, 66]. Bugeja *et al.*, studied the use of urethral catheterisation device (UCD) incorporating a guidewire, in prospective observational cohort study that included 174 patients. The incidence of adverse events was 7% with standard Foley catheterisation vs. 0% with the UCD (no statistical analysis was performed) [67]. A further prospective observational study found that Seldinger technique catheterisation could be used successfully by non-urology trained doctors [68]. These technologies need to be further assessed in prospective raondomised controlled trials (RCTs), incorporating cost-benefit analysis.

Catheter diameter is suggested as a possible contributing factor to urethral stricture due to a pressure effect on the urethral wall [69]. Decreasing the catheter size from 22 Fr to 18 Fr significantly decreased the risk of fossa navicularis strictures (6.9% vs. 0.9%, p=0.02) after radical prostatectomy (RP) [70]. Catheter material may also have an influence on the occurrence of stricture. In the 1970s/80s several comparative studies in patients undergoing cardiac surgery demonstrated that non-coated latex catheters were associated with a greater incidence of urethritis and more stricture formation than silicone catheters [71-73]. Other studies showed no difference [74-76]. Modern latex catheters have polymeric coatings [77] due to the concern with regards to stricture alongside the risk of hypersensitivity and the demonstrable *in vitro* toxicity of latex. Prolonged urethral catheterisation has also been implicated in the aetiology of stricture (e.g., poly-trauma, burns patients) [50].

Summary of evidence	LE
A significant proportion of catheter insertions in hospitalised patients were considered unnecessary.	2b
Educational programs can reduce the incidence of catheter-related urethral injury.	2a
Larger catheter size was associated with a greater risk of navicular fossa strictures.	3
Non-coated latex catheters are associated with a greater degree of urethritis and possibly a greater	1a
risk of urethral strictures, than non-latex catheters or coated latex catheters.	

Recommendations	Strength rating
Avoid unnecessary urethral catheterisation.	Strong
Implement training programmes for physicians and nurses performing urinary catheterisation.	Strong
Do not use catheters larger than 18 Fr if urinary drainage is the only purpose.	Weak
Avoid using non-coated latex catheters.	Strong

#### d.2 Transurethral prostate surgery

Urethral stricture following transurethral prostate surgery occurs in between 4.5-13% of patients [78], whereas bladder neck stenosis (BNS) occurs in between 0.3-9.7% [79]. Transurethral surgery is the most common cause of iatrogenic urethral stricture accounting for 41% of all causes [50]. The most common location for urethral stricture is the bulbomembranous urethra, followed by the fossa navicularis and penile urethra [80, 81]. Postulated mechanisms include friction at the penoscrotal junction, lack of adequate lubrication, repetitive 'in and out' movement of the resectoscope, breach of mucosal integrity leading to urine extravasation and monopolar current leak due to inadequate resectoscope insulation [82]. Bladder neck stenosis may be related to excessive and/or circumferential resection and the use of relatively large resection loops which may generate excessive heat in small intraurethral adenomas leading to scarring [79, 83]. Stenoses of the posterior urethra may also be due to a prolonged period of post-operative inability to void [84].

#### d.2.1 Risk factors for development of urethral stricture and bladder neck stenosis

Several risk factors for the development of urethral stricture and BNS following transurethral prostate surgery have been identified. Both prostatic inflammation (OR: 4.31) and operative time > 60 min (OR: 4.27) were found to be independent predictors of stricture after monopolar transurethral resection of prostate (TURP) [85]. In terms of bipolar TURP, slower resection rate (OR: 0.003), intraoperative urethral mucosa rupture (OR: 2.44) and post-operative infection were shown to be independent predictors (OR: 1.49) [86, 87]. A larger-calibre endoscopic sheath (26 Fr vs. 24 Fr) was associated with a greater risk of bulbar urethral stricture following monopolar TURP (11.4% vs. 2.9%, p=0.018) [88]. Room temperature irrigation solution was associated with a greater risk of urethral stricture following combined transurethral resection and vaporisation of the prostate compared to body temperature irrigation (21.3% vs. 6.3%, p=0.002) [89].

Bladder neck stenosis is known to occur more frequently in smaller prostate glands after both monopolar and bipolar TURP [90, 91]. Lee *et al.*, found that adenoma weight was an independent risk factor for BNS after monopolar TURP [91]. Meanwhile, Tao *et al.*, found total prostate volume (< 46.2 g) (OR: 1.5), but not resected gland weight, to be an independent risk factor [86].

## d.2.2 Incidence of urethral stricture and bladder neck stenosis with different energy modalities

A SR and meta-analysis by Cornu *et al.*, showed no significant differences in urethral stricture and BNS rates by energy modality (monopolar, bipolar, holmium laser enucleation, photoselective vaporisation) [78]. In another meta-analysis assessing outcomes of thulium (Tm:Yag) laser and bipolar TURP, no difference in urethral stricture and BNS rates were found between the two modalities [92]. The presence of potentially confounding factors such as endoscopic sheath diameter, energy setting used, procedural length and length of follow-up make inter-study comparisons between energy modalities problematic. Overall, there is no strong evidence that any single modality is associated with a clinically significant higher incidence of urethral stricture and BNS than others. Selection of modality should be based on a comprehensive evaluation of clinical safety and efficacy. A summary of incidences of urethral stricture and BNS with different modalities is presented in Table 3.1.

# Table 3.1: Incidence of urethral stricture and bladder neck stenosis by transurethral modality (adapted from Chen et al. 2016 [79])

Modality	Urethral stricture	Bladder neck stenosis
Transurethral resection of prostate (TURP)	1.7-11.7%	2.4-9.7%
- monopolar and bipolar		
Holmium enucleation of the prostate (HoLEP)	1.4-4.4%	0-5.4%
Photo-selective vaporisation (PVP)	0-4.4%	1.4-3.6%

# d.2.3 Interventions to prevent urethral stricture and bladder neck stenosis

Sciarra and colleagues conducted a single-blind RCT (n=96) to assess the use of rofecoxib for stricture prevention following TURP. At twelve months follow-up a urethral stricture was found in 17% and 0% of cases in the placebo and rofecoxib groups, respectively (p=0.0039) [93]. Chung *et al.*, conducted a single blinded RCT (n=180) evaluating the effect of urethral instillation of hyaluronic acid (HA) and carboxymethylcellulose (CMC). Urethral stricture on urethrography was diagnosed in 1.25% and 8.64% of patients in the treatment and placebo group respectively (p=0.031). Further RCTs are needed to confirm these findings and the safety of the pharmacological interventions.

Several earlier comparative studies assessed whether routine preliminary urethrotomy with an Otis urethrotome prevented the incidence of stricture following TURP [94-97]. Only one of these reported at least twelvemonth follow-up, finding no significant difference in stricture rate in patients undergoing TURP alone vs. Otis urethrotomy followed by TURP (21% vs. 14%) [98]. Others have suggested performing internal urethrotomy where there are pre-existent meatal or urethral strictures [99].

Adjunctive transurethral incision of the prostate (TUIP) at the end of TURP to reduce the rates of BNS was studied by Lee *et al.* [91]. A total of 1,135 patients of whom 667 underwent TURP and 468 underwent TURP plus TUIP were retrospectively studied. At median follow-up of 38 months, the incidence of BNS was 12.3% for the TURP group vs. 6.0% for the TURP plus TUIP group (p < 0.001). In glands < 30 g, the incidence of BNS in the TURP vs. the TURP plus TUIP group was 19.3% and 7.7%, respectively (p < 0.05). The clinical efficacy and safety of additional surgical interventions to prevent urethral stricture and BNS need to be confirmed in larger prospective RCTs before their use can be recommended.

Summary of evidence	LE
An RCT with more than twelve months follow-up failed to demonstrate a significant reduction in	1b
stricture rate using routine urethrotomy prior to TURP.	

Recommendation	Strength rating
Do not routinely perform urethrotomy when there is no pre-existent urethral stricture.	Strong

#### d.3 Radical prostatectomy

Radical prostatectomy has been associated with vesico-urethral anastomosis stricture (VUAS) in 0.5-30% of patients [79], though most modern series report it in the range of 1-3% [100]. The risk of stricture formation after salvage RP is notably higher (22-40%) [101]. Most VUAS develop within the first two years [101, 102]. A 2012 meta-analysis by Tewari *et al.*, showed no significant difference in VUAS between open-, laparoscopic and robotic RP [103]. In contrast, a more recent analysis of a national cohort in the UK found that VUAS rate after robotic RP was 3.3%, which is significantly lower than following laparoscopic (5.7%) or open RP (6.9%) [104]. These findings are consistent with an earlier similar study conducted in the USA [105]. The difference in VUAS rates may be explained by the level of experience and surgical volume of surgeons [106]. The cohort studies represent "real world" data, including all levels of surgical experience and surgical volumes whereas the meta-analysis is based on clinical studies. Thus, the better outcomes for robotic RP in the population studies may be related to the shorter learning curve [107].

#### d.3.1 Risk factors for development of vesicourethral anastomosis strictures

These include higher grade cancer, more advanced stage, higher prostate volume, coronary artery disease, obesity, hypertension, diabetes mellitus, previous bladder outlet surgery and older age [100, 108, 109]. Surgical factors include the use of non-nerve-sparing technique, anastomotic urine leak, increased operative time and increased estimated blood loss [100, 108, 109]. In addition, low-volume surgeons (< 40/year) were shown to have higher VUAS rates, 27.7%, compared to high-volume surgeons (> 40/year), 22% [110].

#### d.3.2 Interventions to prevent vesicourethral anastomosis strictures

Srougi *et al.*, studied bladder neck mucosal eversion in a prospective RCT of 95 patients. No significant difference was found in rates of VUAS at twelve months follow-up [111]. A meta-analysis by Kowelewski *et al.*, comparing interrupted vs. continuous vesico-urethral anastomosis suturing found no difference in VUAS rates [112]. Another SR by Bai *et al.*, compared barbed sutures to conventional sutures, and although heterogeneity across studies precluded meta-analysis, no patients developed VUAS with either approach [113].

#### d.4 Prostate radiation and ablative treatments

Urethral strictures occur in 1.5% of patients undergoing external beam radiation therapy (EBRT), 1.9% having brachytherapy (BT) and 4.9% who receive combination EBRT-BT at around four years follow-up [114]. These strictures typically occur in the bulbomembranous urethra [115]. As opposed to RP, stricture incidence after irradiation increases with time [101, 114]. For the ablative treatments, the stricture incidence after cryotherapy and high-intensity focused ultrasound (HIFU) is 1.1-3.3% and 1-31%, respectively [101]. The use of these treatment modalities in the salvage setting is associated with increased risk of stricture formation: 3-10% after salvage EBRT, 5-12% after salvage cryotherapy and 15-30% after salvage HIFU [101]. Due to the increasing utilisation of prostate irradiation (EBRT, BT) and ablative treatments (cryotherapy, HIFU), an increasing number of respectively radiation-induced and ablative treatment-induced strictures are expected [116].

#### d.4.1 Risk factors for the development of radiation strictures

Awad *et al.*, performed a multivariate meta-regression analysis including 46 studies, finding combining ERBT + BT and length of follow-up to be significant predictors of urethral stricture following prostate radiation [114]. Factors not shown to predict urethral stricture included biochemical equivalent dose, age, and androgen deprivation therapy [114]. Previous TURP was not included in the analysis, but has been found to be an independent predictor of stricture (HR: 2.81) in a previous multivariate analysis from a single institution [117] as well as PSA level < 10 ng/ml (HR: 0.47) [118].

#### d.4.2 Interventions to prevent radiation induced urethral strictures

Delaying adjuvant or salvage EBRT by nine months is associated with lower rates of urethral stricture (HR: 0.6) [119]. This has to be balanced with risk of delaying treatment in terms of cancer control [79]. In BT, it has been reported that downward movement of needle applicators occurs between fractions [120]. This may explain why strictures occur below the prostatic apex [118] in the so called "hot spot" [121]. Several measures taken together are thought to have contributed to a reduction in urethral stricture formation with BT including reduction of dose to the "hot spot", more careful needle placement, avoiding midline insertion and the introduction of plastic needles rather than steel [114].

#### e. Failed hypospadias repair.

Although urethral strictures after hypospadias repair are sometimes considered as iatrogenic [38], they are a very specific subtype and should be considered as a separate entity. The main reasons for this are the absence of spongiosus tissue at different levels within the penile urethral segment, and the lack of high-quality local tissues for urethral reconstruction [122].

# f. Congenital

The diagnosis of a congenital urethral stricture can only be made in the absence of other possible aetiology, such as iatrogenic, inflammatory, and traumatic causes [25]. Congenital strictures are thought to be consequent to incomplete or incorrect fusion of the urethra formed from the urogenital sinus with the urethra formed following closure of the urethral folds. They typically have a deep bulbar location and are usually short. In general, congenital strictures are diagnosed at a young age (Moorman's ring or Cobb's collar).

# g. Idiopathic

Idiopathic strictures are seen in 34% of all penile strictures and in 63% of all bulbar strictures [123]. Unrecognised trauma is thought to be a possible aetiology of idiopathic urethral strictures [27].

## 3.3.2 Aetiology in females

The cause of FUS was idiopathic in 48.5%, iatrogenic in 24.1%, resulting from prior urethral dilations, difficult/ traumatic catheterisation with subsequent fibrosis, urethral surgeries (mainly diverticulum surgery, fistula repair and anti-incontinence procedures) and trauma (mainly following pelvic fracture) in 16.4% [124-136]. Radiation therapy and infections are rare causes of FUS [137]. The most common segment of urethra affected is the mid-or mid-to-distal (58%). Panurethral strictures are rare (4%) [15, 124, 126, 127, 129-131, 136, 138].

For further information see online supplementary Tables S3.1 and S3.2.

# 4. CLASSIFICATIONS

# 4.1 According to stricture location

Classification according to stricture location is important as this will affect further management.

# 4.1.1 In males

## 4.1.1.1 Anterior urethra

The anterior urethra runs from the meatus to the urogenital diaphragm and is surrounded in its entire length by the corpus spongiosum [11, 139]. Further subdivision is made in three different areas (from distal to proximal) [12]:

*Meatal strictures:* these strictures are located at the external urethral meatus and may extend into the fossa navicularis of the glans.

*Penile strictures:* these are located in the segment between the fossa navicularis and the bulbar urethra. Externally, the penile urethra begins approximately at the balanopreputial sulcus and continues to the penoscrotal junction. The whole penile urethral segment lies in the groove ventral to corpora cavernosa and is surrounded by a thin layer of corpus spongiosum.

*Bulbar strictures:* the bulbar urethra starts at the penoscrotal junction and is surrounded by the bulbospongious muscle. It ends in the membranous urethra proximally at the level of the urogenital diaphragm. The bulbar urethra can be subdivided into a proximal and distal part. The proximal bulbar urethra is defined as the segment within 5 cm of the membranous urethra; the urethra lies eccentrically in this part with abundant ventral spongious tissue. The distal bulbar urethra is defined as the adjoining segment extending to the penoscrotal junction [140]. Strictures extending towards the membranous urethra are termed bulbomembranous strictures (BMS).

*Penobulbar strictures:* these extend from the penile urethra into the bulbar segment, compromising long segments of urethra.

The difference between penobulbar strictures and multifocal strictures should be noted. The latter are defined by two or more narrowed segments, either in the same or different subdivision of the urethra but preserving healthy lengths of urethra between them (e.g., iatrogenic strictures related to TUR procedures which typically affect the fossa navicularis and the penoscrotal junction with healthy urethra in between).

#### 4.1.1.2 Posterior urethra

The posterior urethra is approximately 5 cm long, with three different segments [12]:

• The membranous urethra is the area of the urethra traversing the urogenital diaphragm, between the proximal bulbar and the distal verumontanum.

- The prostatic urethra runs through the prostatic gland, starting at the proximal membranous urethra and extending to the bladder neck.
- The bladder neck is surrounded by the internal urinary sphincter and is the junction between the prostatic urethra and the bladder. Stenosis (or contracture) of the bladder neck implies a prostate *in situ* (i.e., after TURP or simple prostatectomies). If the narrowing or obliteration appears at this level but after a RP, the correct term is VUAS [12].

# 4.1.2 In females

The female urethra is approximately 4 cm long and arbitrarily divided in an upper, mid, and lower part [15, 124, 126, 127, 129-131, 136, 138].

# 4.2 According to stricture tightness

The definition of low- vs. high-grade strictures remains debatable [141-143]. A urethral plate less than 3 mm is considered a high-grade or tight stricture [144]. It has been demonstrated with a normally functioning bladder that flow rate will not diminish until the urethral lumen has a diameter below 10 Fr [142].

Table 4.1 presents a suggested classification for male patients with a normal functioning bladder. This classification was developed by the EAU Urethral Stricture Panel based on a consensus process.

Category	Description	Urethral lumen (French [Fr])	Degree
0	Normal urethra on imaging	-	-
1	Subclinical strictures	Urethral narrowing but $\geq$ 16 Fr	Low
2	Low grade strictures	11-15 Fr	
3	High grade or flow significant strictures	4-10 Fr	High
4	Nearly obliterative strictures	1-3 Fr	
5	Obliterative strictures	No urethral lumen (0 Fr)	

## Table 4.1: EAU classification according to the degree of urethral narrowing

# 4.3 Strictures in transgender men and woman

# 4.3.1 Trans women

After MtF gender confirming surgery, the penile urethra has been resected. Meatal strictures are defined as strictures occurring at the neomeatus, which is formed between the junction of the distal bulbar urethra and the neovagina. The other segments (bulbar and posterior) are the same as in a biological man.

# 4.3.2 Trans men

Four different areas can be identified in the urethra after FtM gender confirming surgeries [145]:

- The native urethra is the female urethral segment which remains preserved during surgery. It goes from
- the bladder neck to the original external meatus.
- The fixed part (pars fixa) or perineal urethra follows the native urethra, starting at the original external
- meatus. This segment is reconstructed using local tissues, typically vestibular mucosa, or anterior vaginal mucosa. Its course is similar to the bulbar urethral segment in males, but without being covered by spongiosal tissue.
- The anastomotic part is the area where the pars fixa joins the neophallus.
- The phallic urethra is the segment located within the neophallus or the metoidioplasty and is usually made of skin tube. Its course is similar to the penile urethra in males, but without being covered by spongiosal tissue.

# 5. DIAGNOSTIC EVALUATION

A comprehensive diagnostic evaluation of urethral stricture disease encompasses clinical history and examination, urinalysis (+/- culture), uroflowmetry and post-void residual (PVR) assessment, radiography, and endoscopy.

# 5.1 Patient history

The purpose of history taking is to assess symptoms including severity and duration, possible aetiology, prior treatments, complications, associated problems, and patient factors that may impact upon surgical outcome.

The clinical presentation of urethral stricture disease is varied. In a retrospective analysis of 611 patients with an endoscopically confirmed diagnosis of urethral stricture, LUTS were the most common presentation (54.3%) followed by acute urinary retention (22.3%), urinary tract infection (UTI) (6.1%) and difficult catheterisation (4.8%) [146]. In a retrospective study of 214 patients who underwent anterior urethroplasty, weak stream was reported as the most common individual LUTS (49%) followed by incomplete emptying (27%) and urinary frequency (20%) [147]. A further retrospective series of 614 patients undergoing anterior urethroplasty found post-void dribble to be present in 73% [148].

Genitourinary pain is a common feature, affecting 22.9-71% [34, 146]. Pain may be felt in the bladder and/or urethra, is associated with more severe LUTS, is more likely to be felt by younger men and resolves in most following reconstruction [34]. Other complaints include spraying (9%), visible haematuria (3.1-5%), urethral abscess/necrotising fasciitis (2.3%), urgency (14%) and incontinence (1-4%) [146, 147].

To establish aetiology, an enquiry about a history of pelvic, genital, or perineal trauma, prior instrumentation, prior surgeries, irradiation or focal therapies and urethritis should be made. It is important to document prior surgical approaches and date of the most recent intervention (e.g., dilatation) as this may impact upon the timing of radiological evaluation or surgical treatment.

Problems of sexual function are common in patients with urethral stricture disease [149, 150] and sexual function may be impacted upon by surgical intervention [151, 152]; therefore, the status of erectile and ejaculatory function should be established and documented using validated tools.

The performance status of the patient should be determined as it may influence the choice of treatment (curative or palliative). A past medical history should assess for factors that may impact upon tissue healing including diabetes, immunosuppression, and smoking. Oral tobacco use or the chewing of betel leaves may increase the risk of morbidity at the harvest site or render oral mucosa too poor for use. Prior harvest of oral mucosa should be noted as alternative sources for tissue transfer may need to be considered [153] or alternative surgical approaches (e.g., perineal urethrostomy [PU]).

# 5.2 Physical examination

The abdomen should be examined for the presence of a palpable bladder. The location of any suprapubic tube should be noted to assess its potential utility for antegrade cystoscopy or the placement of a sound (to facilitate repair) [154]. Examination of the genitalia should note the presence of foreskin, the position and size of the meatus as well as any evidence of scarring suggestive of LS. Pre-operative biopsy to confirm LS may be performed if this alters management and is essential if malignancy is suspected [155].

The presence of penile or perineal fistulae should be noted. The urethra should be palpated to assess for induration suggestive of significant fibrosis. Rarely a mass may signify a urethral carcinoma. A rectal examination to assess for prostatic pathology, which may be the cause of urinary symptoms, should be undertaken. In patients with posterior urethral stenosis rectal adherence to the prostate and the mobility of the surrounding tissues should be assessed [156]. The oral cavity should be examined for the suitability of oral mucosa. Measurement of BMI will identify obese individuals who are at greater risk of leg compartment syndrome when placed in the lithotomy position for a prolonged time period [157]. Assessing hip mobility is important when considering an exaggerated lithotomy position as some patients may have limited hip flexion due to unresolved orthopaedic problems [154].

# 5.2.1 Further diagnostic evaluation

# 5.2.1.1 Patient reported outcome measure (PROM)

The first validated urethral stricture surgery PROM (USS-PROM) was reported in 2011 [158]. It consists of six LUTS questions derived from the International Consultation on Incontinence Questionnaire Male LUTS (ICIQ-MLUTS) module, a LUTS-specific QoL question, the Peeling voiding chart and the EQ-5D to assess overall health-related QoL (HRQoL). The post-operative questionnaire contains an additional two questions to assess overall patient satisfaction. This PROM has been validated in several other languages (German, Spanish, Italian, Dutch, Turkish, Polish, Japanese) and is increasingly used in research studies as well as clinical practice. A further PROM is in development in North America but requires validation [159] (see section 11. Follow-up).

Summary of evidence	LE
A specific urethral stricture surgery patient reported outcome measure was found to have	2a
psychometric validity in the assessment of patient-derived benefit from surgical intervention for	
urethral stricture disease.	
Sexual dysfunction is prevalent in patients with urethral strictures and sexual function can be affected	3
by surgical management of urethral stricture.	

Recommendations	Strength rating
Use a validated patient reported outcome measure to assess symptom severity and impact	Strong
upon quality of life in men undergoing surgery for urethral stricture disease.	
Use a validated tool to assess sexual function in men undergoing surgery for urethral	Strong
stricture disease.	

### 5.2.1.2 Urinalysis and urine culture

Urinalysis is an essential component of the work up of patients with LUTS. If infection is suggested, urine culture should be performed to confirm the diagnosis and identify the causative organism and sensitivity to antibiotics. Bacteriuria should be treated prior to surgical intervention to prevent peri-operative sepsis [160] (see section 10. Peri-operative care).

# 5.2.1.3 Uroflowmetry and post-void residual estimation

A reduced maximum flow rate with a prolonged plateau is characteristic of the constrictive obstruction caused by urethral stricture. However, interpretation of flow patterns is subjective and is not considered a reliable screening tool for the detection of stricture [161]. To overcome this, a statistical model based on uroflowmetry parameters was developed and was found to predict urethral stricture with a sensitivity of 80–81% and a specificity of 77–78% [161]. Uroflowmetry is usually combined with ultrasound (US) estimation of PVR to identify patients with urinary retention who may require emergent bladder drainage. Uroflowmetry parameters can also be used for monitoring patients and in the assessment of treatment response (see section 11. Follow-up).

Urodynamic studies are not indicated in the vast majority of patients with urethral stricture disease. In patients with suspected bladder dysfunction (e.g., severe storage LUTS, history of irradiation or neurological disease), an assessment of bladder function may help surgical decision making and patient counselling. Similarly, when there is concern that flow impairment or increased PVR are due to detrusor underactivity or an acontractile detrusor, a urodynamic study may help predict the likelihood that the patient would need to perform intermittent self-catheterisation (ISC) post-operatively. The only urodynamic parameter found to distinguish a diagnosis of urethral stricture from BPO is urethral closure pressure which is lower in the former due to the constrictive nature of the obstruction (22.07 vs. 28.4 cm H<sub>2</sub>O, p=0.0039, r=0.61, BPO vs. stricture) [162].

#### Summary of evidence

Uroflowmetry pattern interpretation by use of a statistical model was found to be predictive of urethral 3 stricture disease.

Recommendation	Strength rating
Perform uroflowmetry and estimation of post-void residual in patients with suspected	Strong
urethral stricture disease.	

# 5.2.1.4 Urethrography

Retrograde urethrography (RUG) has widely been used as the investigation of choice for evaluating the stricture presence, location, length, and any associated anomalies (e.g., false passages, diverticula) [163].

The reported sensitivity and specificity of RUG in the diagnosis of strictures is 91% and 72%, respectively [164]. The positive predictive value (PPV) was 89% and the negative predictive value (NPV) was 76% [164]. Most reports suggest that RUG underestimates stricture length [165, 166]. Interpretation of RUG findings by urologists were found to be more accurate at predicting urethral stricture location and length as compared to evaluation by an independent physician [167].

Limitations of RUG include difficulty assessing very distal strictures and assessing the proximal extent of strictures which are too narrow to permit passage of adequate contrast. Combining a RUG with voiding

LE

cystourethrography (VCUG) can allow adequate visualisation of the urethra proximal to the stricture and a more accurate assessment of stricture length in (nearly) obliterative strictures, stenoses and gap in pelvic fracture urethral injury (PFUI) [168, 169]. In addition, urethrography provides only a two-dimensional assessment of stricture and the results may be affected by the amount of penile stretch [170], degree of pelvic rotation and patient body habitus [171]. Risks of the procedure include infection, discomfort [162], contrast reaction from intravasation of contrast [172] in addition to the risk of radiation exposure. Urethrographic clamp devices (Brodny, Knutson) are available and were found to be less painful than using the Foley catheter technique [173].

Summary of evidence	LE	
Retrograde urethrography is a widely available and easy to perform method of diagnosing and	2a	
assessing urethral stricture but may underestimate stricture length.		
Retrograde urethrography alone is not able to assess stricture length (or gap) in obliterative strictures		
or stenosis.		
Urethrographic clamp devices are less painful than using the Foley catheter technique.	2a	

Recommendations	Strength rating
Perform retrograde urethrography (RUG) to assess stricture location and length in men with	Strong
urethral stricture disease being considered for reconstructive surgery.	
Combine RUG with voiding cystourethrography to assess (nearly)-obliterative strictures,	Strong
stenoses and pelvic fracture urethral injuries.	
Use clamp devices in preference to the Foley catheter technique for urethrographic	Weak
evaluation to reduce pain.	

# 5.2.1.5 Cystourethroscopy

Cystourethroscopy allows for accurate visual detection of a suspected stricture or can rule out a stricture as cause of obstructive voiding [164]. It can detect narrowing of the urethral lumen before changes in uroflowmetry and symptoms [143]. Cystourethroscopy can also assess the presence of LS or other pathology but cannot usually assess stricture length as the calibre of most cystoscopes is greater than most symptomatic strictures [174]. To overcome this, use of smaller calibre ureteroscopes (6.5 Fr and 4.5 Fr) has been reported [174]. This also allows an assessment of the bladder prior to surgery and may identify other pathology such as bladder stones. Cystourethroscopy is particularly helpful for diagnosing proximal BMS which may be missed on RUG [175].

Retrograde urethroscopy combined with antegrade cystoscopy via the suprapubic tract may be used to evaluate PFUI and plan the surgical approach. It allows an assessment of the length of the defect, the competence of the bladder neck, the involvement of the bladder neck in scarring in addition to identifying the presence of bony spicules or other abnormalities (e.g., fistulae, stones) [176]. Combined retrograde and antegrade cystoscopy was found to provide similar estimates of length of urethral defect in patients with PFUI as combined retrograde and antegrade cystourethrography, but was more likely to detect fistulae, false passages, and calculi [176].

Summary of evidence	LE
Cystourethroscopy will reliably detect the presence of a urethral stricture.	3
Combined retrograde urethroscopy and antegrade cystoscopy is more accurate than retrograde and	3
voiding cystourethrography at identifying associated abnormalities such as fistulae, false passages,	
and calculi in patients with PFUI.	

Recommendations	Strength rating
Perform cystourethroscopy as an adjunct to imaging if further information is required.	Weak
Combine retrograde urethroscopy and antegrade cystoscopy to evaluate pelvic fracture	Weak
urethral injuries as an adjunct to imaging if further information is required.	

# 5.2.1.6 Ultrasound

Ultrasound of the urethra or sonourethrography (SUG) provides a non-invasive three-dimensional assessment of anterior urethral stricture disease; including stricture location, length, and the degree of associated spongiofibrosis [177].

Several studies have compared SUG to RUG and cystoscopic or intraoperative findings. Sonourethrograpy was found to be more accurate at diagnosing stricture presence compared to RUG [173, 178]. Sonourethrography was also found to more accurately estimate stricture length (94% correlation with intraoperative findings) than RUG (59% correlation with intraoperative findings) (p < 0.001) [166]. A further study showed similar findings and found that the closest correlation for stricture length at operation was for strictures in the penile urethra [165]. Intraoperative sonourethrogram findings have also been found to change the planned reconstructive approach (based on pre-operative retrograde urethrogram) in 19% of men undergoing anterior urethral reconstruction [171]. Sonourethrography incorporating real-time elastography can provide a qualitative and quantitative assessment of spongiofibrosis [179, 180]. The clinical relevance of assessing the degree of spongiofibrosis pre-operatively remains to be established. Three-dimensional reconstruction of sonographic images is investigational at present [181].

The advantages of SUG are that it can be performed in the outpatient setting, provides information on the degree of spongiofibrosis and its relatively low cost [177]. Limitations of the technique include lower sensitivity for detection of strictures in the bulbar urethra, operator dependency, and the need for urethral distension requiring intraurethral anaesthesia. Sonourethrography requires specialised training in the use of US and is currently not in widespread usage.

Study	Ν	Segment of	Comparator	Accuracy of SUG		
		urethra studied		Diagnosis	Location	Length
Berne-	113	Anterior and	RUG, VCUG,	SUG more accurate	-	-
Mestre et al.		posterior	surgical	than RUG (p < 0.05)		
2018 [173]			findings			
Ravikumar	40	Anterior and	RUG, VCUG,	Anterior: SUG	-	-
<i>et al</i> . 2014		posterior	surgical	100% sensitivity,		
[178]			findings	100% specificity		
				Posterior: SUG		
				75% sensitivity,		
				50% specificity.		
Kalabhavi	30	Anterior	RUG, surgical	-	-	-
<i>et al</i> . 2018			findings			
[166]						
Krukowski	66	Anterior	RUG, surgical	-	-	-
<i>et al</i> . 2018			findings			
[165]						

#### Table 5.1: Diagnostic accuracy of sonourethrography compared to other modalities and surgical findings

*N* = number of patients; RUG = retrograde urethrography; SUG = sonourethrography; VCUG = voiding cystourethrogram.

#### 5.2.1.7 Magnetic resonance imaging

Magnetic resonance imaging (MRI) has been used to image PFUIs, posterior urethral stenoses and anterior urethral strictures.

Several studies have compared MRI urethrogram to RUG and intraoperative findings. Magnetic resonance imaging urethrogram was found to be as accurate as RUG at detecting stricture site in anterior urethral strictures [182]. In terms of stricture length both MRI urethrogram and RUG reliably correlated with intraoperative findings [182]. On the other hand, a further study of patients with anterior urethral strictures found MRI urethrogram stricture length to correlate more closely with surgical findings than RUG [183].

In a mixed group of anterior urethral strictures and posterior urethral stenoses, MRI urethrogram was as accurate (sensitivity = 100%, specificity = 91.7%) as combined RUG and sonourethrography (sensitivity = 100%, specificity = 91.7%) at diagnosing strictures [184]. There was no significant difference in the measurement of stricture length [184]. In a further study of patients with posterior urethral stenosis, MRI estimation of stenosis length correlated more closely with operative findings compared to RUG [185]. In patients with PFUI, MRI measurement of pubo-urethral stump angle (angle between long axis of pubis and line between the distal end of the proximal urethral stump and lower border of inferior pubic ramus) was predictive of an elaborated approach on multivariate analysis [186].

Magnetic resonance imaging was also found to be more accurate at diagnosing associated pathologies e.g., diverticula, tumours, fistulae, and stones [184]. In cases of fistulation between the urinary tract and pubic symphysis after irradiation for prostate cancer, the fistula tract can be clearly demonstrated on MRI [187]. Other imaging modalities, including computed tomography (CT), may fail to identify the tract and the problem may be misdiagnosed as isolated osteomyelitis of the pubic bone leading to medical management with antibiotics rather than surgical excision [187].

The main advantage of MRI is greater anatomical detail, which is countered by the expense of the procedure and the greater complexity in interpreting images. The technique is not commonly used for routine situations, but it may be helpful in diagnosing associated pathologies which may alter patient management.

Study	Ν	Segment of	Comparator	Accuracy of SUG		
		urethra studied		Diagnosis	Location	Length
Murugesan <i>et al</i> . 2018 [182]	32	Anterior	RUG, Surgical findings	MRI and RUG equivalent (100% sensitivity, 100% specificity)	-	-
Fath El-Bab <i>et al</i> . 2015 [183]	20	Anterior	RUG, Surgical findings	-	-	MRI more accurate than RUG.
El-Ghar et al. 2010 [184]	30	Anterior and posterior	RUG + SUG, Surgical findings	MRI and RUG equivalent (100% sensitivity, 91.7% specificity)	-	MRI and RUG equivalent.
Oh <i>et al</i> . 2010 [185]	25	Posterior	RUG + SUG, Surgical findings	-	-	MRI more accurate than RUG + VCUG.

Table 5.2: Diagnostic accuracy of MRI compared to other modalities and surgical findings

*MRI* = magnetic resonance imaging; *n* = number of patients; *RUG* = retrograde urethrography; *SUG* = sonourethrography; *VCUG* = voiding cystourethrogram.

Summary of evidence	LE
Magnetic resonance imaging is more accurate than retrograde urethrography and voiding	2a
cystourethrography at determining length of posterior urethral stenoses and can detect alternative	
associated pathologies e.g., diverticula, fistulae.	

Recommendation	Strength rating
Consider magnetic resonance imaging urethrography as an ancillary test in posterior	Strong
urethral stenosis.	

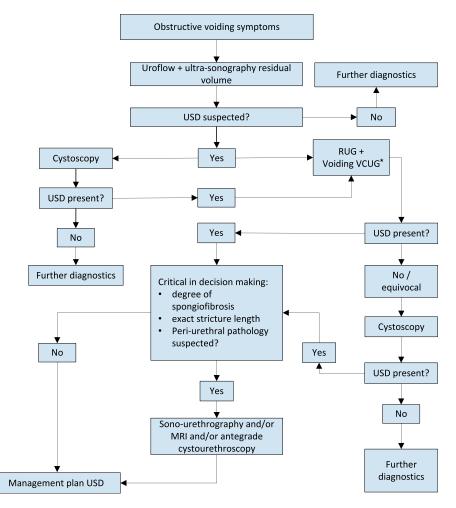


Figure 5.1: Diagnostic flowchart of patients with suspected urethral stricture disease

\*Use VCUG in case of (nearly-) obliterative strictures or stenosis. MRI = Magnetic resonance imaging; RUG = retrograde urethrography, USD = urethral stricture disease; VCUG = voiding cystourethrogram.

# 6. DISEASE MANAGEMENT IN MALES

#### 6.1 Conservative options

#### 6.1.1 **Observation**

A stricture will usually result in diminution in flow once the calibre of the urethral lumen is  $\leq$  10 Fr [142]. In other strictures (> 10 Fr), the diagnosis is often made by coincidence in asymptomatic patients because of a urologic examination for other reasons (e.g., cystoscopy, need for urethral catheterisation) [142]. Purohit et al., performed observation and repeated cystoscopic evaluation of 42 subclinical, incidentally encountered strictures ( $\geq$  16 Fr). After a median follow-up of 23 months, only five (12%) strictures progressed to a low-grade stricture (11-15 Fr). No patient developed symptoms and none of them needed surgical intervention [142]. These patients are candidates for observation although no evidence exist on the long-term evolution of these strictures.

In a series of anatomic stricture recurrence ( $\leq$  16 Fr) after urethroplasty, only 65% of patients were symptomatic [143]. Some asymptomatic patients refused further intervention because they had experienced substantial improvement after their primary urethroplasty. These patients were considered as functional "success" [143]. A multicentric study of the Trauma and Urologic Reconstructive Network of Surgeons observed an important discrepancy between cystoscopic recurrence and need for further intervention [141]. Patients with a large calibre (> 16 Fr) recurrence had a one and two-year need for intervention rate of 4% and 12%, respectively. Of note, patients with small-calibre ( $\leq$  16 Fr) recurrence had a one and two-year need for intervention rate of only 41% and 49%. Patients who needed intervention had poorer PROMs suggesting clinical symptoms and

bother. There is no information on long-term complications in patients with recurrences who did not undergo intervention. In cases of an asymptomatic stricture recurrence, it might be an option not to intervene but to perform regular follow-up.

Care must be taken about the term "asymptomatic" stricture (recurrence) as patients might conceal their bother and symptoms by different means (not drinking, social avoidance) and might only search for medical help once concealment is no longer tenable [188].

# 6.1.2 Suprapubic catheter

Radiation-induced urethral strictures are a difficult to treat population as stricture-free rates for urethral reconstruction are lower compared to those in non-irradiated patients [189]. Fuchs *et al.*, evaluated 75 patients who were initially treated by suprapubic diversion for radiation-induced isolated BMS [190]. Only 51% eventually decided to undergo urethroplasty after a mean follow-up period of 25 months. Although there was no significant difference in overall performance status between patients with a chronic suprapubic catheter vs. those undergoing urethroplasty, all patients with a poor performance score remained with a suprapubic catheter. Patients with concomitant stress urinary incontinence (SUI) opted more often to keep their suprapubic catheter as the SUI improved in 61% of cases. On the other hand, patients who kept their suprapubic catheter suffered from catheter-related complications in 27% of cases. Urinary diversion by ileal conduit was performed in 30% of patients who remained with a suprapubic catheter while this was only the case in 8% who underwent urethroplasty.

A suprapubic catheter is also an option in frail patients not able to undergo surgery or in patients who do not want (further) urethral surgery and are willing to accept the complications of a suprapubic catheter [191].

Summary of evidence	LE
Patients with asymptomatic incidental (> 16 Fr) strictures have a low risk of progression and to	3
develop symptoms.	
Only half of the patients initially treated with a suprapubic catheter for radiation-induced	3
bulbomembranous strictures will proceed with urethroplasty.	

Recommendations	Strength rating
Do not intervene in patients with asymptomatic incidental (> 16 Fr) strictures.	Weak
Consider long-term suprapubic catheter in patients with radiation-induced	Weak
bulbomembranous strictures and/or poor performance status.	

# 6.2 Endoluminal treatment of anterior urethral strictures in males

The ability to treat the majority of strictures by less invasive and time-consuming means, offers obvious benefits particularly when specialist surgical services are not available, or patients simply prefer a more pragmatic immediately available solution.

#### 6.2.1 Direct vision internal urethrotomy

In contemporary practice, direct vision internal urethrotomy (DVIU) is commonly performed as a first-line treatment of urethral strictures [192]. It is usually performed under general or spinal anaesthesia in well-resourced countries but shown to be well tolerated under local anaesthesia with or without sedation [193-195].

## 6.2.1.1 Indications of "cold knife" direct vision internal urethrotomy

6.2.1.1.1 Direct vision internal urethrotomy for primary stricture treatment

In the only high-level evidence study, Steenkamp *et al.*, randomised 210 patients with seemingly comparable non-obliterative strictures at all locations of the urethra to either filiform dilatation vs. DVIU with local anaesthesia on an outpatient basis [196]. They collected objective data with RUG performed at seven follow-up visits (3, 6, 9, 12, 24, 36 and 48 months). This unique study showed that urethral dilatation is equally effective as DVIU but both procedure modalities become less effective with increasing stricture length (see section 6.2.1.1.3.1).

A Cochrane review in 2012 could not identify a single prospective RCT comparing DVIU (or dilatation) with urethroplasty at the anterior urethra [197]. Since then, the randomised Open-label Superiority Trial of Open Urethroplasty vs. Endoscopic Urethrotomy (OPEN) prospectively randomised patients with a recurrent bulbar stricture between open urethroplasty and DVIU but this was for recurrent bulbar strictures only and not as primary treatment [198] (see section 6.2.1.1.2). A retrospective cohort series in boys with bulbar stricture reported a patency rate of 53% for DVIU and 80% for urethroplasty. No statistical analysis was performed and no information on stricture length was available in both cohorts which makes direct comparison hazardous [199].

Patency rates vary considerably between 8% and 77% after DVIU (predominantly without prior urethroplasty) in retrospective cohort studies with minimum follow-up of one year [69, 199-208] (Table 6.1). Median time to recurrence was less than twelve months in most series [69, 200-202, 204-206]. This large variation in patency rate can be in part explained by the heterogeneous nature of the strictures and various definitions of patency used by the authors in these series. Indication to perform DVIU is dependent on various stricture characteristics that are prognostic for a successful outcome.

Study	Ν	Age	Follow-up	Location	Length	Previous	TTR	Patency
		(years)	(months)		(cm)	interventions	(months)	rate (%)
Santucci	76	53 (range:	18 (range:	Bulbar: 37 (49%)	1.5 (0.2-5)	Primary: 100%	7	8
<i>et al.</i> [200]		17-100)	1-30)	Penile: 4 (5%)				
				Penobulbar: 1 (1%)	]			
				Unknown: 34 (45%)	]			
Pansadoro	224	62 (range:	98 (range:	Bulbar: 142 (63%)	1.6 (0.1-6.5)	Primary: 88%	< 12	32
<i>et al</i> . [201]		11-90)	60-216)	Penile: 37 (17%)	]		56%	
				Penobulbar: 45 (20%)	]	Recurrent: 12%	-	-
Al Taweel	301	37 (range:	36	Bulbar: 227 (75%)	1.3 (0.4-4.2)	Primary: 47%	10	8.3
et al. [204]		17-82)		Penile: 50 (17%)	1	D		
				Penobulbar: 24 (8%)	1	Recurrent: 53%	-	-
Barbagli	136	37 (IQR:	55 (range:	Bulbar: 100%	1-2 cm:	Primary: 100%	25	57
et al. [203]		25-48)	36-92)		45%			
					2-3 cm:			
					40%			
					3-4 cm:			
					15%			
Kluth et al.	128	64 (SD: 16)	16 (IQR:6-43)	Penile: 15 (12)	NR	Primary: 66%	8	52
[202]				Bulbar: 112 (88)	1			
				Unknown: 1 (1%)	-	Recurrent: 34%	-	-
Pal et al.	186	39 (SD:15)	1 <sup>st</sup> DVIU: 58	bulbar: 100%	NR	Primary: 69%	8.5	1 <sup>st</sup>
[205]			(SD: 15)			, <b>,</b> , .		DVIU: 30
[]			2 <sup>nd</sup> DVIU: 56			Repeat: 31%	-	2 <sup>nd</sup>
			(SD: 15)			hopedi. 0170		DVIU: 23
			3 <sup>rd</sup> DVIU: 45					3rd
			(SD: 15)					DVIU: 13
Diamond	53	14	30 (range:	bulbar: 100%	NR	Primary: 100%	23	53%
et al. [199]			6-64)					
Launonen	34	6 (range:	79 (range:	Bulbar: 74%	≤ 2 cm:	Primary: 100%	4	26%
et al. [206]		0-16)	7-209)	Bulball 1 170	85%			2070
			1 200)	Penile: 21%	> 2 cm:	-		
					15%			
				Penobubar: 6%	-	-		
Redon-	67	57 (range:	40 (range:	Penile:9%	≤ 1 cm:	Primary: 90%	< 24	63%
Galvez		15-91)	12-120)		82%		~	
et al. [207]			12 120)	Bulbar: 64%	> 1 cm:	Repeat: 10%	-	-
				VUA: 21%	18%	hopean rovo		
				Membranous: 6%				
Harraz	430	50 (SD: 15)	29 (range:	Bulbar: 100%	< 2 cm	NR, prior	NR	58%
et al. [208]		00 (02. 10)	3-132)			urethroplasty		0070
01 07. [200]						excluded		
Yürük	193	65 (SD: 13)	36 (SD: 12)	Bulbar: 100%	< 1 cm: 140	0%	87% of	77%
et al. [69]		00 (00. 10)	00 (00. 12)		(73%)	0,0	recurrence	1170
or un [00]					(,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		≤ 3	
					1-2 cm:		<u>≤</u> 3 100% of	-
					21 (11%)		recurrence	
						-		
					2-3 cm:		≤6	
					32 (17%)			

### Table 6.1: Results of DVIU in series with minimum follow-up > 12 months

DVIU = Direct vision internal urethrotomy; IQR = interquartile range; N = number of patients; NR = not reported SD = standard deviation; TTR = time to recurrence.

# 6.2.1.1.2 Direct vision internal urethrotomy for recurrent strictures and as salvage treatment after failed urethroplasty

In the OPEN trial, a recurrent stricture was defined as at least one previous failed intervention (endoscopic urethrotomy, urethral dilatation, urethroplasty) [209]. The previous intervention was predominantly DVIU. Despite poor recruitment, 108 and 112 patients were randomised to urethroplasty and DVIU respectively in a 24-month study protocol. Both groups had a similar improvement in voiding score symptoms after intervention. However, patients undergoing urethroplasty had 2.6 higher odds of experiencing an improvement of  $\geq$  10 ml/s in their maximum urinary flow compared to those undergoing urethrotomy (p=0.001) [209]. Need for re-intervention was observed in 13.8% vs. 25.9% of cases respectively allocated to urethroplasty and DVIU resulting in a 48% lower risk for re-intervention with urethroplasty (HR: 0.52; 95% CI: 0.31-0.89; p=0.017) [209]. Of note, self-dilatation was not considered a re-intervention [209]. Direct vision internal urethrotomy is also used as salvage treatment for recurrent strictures after urethroplasty. Brown et al., used DVIU for stricture recurrence (mean length: 4 cm; range: 1.5-7 cm) after excision and primary anastomosis (EPA), buccal mucosa grafts (BMG) urethroplasty and penile skin graft urethroplasty [210]. Patency was obtained in thirteen out of 37 cases (35%) after a single DVIU. After free graft urethroplasty (FGU), a short, veil-like stricture (or "diaphragm") might develop at the distal or proximal end of the graft. Rosenbaum et al., used DVIU to a selected cohort of 43 patients with a short (< 1 cm), veil-like stricture after BMG urethroplasty [211]. After a mean follow-up of twelve months, patency rate was 51%. Farrell et al., performed DVIU with mitomycin C (MMC) injection in seventeen patients with a short (median 2 cm; interquartile range [IQR] 1-2.5 cm) recurrence after bulbar urethroplasty (no details on technique available) and patency was achieved in twelve (71%) patients [212].

#### 6.2.1.1.3 Predictors of failure of "cold knife" direct vision internal urethrotomy

Several groups tried to identify prognostic factors to predict which patients are most likely to fail initial treatment (Table 6.2).

#### 6.2.1.1.3.1 Stricture length

Stricture length was identified as an important predictive factor for recurrence in several series. For bulbar strictures, Pansadoro *et al.*, found a 71% and 18% patency rate for < 1 cm and  $\geq$  1 cm strictures respectively (p < 0.001) [201]. In the series of Al Taweel *et al.*, no patient with a stricture > 1 cm who achieved patency was stricture-free, whereas this was 27% for strictures < 1 cm (p < 0.001) [204]. Barbagli *et al.*, reported an estimated five-year patency rate of 71%, 51% and 39% for 1–2 cm, 2–3 cm and 3–4 cm strictures respectively (p < 0.0001) [203]. Pal *et al.*, reported no patency in case of strictures > 1 cm [205]. In their prospective study, Steenkamp *et al.*, reported that for each 1 cm increase in the length of the stricture the risk of recurrence was increased by 1.22 (95% Cl: 1.05–1.43) [196]. In a paediatric series, a 0% patency rate was obtained for strictures > 2 cm [206]. Redon-Galvez *et al.*, reported a 25% patency rate for strictures > 1 cm, whereas strictures  $\leq$  1 cm had a 71% patency rate (p=0.006). This difference remained statistically significant in the multivariable analysis, when adjusted for stricture location (HR: 1.75; p=0.025) [207]. A SR of case series calculated a weighted average patency rate of 71.2% vs. 23.2% for strictures less and more than 1 cm respectively (p < 0.0001) [213].

#### 6.2.1.1.3.2 Stricture tightness (calibre)

Pansadoro *et al.*, reported a patency rate of 69% and 34% for strictures more than and less than 15 Fr in calibre, respectively (p < 0.001) [201]. Using pre-operative maximum urinary flow ( $pQ_{max}$ ), as surrogate for urethral calibre, Barbagli *et al.*, stratified patients into three groups ( $pQ_{max} < 5 \text{ vs.} 5-8 \text{ vs.} > 8 \text{ ml/s}$ ) and reported an estimated five-year patency rate of 31% vs. 53% vs. 83%, respectively (p < 0.0001) and the importance of  $pQ_{max}$  was confirmed in multi-variate analysis [198]. Kluth *et al.*, could not confirm the significance of  $pQ_{max}$  on the outcome of DVIU [202].

#### 6.2.1.1.3.3 Number of strictures

Pansodoro *et al.*, found poorer patency rates in case of DVIU for multiple strictures compared to a single stricture at both the bulbar (18% vs. 50%; p < 0.001) and penile urethra (8% vs. 35%; p=0.013) [201]. Pal *et al.*, reported a 0% patency rate in case of multiple strictures whereas this was 35% for a single stricture (p=0.03) [205].

#### 6.2.1.1.3.4 Stricture aetiology

Harraz *et al.*, identified idiopathic stricture aetiology as an independent risk factor for failure (HR: 3.11; p=0.035) [208]. On the other hand, stricture aetiology was not a predictive factor in many other series [201, 205, 206].

#### 6.2.1.1.3.5 Stricture location

Several series have reported a better patency rate for bulbar strictures compared to penile stricture or penobulbar strictures [196, 201, 204]. Kluth *et al.*, could not identify stricture location as an independent prognostic factor but only 12% of patients had a stricture at the penile urethra [202].

#### 6.2.1.1.3.6 Previous interventions

Pansodoro *et al.*, [201], Al Taweel *et al.*, [204] and Heyns *et al.*, [214] found a 0% patency rate after two or more prior failed DVIU, whereas this occurred after three and four prior failed DVIUs in the series of Santucci *et al.*, [200] and Launonen *et al.*, [206], respectively. Kluth *et al.*, identified secondary DVIU for a recurrent stricture as an independent risk factor for stricture recurrence (HR=1.78; 95% Cl: 1.05-3.03; p=0.032) [202]. Pal *et al.*, found significantly better patency rates after a 1<sup>st</sup> DVIU compared to a 2<sup>nd</sup> or 3<sup>rd</sup> DVIU [205].

#### 6.2.1.1.3.7 Other factors

Two series could not identify age, diabetes, hypertension, obesity and smoking as independent predictive factors [202, 203]. However, Harraz *et al.*, identified that older age at presentation and obesity are independent predictors of failure after DVIU [208].

In the absence of well-designed, adequately powered multi-centre trials it is difficult to answer the question as to which clinical factors are predictive of failure of DVIU in men with urethral strictures. However, based on the predictors evaluated above and further supported by consensus papers [215-217], one can summarise that the best candidates are previously untreated patients with a single, short (max. 2 cm) bulbar stricture. In a selected group of patients (n=60), a patency rate of 77% was reported for a single, short, primary bulbar stricture with a minimum follow-up of five years [201]. This is confirmed by a more contemporary cohort of patients with untreated short (1-2 cm) bulbar urethral strictures, in which the estimated five-year patency rate was 71% [203].

Author	Location	Length	Calibre	Multiplicity	Prior DVIU
Pansodoro et al.	Penile: 16%	< 1 cm: 71%	< 15 Fr: 34%	Single: 50%	None: 36%
[201]	Penobulbar: 11%	> 1 cm: 18%	> 15 Fr: 69%	Multiple: 16%	1:6%
	Bulbar: 42%	-	-	-	> 1: 0%
Steenkamp et al.	RR for recurrence	< 2 cm: 60%	NR	NR	None: 50-60%
[196] / Heyns [214]	penile vs. bulbar:	(@12 months)			(@48 months)
	1.85 (95% CI: 0.94 to				
	3.67, p = 0.077)				
	-	2-4 cm: 50%	-	-	1: 0-40% (@48 months)
		(@12m)			
	-	> 4 cm: 20%	-	-	2: 0% (@24 months)
		(@12 months)			
Santucci et al. [200]	NR	NR	NR	NR	0: 8%
	-	-	-	-	1:6%
	-	-	-	-	2: 9%
	-	-	-	-	> 2: 0%
Al Taweel et al. [204]	Bulbar: 11%	< 1 cm: 27%	NR	NR	0: 12.1%
	Penile: 0%	1-2 cm: 0%	-	-	1: 7.9%
	Penobulbar: 0%	> 2 cm: 0%	-	-	> 1: 0%
Barbagli et al. [203]	NA	1-2 cm: 71%	pQ <sub>max</sub>	NA	0: 62%
		(@60 months)	< 5 ml/s: 31%		
	-	2-3 cm: 51%	pQ <sub>max</sub>	-	1: 37%
		(@60 months)	5-8 ml/s: 53%		
	-	3-4 cm: 39%	pQ <sub>max</sub>	-	-
		(@60 months)	> 8 ml/s: 83%		
Kluth et al. [202]	Location no predictor	NR	pQ <sub>max</sub> no	NR	0: 60%
			predictor		
	-	-	-	-	≥ 1: 39%
Pal et al. [205]	NA	< 1 cm: 45%	NR	Single: 35%	0: 30%
	-	1-1.5 cm: 0%	-	Multiple: 0%	1: 23%
	-	> 1.5 cm: 0%	-	-	2: 13%

#### Table 6.2: Predictors for urethral patency after direct vision internal urethrotomy

Launonen [206]	Bulbar: 76%*	< 2 cm: 83%*	NR	NR	0:26%
	Penile: 71%*	> 2 cm: 0%*	-	-	1:33%
	-	-	-	-	2:26%
	-	-	-	-	3: 11%
	-	-	-	-	4: 0%
Redon-Galvez [207]	NR	≤ 1 cm: 71%	NR	NR	NR
	-	> 1 cm: 25%	-	-	-

DVIU = Direct vision internal urethrotomy; NA = not applicable; NR = not reported; pQmax = pre-operative maximum urinary flow.

\*patency rates are reported after repetitive treatments.

# 6.2.1.2 Indications of "hot-knife" direct vision internal urethrotomy

# 6.2.1.2.1 Laser urethrotomy

Lasers available for urological applications, including Neodymium:YAG, Argon, Holmium:YAG, Potassium titanyl phosphate (KTP) and Tm:Yag, have been used for the treatment of urethral strictures. A SR identified four RCTs comparing laser urethrotomy and the "cold knife" urethrotomy. All studies were limited by short-term outcome evaluation and none of these four studies specified the results based on the location of the stricture. Two of these studies reported specific recurrence rates and meta-analysis showed a RR for recurrence of 0.55 (95% CI: 0.18-1.66; p=0.29), 0.39 (95% CI: 0.19-0.81; p=0.01) and 0.44 (95% CI: 0.26-0.75; p=0.003) in favour of laser urethrotomy after three, six and twelve months respectively [218]. Jin *et al.*, performed a SR including 44 case series on laser urethrotomy or "cold knife" DVIU [213]. This included nineteen articles on laser urethrotomy and 25 articles on "cold knife" DVIU. The overall weighted average stricture-free rate was 74.9% (371/495) and 68.5% (1874/2735) for laser vs. "cold knife" DVIU, respectively (p=0.004). Although statistically significant, the results must be interpreted with caution because of heterogeneity and because no details are provided on follow-up duration. Specifically looking at first DVIU, laser and "cold knife" DVIU obtained a stricture-free rate of 58.6% and 42.7% respectively and the difference was no longer statistically significant (p=0.09). At the bulbar urethra, laser and "cold knife" DVIU yielded a stricture-free rate of 52.9% and 60%, respectively (p=0.66) [213].

After publication of this SR, the EAU Guideline Panel scope search identified two additional RCTs [219, 220] and one retrospective cohort series [221]. In the RCT of Yenice *et al.*, patients with a primary, bulbar stricture were randomised either to "cold knife" DVIU (n=29) or holmium:YAG laser urethrotomy (n=34). After twelve months follow-up, no significant difference in patency rate was identified (79% for "cold knife" DVIU vs. 68% for laser urethrotomy, p=0.3) [220]. In their RCT, Chen *et al.*, reported a better patency rate after one year with laser (n=24) compared to "cold knife" (n=22) DVIU (respectively 88% vs. 18%; p < 0.05). However, after two years the benefit for laser disappeared and after five years both techniques showed a low patency rate: 9% for "cold knife" DVIU vs. 12% for laser DVIU (p > 0.05) [219]. In both these RCTs, operation time was slightly but significantly longer with laser DVIU as compared to "cold knife" DVIU [219, 220]. Holzhauer *et al.*, evaluated in a retrospective comparative study "cold knife" (n=127) with laser (n=65) DVIU at a mean follow-up of sixteen and eighteen, respectively. They reported patency rates of 42% for "cold knife" DVIU vs. 31% for laser DVIU (p=0.1) [221].

# 6.2.1.2.2 Plasmakinetic (bipolar) urethrotomy

Cecen *et al.*, conducted an RCT comparing plasmakinetic with "cold knife" DVIU (n=136) [222]. They reported patency rates for plasmakinetic and "cold knife" urethrotomy at nine months in respectively 86% and 70% of cases (p=0.025). At eighteen months, patency rates for plasmakinetic and "cold knife" urethrotomy were 63% and 67%, respectively (p=0.643) [222]. A prospective cohort study on primary strictures < 2 cm reported a patency rate at twelve months in 23/30 (77%) cases for plasmakinetic DVIU vs. 19/30 (63%) cases with "cold knife" DVIU (p=0.04) [223]. A retrospective case series (n=27) reported a 74% patency rate for short (1-2.5 cm) strictures after a mean follow-up of fourteen months [224]. They reported negligible blood loss during the procedure and no post-operative incontinence.

Based on the conflicting results described above and considering the heterogeneity of series and absence of long-term follow-up, overall, the available studies do not support the efficacy of one technique of DVIU over another. Given the similar complication rates between techniques (see section 6.2.1.3), no recommendation can be made in favour of one technique over another.

#### 6.2.1.3 Complications of direct vision internal urethrotomy

6.2.1.3.1 Complications of "cold knife" direct vision internal urethrotomy

An overall complication rate of 6.5% was reported in a SR of Jin *et al.*, based on twelve articles including 1,940 patients [213] (Table 6.3).

Notably, erectile dysfunction (ED) was reported in 5.3% of cases in this review [213]. In addition, Graversen *et al.*, reported ED in eleven out of 104 (10.6%) patients [225]. This risk appears higher in strictures located in the penile urethra and, in addition to the poor patency rates, the use of DVIU in the penile urethra must be discouraged [217, 225].

6.2.1.3.2 Complications of "hot knife" direct vision internal urethrotomy The SR of Jin *et al.*, reported a total complication rate of 11.8% (39/330) [213] (Table 6.3).

6.2.1.3.3 Complications of "cold knife" vs. "hot knife" direct vision internal urethrotomy

In a SR of RCTs comparing "cold knife" DVIU vs. laser DVIU, only 1/4 series reported complications [218]. In the laser group, an 8.9% complication rate was found due to contrast extravasation to the perineum and stricture recurrence. For the "cold knife" DVIU, a 15.5% complication rate was reported related to bleeding [218]. Two later RCT's reported similar rates of urinary extravasation [219, 220] and urinary incontinence (UI) [219] with both techniques.

The SR of retrospective case series of Jin *et al.*, found no significant differences in the incidence rates of UI, urinary extravasation and UTI between laser and "cold knife" DVIU [213]. However, urinary retention and haematuria were more frequent with laser compared to "cold knife" DVIU [213]. Conversely, In the series of Yenice et al., haematuria was only reported after "cold knife" DVIU but not after laser DVIU (p=0.6) [220] (Table 6.3).

Study/Complication	"Cold knife" DVIU (%)	Laser DVIU (%)	p-value
Jin et al. [213]			
Urinary extravasation	2.9	3.1	0.938
Urinary incontinence	4.1	2.1	0.259
Urinary tract infection	2.1	2.7	0.653
Urinary retention	0.4	9	< 0.0001
Haematuria	2	5.2	0.034
Epididymitis	0.5	NR	NA
Fever	2.3	NR	NA
Scrotal abscess	0.3	NR	NA
Erectile dysfunction	5.3	NR	NA
Urinary tract irritation	NR	11.4	NA
Urinary fistula	NR	1.5	NA
Dysuria	NR	5.1	NA
Yenice et al. [220]		·	
Urinary extravasation	0	2.9	0.6
Haematuria	10	0	
Chen et al. [219]			
Urinary extravasation	9.1	4.2	0.5
Urinary incontinence	4.5	4.2	

#### Table 6.3: Complications after "cold knife" DVIU vs. laser DVIU

DVIU = direct vision internal urethrotomy; NA = not applicable; NR = not reported.

6.2.1.3.4 Complications of direct vision internal urethrotomy vs. dilatation

A Cochrane review found no significant differences for overall intra-operative complications (single dilatation vs. DVIU respectively 14% vs. 11%; RR: 0.75; 95 CI: 0.36-1.55) nor for individual complications (difficulty urinating, haematuria, false passage, pain, knotting/breaking/bending filiform leader) [196, 197]. The low rate of false passage for both DVIU and dilatation (respectively 0.96 and 0.94%) might be explained by the systematic use of a filiform leader in both groups which was inserted endoscopically in the dilatation group followed by coaxial dilatators [196, 197].

A small retrospective study comparing balloon dilatation (n=31) with DVIU (n=25) showed less urethral bleeding (6.5 vs. 32%; p=0.017) and UTI (3.2 vs. 24%; p=0.037) with balloon dilatation [226].

Apart from acute peri-operative complications described above, the stricture length was reported to increase after DVIU treatment requiring complex urethral reconstruction, but the authors of this retrospective study clearly state the limitations of the study design in the absence of consistent baseline investigations [200]. Other

authors mention that repeat urethral manipulations (DVIU and/or dilatation) can increase stricture complexity and delays time to urethroplasty [227, 228].

6.2.1.3.5 Complications of "cold knife" direct vision internal urethrotomy vs. urethroplasty

The OPEN-trial reported adverse events of any type in 61% and 26.1% after urethroplasty (all types) and DVIU respectively [209]. In the urethroplasty group, mouth pain (related to oral mucosa graft [OMG] harvesting) and wound infection was noted as complication in respectively 14.6% and 4.9% of cases. Erectile dysfunction was 4.9% and 2.6% after urethroplasty and DVIU, respectively. Serious adverse events were reported in 8.5% and 8.7% after urethroplasty and DVIU respectively [209].

Summary of evidence	LE
Direct vision internal urethrotomy performs poorly in penile strictures. Direct vision internal	1b
urethrotomy at the penile urethra might provoke venous leakage from the corpora cavernosa with	
subsequent risk of erectile dysfunction.	
Increased stricture length is associated with higher risk of failure of DVIU.	1b
In selected patients with a primary, single, short (< 2 cm) and non-obliterative bulbar stricture, a five-	3
year stricture-free rate of up to 77% can be expected.	
Direct vision internal urethrotomy has a stricture-free rate of 51-71% if performed for a short (< 2 cm)	3
recurrent stricture after prior bulbar urethroplasty.	
There is conflicting evidence that "hot knife" (laser, plasmakinetic) DVIU would be superior compared	1a
to "cold knife" DVIU after more than one year of follow-up.	

Recommendations	Strength rating
Do not use direct vision internal urethrotomy (DVIU) for penile strictures.	Strong
Do not use DVIU/dilatation as solitary treatment for long (> 2 cm) segment strictures.	Strong
Perform DVIU/dilatation for a primary, single, short (< 2 cm) and non-obliterative stricture at	Weak
the bulbar urethra.	
Perform DVIU/dilatation for a short recurrent stricture after prior bulbar urethroplasty.	Weak
Use either "hot" or "cold knife" techniques to perform DVIU depending on operator	Weak
experience and resources.	

# 6.2.2 Single dilatation

#### 6.2.2.1 Modalities of dilatation and results

Dilatation can be done in the office, under local anaesthesia and without complex resources [216, 229]. With dilatation, the urethral mucosa at the stricture site is stretched and the scarring is disrupted. This is opposed to DVIU where the stricture is incised. However, both treatment modalities use the same principle to achieve urethral patency: a breach of the urethral mucosa at the site of the stricture in which re-epithelialisation should occur faster than wound contraction [197].

When dilators are used to dilate bulbar urethral strictures, considerable experience is required to avoid accidental perforation of the urethra at the level of the stricture. In order to reduce the risks (esp. false passage, spongiosal perforation, urethral bleeding) of "classic" blind dilatation with rigid sounds [229], other strategies have been developed and evaluated in which the dilatation is visually controlled:

- endoscopic/fluoroscopic guidewire placement and progressive dilatation with Amplatz renal dilators [229, 230];
- endoscopic/fluoroscopic guidewire placement and balloon dilatation [226, 231];
- endoscopic/fluoroscopic guidewire placement and S-curved coaxial dilators [232].

Although no direct comparative studies of blind vs. visually controlled dilatation are available, several studies have reported a low complication rate with visually controlled modifications of dilatation. The recurrence rate with short follow-up largely varies between 7.7-64.5% (Table 6.4). Chhabra *et al.*, identified focal/short (< 1.5 cm) strictures and strictures at the bulbar urethra as predictors for a favourable outcome [231].

#### Table 6.4: Results of visually controlled dilatation

Study	Technique	Ν	FU (mo)	recurrence	Definition of	Complications			
					failure	Haematuria	False	Procedural	UTI
							passage	failure	
Akkoc	Amplatz	26	12-21	2 (7.7%)	Need for	3 (11.5%)	0 (0%)	NR	NR
et al. [229]					additional				
					intervention				
Chhabra	Balloon	144	24 (3-52)	21 (15.6%)	Need for	NR	0 (0%)	3 (2.1%)	14 (9,7%)
<i>et al.</i> [231]	+ ISD				additional				
	(permanent)				intervention				
Kallidonis	Coaxial	310	12	90 (33%)	No recurrence	11 (3.5%)	0 (0%)	7 (2.2%)	33 (10.6%)
et al. [232]	S-curved				@1 yr with				
					maximum				
					one additional				
					procedure				
Nomikos	Amplatz +	34	12	8 (23.5%)	Stricture	2 (5.8%)	NR	NR	3 (8.8%)
et al. [230]	DVIU + ISD				recurrence on				
	(1 yr.)				urethroscopy/				
					urethrography				
Yu et al.	Balloon	31	15 (5-36)	20 (64.5%)	Need for	2 (6.5%)	0 (0%)	NR	1 (3.2%)
[226]					subsequent				
					urethroplasty				

DVIU = direct vision internal urethrotomy; FU = follow-up; ISD = intermittent self-dilatation; mo = months; N = number of patients; NA = not applicable; NR = not reported; UTI = urinary tract infection; yr = year.

#### 6.2.2.2 Effectiveness of dilatation compared with direct vision internal urethrotomy

A SR identified only one prospective RCT comparing dilatation with DVIU and failed to detect any differences [196, 197]. In a small (n=56) retrospective cohort study, the three-year estimated stricture recurrence-free survival was 35.5% and 28% for respectively balloon dilatation and DVIU (p=0.21) [226].

At present, there is lack of evidence to support the claim that dilatation is superior to DVIU (or *vice versa*) and therefore, the indications for single dilatation are the same as for DVIU.

Repetitive dilatation/DVIU with curative intent (see also section 6.2.1.1.3.6 Previous interventions) should be avoided as no long-term freedom of recurrence can be expected [216] and because of the significant risk of increasing stricture length and complexity [227, 228] and prolonging the time to urethroplasty (which has better patency rates) [228].

Summary of evidence	LE
Visually controlled dilatation after endoscopic or fluoroscopic guidewire placement has a low	3
complication rate.	
Repetitive dilatations/DVIU have no long-term freedom of recurrence and increase stricture	1b
complexity.	

Recommendations	Strength rating
Use visually controlled dilatation in preference to blind dilatation.	Weak
Do not perform repetitive (> 2) direct vision internal urethrotomy/dilatations if urethroplasty	Strong
is a viable option.	

#### 6.2.3 Post-dilatation/direct vision internal urethrotomy strategies

Several strategies have been developed and evaluated to prevent wound contraction, improve the stricture-free rate and time to stricture recurrence after dilatation or DVIU.

It is noteworthy that these strategies tend to stabilise the stricture rather than to keep the patient stricture-free and the reported outcomes should be understood in this respect.

# 6.2.3.1 Intermittent self-dilatation

# 6.2.3.1.1 Results

A SR identified six randomised and quasi-randomised trials comparing ISD with no ISD with a follow-up between eight and 24 months [233]. Stricture recurrence was reduced in men performing ISD (85/197, 43%) vs. those who did not (128/207, 62%) (RR: 0.70; 95% CI: 0.48-1.00; p=0.05). There was significant heterogeneity, and the quality of included studies was very low, which led the authors to conclude there is uncertainty about the estimate [233]. This review found no significant difference in adverse events between ISD and no ISD (RR: 0.60; 95% CI: 0.11-3.26; p=0.56) [233]. One trial containing 48 patients found no significant difference in six vs. twelve months duration of ISD (RR: 0.67; 95% CI: 0.12-3.64) and another trial (n=59) found no significant difference from using a low-friction hydrophylic vs. a polyvinyl chloride catheter (RR: 0.32; 95% CI: 0.07-1.40) [233]. Other studies have been published after this SR of 2014. Chhabra *et al.*, reported that patients complying with ISD after dilatation had a lower need for re-intervention than those who did not, 12.3% vs. 20.5% respectively (p=0.2) [231]. After a mean follow-up of 25 months, Greenwell *et al.*, found a need for subsequent intervention in 13/31 (42%) men performing ISD vs. 47/95 (49%) who did not (p=0.46). The number of reoperations in patients with need for subsequent intervention was lower in the group performing ISD vs. those who did not (2.6 vs. 3.4). No major complications were reported in both groups [234].

## 6.2.3.1.2 Complications

The potential benefit of ISD in stabilising the stricture must be balanced against the drawbacks. Commonly reported complications are urethral bleeding (7.1%) [235] and UTI/epididymitis (4.7-18.1%) [236, 237]. A multicentric prospective study (n=85) reported that respectively 35% and 26% of patients had moderate to severe difficulties in catheterisation and respectively 32% and 17% of patients suffered moderate to severe pain while performing ISD. This had a serious impact on QoL which was rated moderate and poor in 32% and 55% of patients, respectively [35]. Younger age was identified as predictor for poor QoL, and QoL was more impaired in proximal stricture location (posterior and bulbar) [35]. In a study of 286 patients (mainly > 60 years old) performing ISD, 20% experienced problems with ISD and 33% had at least one infection annually. After a mean follow-up of 58 months 67% still continued with ISD [238]. Khan *et al.*, reported eight "drop-outs" of 30 (26.7%) men randomised to ISD [237]. Of these eight "drop-outs", two were unable to perform ISD and one stopped because of pain.

As mentioned above, repetitive dilatation (including ISD) increases stricture complexity and delays time to urethroplasty [227, 228].

### 6.2.3.1.3 Intermittent self-dilatation combined with intra-urethral corticosteroids

To delay wound contraction at the stricture site, intra-urethral corticosteroids (as a catheter lubricant) have been used to improve the results of ISD. In 2014, a SR identified three prospective RCTs comparing ISD and local steroid (triamcinolone) ointment vs. ISD without local steroid ointment [239]. These three studies included a total 67 and 68 patients randomised to local steroid, or not, with a follow-up ranging between twelve and 36 months. There were fifteen (22.4%) recurrences in the steroid group and 25 (36.7%) in the control group (OR: 0.51; 95% CI: 0.24-1.10; p=0.09) [239]. Time to recurrence was longer in the steroid group vs. the control group (weighted mean difference = 0.29; 95% CI: 0.08-1.00; p=0.05). There was no difference in adverse events between groups [239].

Since 2014, two additional RCTs have been published. Ergun *et al.*, evaluated patients after DVIU for primary short (< 2 cm), bulbar (82%) or posterior (18%) strictures that were further randomised between ISD (n=30) and ISD + triamcinolone ointment (n=30) for six weeks. Stricture recurrence rate after 24 months was not significantly different between ISD and ISD + triamcinolone (respectively 33.3 and 30%) [240]. On the other hand, Regmi *et al.*, found a lower stricture recurrence rate (22% vs. 46%, p=0.04) in patients performing ISD + triamcinolone (n=27) vs. ISD alone (n=28) [241]. In this study, median time to recurrence was 7.4 ± 4.5 months vs. 11.9 ± 3 months in respectively ISD alone and ISD + triamcinolone (p=0.16). Both studies reported no complications related to ointment of triamcinolone [240, 241].

In a small (n=28) cohort with LS-related strictures, an intra-urethral steroid regimen was successful (no need for subsequent escalation of therapy) in 25 (89%) patients after a mean follow-up of 25 months [155]. This regimen consisted of applying clobetasol cream 0.05% as lubricant on a calibration device (10-16 Fr catheter or dilator) twice a day during a minimum of two months. As most of these patients further continued with instillation of steroids on a calibration device, this high "success" rate must be viewed with caution and should be considered as a stabilisation of the stricture rather than a cure. Eventually, twelve (42.8%) patients could reduce the interval of instillation/dilatation and three (10.7%) of them could finally stop the treatment [155].

Summary of evidence	LE
Stricture recurrence was reduced in men performing ISD vs. those who did not.	1a
Intra-urethral corticosteroids in addition to ISD delays the time to recurrence.	1a

Recommendations	Strength rating
Perform intermittent self-dilatation (ISD) to stabilise the stricture after dilatation/direct vision	Weak
internal urethrotomy if urethroplasty is not a viable option.	
Use intra-urethral corticosteroids in addition to ISD to stabilise the urethral stricture.	Weak

## 6.2.3.2 Intralesional injections

The rationale of adjuvant intralesional injections is to reduce fibroblast proliferation and excessive urethral scaring [215].

## 6.2.3.2.1 Steroids

A 2014 SR identified five studies comparing intra-urethral submucosal steroid injection vs. no intra-urethral submucosal steroid injection after DVIU, of which two were RCTs [239]. Meta-analysis of these two RCTs with 57 and 58 patients in, respectively, the steroid and control group showed no statistical difference in recurrence rate (OR: 0.53; 95% CI: 0.25-1.13; p=0.10).. Time to recurrence was significantly longer in the steroid group (weighted mean difference = 4.43; 95% CI: 2.77–6.09, p < 0.00001). There were no significant differences regarding adverse events (infection, bleeding, extravasation) between both groups (weighted mean difference = 1.59; 95% CI: 0.71–3.58, p=0.26).

## 6.2.3.2.2 Mitomycin C

An RCT (n=40) by Moradi *et al.*, reported that MMC hydrogel significantly reduced recurrent stricture formation (10% with MMC vs. 50% without MMC; p=0.001) at one year in patients with anterior strictures < 1.5 cm and no or mild spongiofibrosis on US [242]. The authors reported no significant complications related to MMC injection [242]. Another RCT (n=151) with eighteen months follow-up in predominantly bulbar strictures reported a stricture-free rate of 86% and 63% after DVIU with and without MMC, respectively (p=0.002) [243]. The mean stricture length was less than 2 cm in both groups. No significant complications, such as necrosis of the urothelium, extravasation, or systemic absorption, were recorded in the MMC group [243].

Farrell *et al.*, conducted a retrospective study in 44 patients with recurrent bulbar and BMS with a median stricture length of 2 cm (IQR: 1-2.5 cm) [212]. They reported patency in 75% after a median follow-up of 26 months. No long-term complications attributed to MMC were observed.

In a prospective case-series (n=103), Kumar *et al.*, evaluated adjuvant intralesional injections of a cocktail of triamcinolone, MMC and hyaluronidase after DVIU for predominantly (78%) bulbar strictures with a median follow-up of fourteen months. A stricture-free rate of 81% was reported and none of the patients suffered local or systemic side effects related to the injection [244].

Despite the encouraging results reported with MMC, the use of MMC in urethral stricture management is still off-label and not widespread. Severe complications with MMC injection are possible. Redshaw *et al.*, reported in a multi-institutional series that 4/55 (7%) patients experienced serious complications with osteitis pubis, rectourethral fistula and necrosis of the bladder floor when MMC was injected after endoscopic incision to treat BNS [245]. Given this safety concern and in the absence of well-conducted and adequately powered RCTs, MMC adjuvant to DVIU should only be used in the framework of a clinical trial.

See supplementary <u>Table S6.1</u> for further information.

#### 6.2.3.2.3 Platelet rich plasma

Rezaei *et al.*, conducted an RCT comparing DVIU + platelet rich plasma (PRP) (n=44) vs. DVIU + saline (n=43) in primary, bulbar strictures < 1.5 cm in length [246]. The two-year stricture-free rate was 78% vs. 56% after DVIU with or without PRP, respectively (p=0.034). Complications were frequent but not significantly different between both groups (DVIU + PRP: 70%; DVIU + saline: 79%). All complications (urethral bleeding, haematuria, urethral pain, pelvic pain, urinary leakage and genitoperineal swelling) were classified as grade 1 according to the Clavien-Dindo system. Further validation of this treatment is needed before general clinical implementation.

Summary of evidence	LE
Intralesional injections after DVIU might improve stricture-free rates on the short-term compared to	1a
DVIU alone. Experience is limited and the use of these drugs are off-label.	

Recommendation	Strength rating
Do not use intralesional injections outside the confines of a clinical trial.	Weak

## 6.2.3.3 Urethral stents

Urethral stents are designed with the aim to oppose wound contraction after dilatation or DVIU [247, 248]. Stent insertion is a short procedure (< 60 minutes) that can be done under local or spinal anaesthesia as "one-day" surgery [247, 249, 250]. Urethral stents are classified as permanent or temporary (removable, after six to twelve months).

# 6.2.3.3.1 Results

Permanent stainless-steel mesh stents are no longer commercially available. An RCT comparing dilatation/ DVIU only vs. dilatation/DVIU followed by temporary stent insertion for bulbar strictures reported a significantly longer stricture-free survival time in favour of dilation/DVIU followed by stent (median 292 vs. 84 days; p < 0.001) [251]. Only 20.6% of patients treated with a stent developed a recurrent stricture within one year vs. 82.8% in the control group. These results are corroborated by a prospective series of Wong *et al.*, who found a median stricture-free survival of two months after DVIU alone vs. 23 months after DVIU followed by temporary (three months) stent for bulbar strictures [248].

Failure and need for re-intervention are frequent (30-53%) and are usually because of stricture recurrence, stent encrustation, stent migration and urethral hyperplasia. Other complications include recurrent UTI, recurrent haematuria and genito-perineal pain (Table 6.5). Although stents are mainly used to treat bulbar strictures, they have been used for posterior stenoses as well. Stents used in the posterior urethra have a high risk (82-100%) of causing UI and this is most pronounced in patients with previous irradiation and/or strictures extending into the membranous or bulbar urethra [252]. In the bulbar urethra, the risk of UI is higher if stent placement is adjacent to the external sphincter [253]. The use of stents in the penile urethra is anecdotal. Jung *et al.*, reported stent failure in 4/7 (57%) patients with a penile stricture after a mean follow-up of eight months. Of those patients who failed, no patient with distal or pan-penile strictures was rendered stricture-free [254]. In their series, stricture recurrence after stenting of the penile urethra was significantly higher when compared to the bulbar urethra [254]. Although no direct comparison is available, temporary stents tend to have fewer and less severe complications compared to permanent stents (Table 6.7).

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s associated v
omplication
and c
e rate
Failure rate
able 6.5: Failure
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Study	Type of	Duration	z	Ŀ	Stricture	Stricture location Previous	Previous	Failure	<b>Defintion failure</b>	Compli	Complications					
	stent			(months)	length (cm)		interventions	rate		E	haematuria	stent	stent	urethral Local		5
												encrustation/ migration hyper- stone plasia	migration	hyper- plasia	pain	
												formation				
Abdallah	Thermo-	Temporary	23	17 (6)	3.6 (1.2)	Bulbar	DVIU/	12	Need for	4	3 (13%)	3 (13%)	5 (22%)	2 (8%)	9	NR
<i>et al.</i> [247]	expandable nitinol						urethroplasty: all	(52%)	re-intervention	(17%)					(26%)	
Jordan et	Thermo-	Temporary	63	12	2.7 (1.6)	Bulbar	DVIU only: all	28	Inability to pass 16	31	10 (16%)	3 (4.7%)	8 (13%)	NR	19	12
<i>al.</i> [251]	expandable nitinol							(44%)	Fr cystoscope	(49%)					(30%)	(19%)
Temeltas	Polymer-	Temporary	28	29 (7-46)	1.9 (0.5-3.5)	Bulbar	DVIU only: all	10	Stricture recurrence	NR	NR	1 (3.6%)	3 (11%)	RN	0 (0%)	NR
<i>et al.</i> [250]	coated							(36%)	on urethroscopy/							
									graphy, Q <sub>max</sub>							
11/2000	The sume of	Tempore	ç					1/000/ 2	< 15 m/s, UTI	1/00/ 0		1,00/ 0	111 5011	1/00/ 0		
wong er	Inermo-	lemporary	22	23 (9-31)	(c.+-1) +.2	Bulbar	DVIU ONIY: all	( (32%)	_	0%N) N	YN	0 (0%) N	1 (%C.4) 1	0%)U	(%n) n	Ĩ
<i>al.</i> [248]	expandable								17 Fr cystoscope,							
	nitinol								$Q_{max} < 10 \text{ ml/s or}$							
									recurrent obstructive							
									symptoms							
Atesci et	Thermo-	Permanent	20	144 (120	2.5 (0.5-5.5)	Bulbar	DVIU/	9	Need for	NR	NR	4 (20%)	2 (10%)	0 (0%)	8	1 (5%)
<i>al.</i> [249]	expandable			-192)			urethroplasty:	(30%)	re-intervention						(%07)	
	nitinol						all									
Sertcelik	Thermo-	Permanent	47	101 (84-	2 (0.5-5)	Bulbar (45),	urethroplasty	22	Need for	NR	NR	12 (26%)	2 (4%)	7 (15%)	20	0
<i>et al.</i> [253]	expandable			125)		bulbomem-	(19%)/	(47%)	re-intervention						(43%)	(19%)
	nitinol					branous (2)	DVIU (64%)/									
							railroading (17%)									
Erickson	Self-	Permanent	38	28 (30)	3 (1.7)	Posterior	DVIU only: all	20	Need for	7	3 (8%)	6 (16%)	NR	NR	9	31
<i>et al.</i> [252]	expandable					(prostate cancer		(23%)	re-intervention	(18%)					(16%)	(82%)
	super alloy					related); VAUS 24;										
	mesh					prostatic urethra										
						(irradition) 14										
DVIU = dire	ct vision inte	mal urethro	tomy	r; FU = follc	w-up; NR =	not reported; UI =	urinary incon	tinence;	DVIU = direct vision internal urethrotomy; FU = follow-up; NR = not reported; UI = urinary incontinence; UTI = urinary tract infection; VUAS = vesico-urethral anastomotic stricture;	infectior	ı; VUAS = ve	sico-urethral a	inastomoti	c strictur€		

Q<sub>max</sub>= maximum flow rate

# 6.2.3.3.2 Treatment of stent failure

In the case of stent failure, subsequent urethroplasty (usually with stent removal) is possible, but this urethroplasty is very likely to be more complex than it would have been had it been performed initially [255-257]. Due to the fact that the stainless-steel wires are fully embedded into the urethral wall, over time the urethral spongiosum is severely damaged. Horiguchi et al., found that a history of urethral stenting was an independent significant predictor of increased stricture complexity (OR: 13.7; 95% CI: 1.7-318.3; p=0.01) and need for more complex urethroplasty (OR: 6.9; 95% CI: 1.1-64.5; p=0.04) [227]. The majority (62%) of patients in this study had a permanent stent and tend to be difficult to remove because they are epithelialised, usually within six months [227]. The type of urethroplasty required depends on the length of the stricture and quality of local tissues [256]. In the majority of cases, it is possible to preserve the urethral plate and to perform a one-stage substitution urethroplasty [255, 256, 258]. The patency rates after different types of urethroplasty vary greatly between 16.7-100% [255-258] and this variation probably reflects variation in complexity of the stricture, rather than that the superiority of one technique of urethroplasty over another (for further information see supplementary Table S6.2). Due to these limitations, the use of stents should be avoided if subsequent urethroplasty is considered [247, 257]. Urethral stents are not a first-line treatment for urethral strictures but can be considered in co-morbid patients who have a recurrent stricture after DVIU/dilatation and are unable to have more complex urethroplasty or who refuse urethroplasty [247, 251, 252].

Summary of evidence	LE
Permanent urethral stents have a high complications and failure rate and make subsequent	3
urethroplasty more challenging if they fail.	
Stents have a higher failure rate in the penile urethra.	3
Temporary stents after DVIU/dilatation at the bulbar urethra prolong time to next recurrence compared	1b
to DVIU/dilatation alone.	

Recommendations	Strength rating
Do not use permanent urethral stents.	Strong
Do not use urethral stents for penile strictures.	Strong
Use a temporary stent for recurrent bulbar strictures after direct vision internal urethrotomy	Weak
to prolong time to next recurrence only if urethroplasty is not a viable option.	

# **6.3** Open repairs (urethroplasty): site and aetiology (clinical scenario) treatment options 6.3.1 The role of urethroplasty in the management of penile urethral strictures

Due to the specific aetiology and the associated problems, strictures related to failed hypospadias repair and LS will be discussed separately. However, many series reporting on the outcome of penile strictures have a mixed aetiology also including failed hypospadias repair and/or LS [259, 260]. Due to their specific location, distal penile strictures will be discussed separately.

# 6.3.1.1 Staged augmentation urethroplasty

Classically called "two-stage" urethroplasty, this approach may become a multi-stage urethroplasty as revision (usually due to graft contracture) after the 1<sup>st</sup> stage has been reported in 0-20% of cases [260-263]. Therefore, the term "staged" should be used instead [264]. Revision rates before 2<sup>nd</sup> stage were 0-20%, stressing that a two-stage urethroplasty might become a multi-stage urethroplasty. In general, reconstructive urologists tend to follow this approach in men with more complex urethral stricture disease (multiple interventions in the past, unfavourable clinical findings such as significant spongiofibrosis or scarring that requires excision, poor quality of the urethral plate). An interval of at least four to six months has been proposed before proceeding to the tubularisation of the urethra, provided that the graft has healed uneventfully [265-267].

A SR by Mangera *et al.*, has shown an average patency rate of 90.5% with the use of all types of grafts for staged penile urethroplasties with an average follow-up of 22.2 months [268]. Patency rates of staged OMG urethroplasty in specific locations vary between 73.3 and 100% [259, 260, 262, 263]. Post-operative urethrocutaneous fistula (UCF) rates were 17.2% and 2.6% in the studies of Ekerhult *et al.* and Joshi *et al.*, respectively, and either not reported or unclear in the remaining studies [259, 260].

# 6.3.1.2 Single-stage augmentation urethroplasty

Single-stage urethroplasty offers the option for reconstruction of the stricture without the need for multiple operations, the associated peri-procedural risks, and the cosmetic and functional implications that by definition follow the first part of staged urethroplasties [269-271]. There is some evidence to suggest a considerable

number of patients (50% or more in some studies) who were offered 1<sup>st</sup> stage urethroplasty never returned for the 2<sup>nd</sup> stage because they were either satisfied with their functional status after the 1<sup>st</sup> stage (this particularly applied to older men or patients with multiple failed procedures in the past) or they were disappointed with the need for another operation [269, 270].

In the SR of Mangera *et al.*, overall patency rate for all types of single-staged graft urethroplasties is 75.7% with an average follow-up of 32.8 months [268].

The patency rate for different one-stage techniques in specific are:

- dorsal OMG (n=190): 70-100% [263, 272-277];
- ventral OMG (n=47): 55-92.6% [278, 279];
- dorsal + ventral OMG (n=10): 80% [276];
- double (dorsal + ventral) onlay with penile/scrotal skin graft /OMG (n=14/8/4): 88.5% [273];
- dorsal penile skin graft (n=44): 62-78% [273, 274];
- penile skin flap (n=315): 67-100% [273-275, 280, 281].

No high-level evidence exists to state that one technique is superior to another, but it seems that the dorsal graft location is more commonly used compared to the ventral one. Mangera *et al.*, reported that the patency rate was better with OMG compared to other grafts (mainly penile skin) [268]. Jiang *et al.*, showed that combined (dorsal + ventral) BMG onlay had significantly better stricture-free rates for penoscrotal strictures (patency rate 88.9% vs. 60.9% with single-onlay approach); however, follow-up was significantly shorter in the double-onlay group [282]. Few studies have reported dedicated results on sexual function parameters that do not appear to be significantly impaired post-operatively [262, 283, 284].

A critical factor with respect to single-staged procedures is the careful selection of patients, as men with long and complex strictures might not be good candidates for single-stage reconstruction and attempts to offer single-staged operations in these patients might lead to higher recurrence rates. Sometimes, this selection can only be done based on intra-operative findings. Therefore, any scheduled single-staged procedure might be converted into a staged one [269, 285]. Palminteri *et al.*, highlighted the fact that single-stage augmentation urethroplasties in men with LS-related strictures enlarge rather than remove the diseased segment of the urethra; therefore, there is always a risk of recurrence in the future [286]. The role of previous interventions (especially multiple urethrotomies or history of previous urethroplasties) remains unclear as several studies on single-staged operations do not provide information on previous procedures, or excluded patients with operations in the past [275, 284]. Although favourable outcomes in patients with previous history of urethroplasties were reported by Barbagli and Kulkarni, in the study by Pfalzgraf *et al.*, all recurrences post-previous urethroplasty took place in the single-stage group while Ekerhult *et al.*, identified prior history of urethral operations as a risk factor for recurrence in the group of single-stage procedures [259, 262, 263, 273]. In addition to previous urethroplasty [259].

#### 6.3.1.3 Anastomotic urethroplasty in men with penile urethral strictures

Historically, the use of anastomotic urethroplasty in the management of urethral stricture disease has been discouraged due to the risk of chordee post-operatively [267, 287]. Nevertheless, it has been performed in selected patients with very short strictures (usually < 1 cm) with a 93% patency rate, with satisfactory QoL and sexual function and without any case of chordee [288].

Summary of evidence	LE
Stricture-free rates for single-stage penile augmentation urethroplasties range from 70-100% for	2b
dorsal OMG augmentation, 67-100% for penile skin flap (PSF) augmentation, 55-92.6% for ventral	
OMG augmentation and 62-78% for dorsal SG augmentation. Overall stricture-free rates for staged	
OMG penile augmentation urethroplasties range from 70-100%.	
In staged urethroplasties, an interval of at least four to six months has been proposed before	4
proceeding to the tubularisation of the urethra, provided that the graft has healed uneventfully.	
The use of anastomotic urethroplasty in the management of urethral stricture disease has been	3
discouraged due to the risk of chordee post-operatively. Anastomotic urethroplasty can be offered in	
selected cases of very short (< 1 cm), injury-associated penile strictures.	
In case of adverse intra-operative findings, a single-stage approach might not be feasible and must be	3
converted into a staged approach.	

Recommendations	Strength rating
Offer men with penile urethral stricture disease augmentation urethroplasty by either a	Strong
single-stage or staged approach taking into consideration previous interventions and	
stricture characteristics.	
Offer an interval of at least four to six months before proceeding to the second stage of the	Weak
procedure provided that outcome of the first stage is satisfactory.	
Do not offer anastomotic urethroplasty to patients with penile strictures > 1 cm due to the	Strong
risk of penile chordee post-operatively.	
Counsel patients with penile strictures that single-stage procedures might be converted to	Strong
staged ones in the face of adverse intra-operative findings.	

## 6.3.1.4 Specific considerations for failed hypospadias repair-related strictures

The term "failed hypospadias repair" (FHR) includes a wide range of abnormalities after previous attempts for reconstruction, such as glans deformity, recurrent urethral stricture, glans/urethral dehiscence, UCF and penile chordee [289-291]. The management of FHR is challenging as the urethral plate, penile skin and dartos fascia are often deficient/non-existent. Management of these patients is often made more difficult due to incomplete health records and a lack of critical information (original meatal site, number, and type of previous repairs) [265, 292]. In addition, multiple operations might need to be offered to reach satisfactory outcomes [289]. As a result, FHR should always be considered as a complex condition and it is advised that FHR management takes place in high-volume centres [290, 291, 293, 294].

"Hypospadias cripples" is a term widely used to describe the group of men with multiple previous failed attempts to correct the condition resulting in unfavourable results such as severe scarring, penile deformity and shortening, hair or stones in the urethra, UCF, chordee and functional disorders (e.g., urinary, or sexual dysfunction). This term should be avoided and a more neutral one should replace it as it further stigmatises men with hypospadias who have been shown to have reduced self-esteem and confidence due to unsatisfactory cosmesis, and problematic urinary and sexual function. Moreover, it has been reported that FHR patients experience high rates of disappointment after failure of attempted repair and a sense of helplessness as they are frequently advised that their failed hypospadias is too complex to correct and they should not pursue further repair [290-292, 295, 296].

Two main approaches are applicable: single-stage or staged procedures. In general, it is advised that staged procedures should be followed when the urethral plate is inadequate for a single-stage operation. Surgeons should consent patients for both types of urethroplasty as the surgical approach might need to be modified intra-operatively depending on favourable/unfavourable intra-operative findings. Besides poor-quality of the urethral plate, these unfavourable findings include high degree of scarring and presence of concomitant LS, UCF and/or chordee. It is not uncommon for men with FHR to have scarred skin or concurrent LS and thus, skin grafts or flaps should be avoided as the risk of recurrence due to LS is very high (90% in long-term follow-up as reported by Depsaquale *et al.* [41]) [297, 298].

Staged repairs (using mainly BMG) reported patency rates ranging from 71-95% [261, 295, 297, 299, 300], while single-stage repairs had patency rates from 80-100% [297, 299, 301-304]. It needs to be highlighted that, as FHR is an umbrella term that covers various clinical conditions apart from urethral stricture disease only (such as UCF, chordee, penile deformity), "success" rates as reported by the authors in their studies do not represent urethral patency rates only. Unfortunately, the number of previous operations is either not reported or refers to the whole FHR study group collectively rather than to the subgroups of staged/single-staged procedures.

A comparative analysis is reported by Barbagli *et al.*, in 345 FHR patients at five-year follow-up. Overall failurefree survival rate was 48% for all urethroplasties, and in sub-analysis, staged techniques had significantly lower treatment failure-free survival rates compared to single-stage techniques [305]. However, it is unclear whether these groups were comparable in terms of baseline characteristics such as age, length of stricture, number of procedures, comorbidities etc. [305]. If the patients in the staged group had a more unfavourable background, this on its own could explain the final outcome rather than the surgical approach itself.

Kozinn *et al.*, reported a 16% and 14% revision rate after the 1<sup>st</sup> and 2<sup>nd</sup> stage, respectively, and observed that these revision rates were higher in the FHR group compared to non-FHR patients with penile strictures [261]. There is conflicting evidence whether FHR as aetiology is a poor prognostic factor in the outcome of urethroplasty for penile strictures [259, 306-308]. Concomitant UCF can be successfully managed at the same time of urethroplasty [305].

For further information see supplementary Table S6.3.

Summary of evidence	LE
Men with FHR have history of multiple interventions, and poor-quality tissues, and might require complex procedures for a satisfactory functional and cosmetic outcome.	4
Men with FHR may have low self-esteem due to urinary and sexual dysfunction and unsatisfactory cosmesis.	2b
Men with FHR can have scarred penile skin or concurrent LS and outcomes with skin grafts or flaps can be unsatisfactory.	3

Recommendations	Strength rating
Men with failed hypospadias repair (FHR) should be considered complex patients and	Weak
referred to specialist centres for further management.	
Propose psychological and/or psychosexual counselling to men with unsatisfactory	Weak
cosmesis and sexual or urinary dysfunction related to FHR.	
Do not use penile skin grafts or flaps in failed FHR patients with lichen sclerosus or scarred	Strong
skin.	

#### 6.3.1.5 Specific considerations for lichen sclerosus-related penile urethral strictures

Given the fact that LS affects the skin, the use of genital skin as a flap or graft is not advised as the risk of disease recurrence has been reported to be high (50-100%) and while most of recurrences tend to occur within the first two to three post-operative years, late recurrences have been reported [309].

Main strategies are single-stage or staged oral mucosa graft urethroplasty.

The EAU Urethral Strictures Guidelines Panel conducted a SR [6] to explore the role of single-stage oral mucosa graft urethroplasty in the management of LS-related urethral strictures and to compare its outcomes with alternative management options (surgical dilatations +/- ISD; surgical dilatations + local steroids +/- ISD; staged oral mucosa urethroplasty; penile skin urethroplasty; meatotomy/meatoplasty; urethrotomy [Otis, DVIU]; perineal urethrostomy; urinary diversion [e.g., suprapubic catheterisation]).

In total, fifteen studies met the inclusion criteria, recruiting a total of 649 patients (366 from five nonrandomised comparative studies and 283 from ten, single-arm retrospective observational studies). Singlestage OMG urethroplasty resulted in success rates ranging from 65-100% after twelve to 67 months mean or median follow-up. For staged OMG urethroplasty, the most commonly reported comparator, the success rates were somewhat lower and varied between 60-79%. Methodological issues (mainly selection bias) could explain the difference in success rates rather than the intervention itself. Complications were uncommon (0-12%) and mainly comprised Grade 1-3 events.

Due to the overall very poor quality of evidence, the SR did not provide a clear answer as to whether singlestage OMG urethroplasty is superior to other management options, although careful patient selection is highlighted. In the absence of adverse local tissue conditions, a single-stage approach could lead to high success rates with an improvement in voiding symptoms and QoL.

Summary of evidence	LE
Lichen sclerosus is a skin condition that can lead to scarring, and recurrence rates after skin graft/flap	4
augmentation urethroplasties have been reported to be high (50-100%).	
Single-stage OMG urethroplasty provides patency rates between 65-100% and is not inferior to	3
staged OMG urethroplasty.	

Recommendations	Strength rating
Do not use genital skin in augmentation penile urethroplasty in men with lichen sclerosus (LS)	Strong
related strictures.	
Perform single-stage oral mucosa graft urethroplasty in the absence of adverse local	Weak
conditions in men with LS related strictures.	

6.3.1.6 Distal urethral strictures (meatal stenosis, fossa navicularis strictures)

Open repair of distal urethral strictures can be in the form of Malone meatoplasty, skin flap meatoplasty or graft (skin [SG]/OMG) urethroplasty.

For short distal meatal strictures, the Malone meatoplasty (dorsal + ventral meatotomy) provides a technique with patency rates up to 100%, and 83% patient-reported satisfaction with the cosmetic results [310].

Skin flap meatoplasty showed excellent patency rates ranging from 85-100% based on three studies comprising 53 patients [311-313]. In addition, based on their results, patient satisfaction with post-operative outcomes and cosmesis was high, there were no cases of ED and functional complaints were minimal (mainly spraying of the urine flow). Barbagli *et al.*, in their study from 2008, had lower success (57%) with the use of skin flaps; however, this was in only seven patients [273].

Patency rates with the use of grafts (OMG or SG) ranged from 69-91% in 85 patients overall [273, 302, 312, 314]. Where reported, patients were satisfied with cosmesis, and mild spraying of the urine flow self-resolved. Although tubularised grafts in a single-stage procedures are not routinely recommended (see also section 9. Tissue transfer), one series reported an 89.9% patency rate for this approach ("two-in one approach") in selected patients with mainly distal penile strictures [315].

For further information see supplementary Table S6.4.

Summary of evidence	LE
Post-meatoplasty/urethroplasty patency rates in men with meatal stenosis or fossa navicularis/distal	3
urethral strictures range between 57-100% depending on type of surgical intervention with high	
patient satisfaction and minimal complications.	

Recommendation	Strength rating
Offer open meatoplasty or distal urethroplasty to patients with meatal stenosis or fossa	Weak
navicularis/distal urethral strictures.	

# 6.3.2 Urethroplasty for bulbar strictures

# 6.3.2.1 "Short" bulbar strictures

The length of a "short" bulbar stricture is poorly defined. In general, "short bulbar strictures" are those amenable to stricture excision and subsequent tension-free anastomotic repair. The limit is usually around 2-3 cm but can be longer depending on the patient's anatomy and stricture location within the bulbar urethra [316].

In fit patients, the choice of urethroplasty is between EPA (transecting or non-transecting) and FGU.

# 6.3.2.1.1 Excision and primary anastomosis

6.3.2.1.1.1 Excision and primary anastomosis with transection of corpus spongiosum (transecting EPA) Transecting EPA (tEPA) is based on the full thickness resection of the segment of the bulbar urethra where the stricture and surrounding spongiofibrosis is located. Reconstruction is performed by a tension-free spatulated anastomosis.

#### 6.3.2.1.1.1.1 Patency rates

The International Consultation on Urological Diseases (ICUD) performed an extensive review of the literature and reported a composite patency rate of 93.8% for tEPA [317]. Based on this, they endorsed tEPA as treatment of choice for short bulbar strictures if other techniques have an expected patency rate below 90%. However, ED was not taken into account for this advice and as discussed below, ED is a concern with tEPA.

After publication of the ICUD review, several other series have been published and the reported patency rates (76-97%) are in line with the findings of the ICUD review [318-330].

Usually, no need for further intervention is used to evidence that the urethra is patent. In the few studies using an anatomic definition for failure (an inability to pass a 16 Fr endoscope) tEPA urethroplasty achieves a similar patency rate, ranging between 85.5-97% [143, 323, 329, 331] (Table 6.12). The median time for recurrence after tEPA is between 3.5 and thirteen months [143, 320, 321].

Several authors suggested that tEPA is the technique of choice for short post-traumatic bulbar strictures with complete obliteration of the urethral lumen and full thickness spongiofibrosis [331, 332]. These strictures are a specific entity and usually the result of a straddle injury with complete or nearly complete rupture of the bulbar urethra. These obliterations are predominantly short and can be treated with tEPA yielding a patency rate of 98.5% as reported in the series of Horiguchi *et al.* [333]. They also reported an improvement in erectile function after urethroplasty measured one year post-operatively. Straddle injury (and perineal trauma) are a common aetiology in papers published about tEPA; however, separate data on the outcomes for this specific aetiology is usually lacking.

For further information see supplementary Tables S6.5 and S6.6.

#### 6.3.2.1.1.1.2 Complications

Granieri *et al.*, [322] specifically focused on complications after bulbar urethroplasty. Peri-operative complications (haematoma, neuralgia), infectious complications, anatomic complications and voiding complications were not significantly different between EPA, augmented anastomotic repair (AAR) and FGU. Erectile dysfunction after bulbar urethroplasty is usually transient, with improvement after three to six months [334]. Chordee is one of the complications attributed to EPA urethroplasty but is rarely reported. A large case series (n=352), reported an incidence of 0.3% [331]. Another large case series (n=94), reported five cases (5.3%), with a mean stricture length of 2 cm (range 1.5-4) in patients with this complaint [318].

Other complications of tEPA are a cold feeling in the glans (1.6-3.2%) and decreased glandular tumescence (6%) [334, 335]. These latter complications (as well as ED) might be attributed to complete transection of the corpus spongiosum at the level of the stricture, thereby disrupting the antegrade blood flow of the urethra and corpus spongiosum. To spare this, the non-transecting EPA (ntEPA) has been described [336] and later modified [337].

#### 6.3.2.1.1.2 Non-transecting excision and primary anastomosis

#### 6.3.2.1.1.2.1 Patency rates

Except for straddle injuries that are usually associated with complete obliteration of the lumen and full thickness scarring of the corpus spongiosum [317, 331], ntEPA is a good alternative for short bulbar strictures of all other aetiologies. With median follow-ups ranging between 17.6 and 37.1 months, the patency rates reported are 93.2-99%; with the lack of further intervention as success criteria [330, 332, 338]. Even with the anatomic criteria (16 Fr cystoscopy passage) the success rate achieved was 97.9% at twelve months [331] (see supplementary Table S6.7).

Two comparative analyses evaluated tEPA vs. ntEPA. Waterloos *et al.*, reported patency rates of 88.4% and 93.2%, respectively, for tEPA and ntEPA (p=0.33) but with significantly longer follow-up for tEPA (118 vs. 32 months, p < 0.001). Of patients scheduled for ntEPA, 11.1% were converted to tEPA, highlighting that ntEPA is not always possible. Chapman *et al.*, using anatomic success criteria (16 Fr cystoscope passage), reported patency in 93.8% of tEPA vs. 97.9% of ntEPA. Follow-up was also significantly shorter at 74.1 (SD: 45.4) months for tEPA vs. 37.1 (SD: 20.5) months for ntEPA (p < 0.001) [331].

#### 6.3.2.1.1.2.2 Complications

When erectile function after urethroplasty was assessed (at six months), ntEPA had significantly lower ED rates (a decrease of > 5 points on the sexual health inventory for men [SHIM] scale) compared to tEPA (4.3 vs. 14.3%, respectively) [331]. Urethral transection performed during tEPA was the only factor associated with sexual dysfunction in a multivariate analysis [331]. Other series reported ED lasting for more than six months in 2-6% of cases after ntEPA [332, 338, 339]. Grade  $\geq$  2 Clavian-Dindo complications were 3.6-8.1% vs. 4.3-6.8%, respectively, for tEPA and ntEPA, without reaching statistical significance [330, 331].

To date, no trials comparing ntEPA with FGU have been published to report on comparative patency outcomes and complications.

#### 6.3.2.1.2 Free graft urethroplasty

Despite the very high patency rates of EPA, FGU has been performed for short bulbar strictures as well. This is mainly driven by reports of ED after EPA. A meta-analysis of ten papers [340] comparing tEPA with BMG FGU for short strictures, found that tEPA is better than BMG FGU in terms of patency rates (91.5% vs. 70%), whilst BMG FGU has less erectile complications (9% vs. 25%). However, the methodology of this meta-analysis must be disputed as it was performed on cohort studies without risk of bias assessment and without further specification of timing of assessment of ED. On the other hand, two prospective, non-randomised papers

[143, 341] comparing tEPA with BMG FGU, found no significantly different patency rates for EPA compared to BMG FGU (87-90% vs. 84-87%, respectively) and no significant differences in erectile complications for tEPA compared to BMG FGU (6.7% vs. 2.2%, respectively). However, the operation technique used was dependent upon the length of the stricture, with tEPA utilised for shorter strictures (< 2 cm) and BMG for longer (> 2 cm) [341] or when a tension-free anastomosis was not possible [143]. Appropriate choice of procedure for stricture length and other patient and stricture parameters appear to equalise outcomes. Another prospective trial [342] involving both penile and bulbar strictures could not find any influence on erectile function of urethral transection. A prospective study on ejaculatory function following different urethroplasties by Erickson *et al.*, [343] found no overall difference in ejaculatory score pre- and post-operatively, although patients with a poor score preoperatively improved significantly and those with a good score pre-operatively did not decrease post-operatively.

Dogra *et al.*, [283] looked prospectively at sexual function in 87 patients after different urethroplasties (EPA, penile/bulbar substitution) and found a 20% reduction in sexual function in all groups, which resolved after six months.

Details on where to place the graft during FGU are discussed below.

Summary of evidence	LE
For short post-traumatic strictures tEPA has good patency rates.	3
For short bulbar strictures not related to straddle injury tEPA, ntEPA and FGU have the same patency	3
rates, but ntEPA and FGU have less erectile dysfunction than tEPA.	

Recommendations	Strength rating
Use transecting excision and primary anastomosis (tEPA) for short post-traumatic bulbar	Strong
strictures with (nearly) complete obliteration of the lumen and full thickness spongiofibrosis.	
Use non-transecting excision and primary anastomosis or free graft urethroplasty instead of	Weak
tEPA for short bulbar strictures not related to straddle injury.	

# 6.3.2.2 "Longer" bulbar strictures

# 6.3.2.2.1 Free graft urethroplasty

For strictures not amenable to EPA, FGU is the technique of choice and buccal mucosa is, at the moment, the most widely used graft. Other grafts (and flaps) are possible and discussed in the tissue transfer chapter. Patency rates of FGU of the bulbar urethra are 88-91% with twelve to 40 months follow-up [268, 344].

During bulbar urethroplasty, the bulbospongiosus muscle is usually separated at the midline which may cause damage to the muscle and perineal nerves. This might subsequently provoke post-void dribbling and ejaculation disorders. In order to reduce this, the muscle and nerve-sparing perineal approach has been introduced [345]. Although it is mostly used in graft urethroplasty, this approach is also possible for EPA as well [346]. Elkady *et al.*, [339] randomised 50 patients between a muscle and nerve-sparing perineal approach vs. a classic perineal approach and found no difference in operative time (100 vs. 105 min), but significantly less dribbling (4% vs. 36%, p=0.01), and significantly less ejaculatory changes (8% vs. 40%, p=0.02) in the nerve and muscle-sparing group. Fredrick *et al.*, [346] did the same in 50 patients in a multicentric study with bulbar urethroplasty but could not find a statistical difference regarding post-void dribbling and ejaculatory changes. Due to the limited and conflicting evidence, no recommendation can be made about the routine use of nerve and muscle-sparing modification during bulbar urethroplasty.

See supplementary <u>Table S6.8</u> for further information.

# 6.3.2.2.2 Augmented anastomotic repair

Augmented anastomotic repair is also an option for these strictures. It has been mainly performed in cases where the stricture was just too long (+/- 2-4 cm) for tension-free EPA [328]. It can also be performed for longer strictures with a shorter (nearly) obliterative segment [347]. In this case, only the most obliterative segment is excised, the urethral plate is anastomosed, and the urethra is further reconstructed with an onlay graft [347]. Patency rates after AAR vary between 91.1 - 91.9% with twelve to 28 months follow-up [322, 328] (see supplementary Table S6.9).

A non-transecting alternative has also been described to overcome the previously mentioned inconveniences related to spongiosal transection (augmented non-transecting anastomotic bulbar urethroplasty [ANTABU]). With this technique, Bugeja *et al.*, [348] reported a 100% patency rate in sixteen patients after a median follow-up of thirteen months. One patient (6.7%) suffered permanent ED.

Summary of evidence	LE
For strictures not amenable to EPA, FGU provides an 88-91% patency rate.	1b
Augmented anastomotic repair provides good patency rates for bulbar strictures with a nearly	3
obliterative segment.	

Recommendations	Strength rating
Use free graft urethroplasty for bulbar strictures not amendable to excision and primary	Strong
anastomosis (EPA).	
Use augmented anastomotic repair for bulbar strictures not amenable to EPA but with a	Weak
short, nearly obliterative segment within the whole strictured segment.	

### 6.3.2.2.3 Location of the graft during urethroplasty for bulbar strictures

The best location for graft positioning into the bulbar urethra remains to be determined. There are many techniques described with ventral, lateral, dorsolateral, or dorsal graft as an onlay or an inlay. Onlay means from the outside onto the urethra, inlay means from the inside after opening the urethra.

Regarding the site of graft placement, the Panel has conducted a SR assessing the literature from 1996 onwards, including studies with at least 20 patients and a minimum of twelve months follow-up [7]. This yielded one RCT, four non-randomised comparative series and 36 case series comprising 3,683 patients. The RCT of Vasudeva *et al.*, compared ventral (n=40) with dorsal (n=40) onlay BMG urethroplasty and reported a patency rate of 90 - 92.5% respectively at twelve months follow-up (p=0.51) [344]. The non-randomised comparative studies could not identify any significant differences in patency rates for dorsal onlay vs. ventral onlay, dorsal inlay vs. ventral onlay or dorsal onlay vs. ventral onlay vs. dorsolateral onlay. Case series reported a patency rate of 62.1-98.3% for dorsal onlay, 74.3-94.4% for ventral onlay and 78.4-92% for dorsal inlay. There are no arguments to assume a higher risk of ED with one of the four techniques. Post-void-dribbling was reported in 0-28.1% with dorsal onlay and in 20-21% with ventral onlay. Other complications were also similar in incidence between techniques. Urethrocutaneous fistula and urethral diverticulum were only reported with the ventral onlay technique although this consisted of only two and one cases, respectively.

Double ventral-dorsal onlay, proposed by Palminteri *et al.*, [144] for high-grade strictures, yielded a patency rate of 91% after 22 months follow-up.

Summary of evidence	LE
Location of the graft has no impact on patency rates.	1b

Recommendation	Strength rating
Use dorsal, dorsal-lateral, or ventral approach according to surgical practice, expertise, and	Strong
intra-operative findings.	

#### 6.3.2.3 Staged urethroplasty for bulbar urethral strictures

#### 6.3.2.3.1 Indications

Staged urethroplasty may be considered when:

- there are locally adverse conditions such as fistula, false passage, abscess, cancer [285, 349, 350];
- there has been a previously unsuccessful complex urethroplasty including failed hypospadias repair [261, 349];
- there is a lack of certainty on behalf of the surgeon regarding the most appropriate form of urethroplasty for the patient [349];
- the stricture is radiotherapy induced [261];
- the stricture is consequent to LS [261] (this is controversial and for some groups LS is a contraindication for a staged urethroplasty [307]; Kozinn *et al.*, recommend leaving at least ten months between 1<sup>st</sup> stage and 2<sup>nd</sup> stage re-tubularisation in patients with LS to allow graft complication to develop) [261];
- there is severe spongiofibrosis [351].

### 6.3.2.3.2 Outcomes

Patency rates of 33.3-94.6% at mean follow-up of 11.2-50 months have been described for staged urethroplasty in series which include men with bulbar urethral stricture disease [261, 307, 329, 351-353]. Grafts (mesh graft, preputial skin, oral mucosa) can be used in staged augmentation as well as marsupialisation [329, 351]. In patients affected by LS, a 52.2% patency rate for staged urethroplasty was reported whereas this was 86% for single-stage buccal mucosa urethroplasty (p < 0.01) [307]. It is highly likely that different stricture and patient characteristics contributed to the differences reported and this should be kept in mind when interpreting the data. Of note, 19-45.5% of patients planned for staged urethroplasty declined to proceed to 2<sup>nd</sup> stage re-tubularisation [261, 352].

Early complications after staged procedures include wound dehiscence, UTI, epididymitis, scrotal abscess, and penile numbness. Specific to 2<sup>nd</sup> stage Johanson urethroplasty UCF occurs in 3-15%. The actual incidence of UCF is probably higher as many small fistulae close spontaneously with conservative management and are not formally reported [307, 329, 351].

Late complications of 1<sup>st</sup> stage urethroplasty include a need for revision in up to 19% - as a consequence of recurrence of LS in graft(s) (8.8%), graft contracture (6.6%) and stomal stenosis (3.3%) [261]. Late complications of 2<sup>nd</sup> stage urethroplasty include post-micturition dribble in 14-18%, SUI in up to 16%, penile curvature in up to 9%, ED in up to 4%, urethral diverticulum formation in 1% and cold glans [307, 351, 353]. Stress urinary incontinence, penile curvature and ED appear to be particularly associated with mesh graft stage urethroplasty [351, 353].

After their procedure, 86% and 96.6% of men with, respectively, mesh graft and buccal mucosa graft staged urethroplasty were satisfied. The patient groups included in the review were too small to detect significant differences [351]. All are retrospective series – with heterogenous indications, stricture locations (not exclusively bulbar), stricture lengths and patient groups. It is consequently difficult to draw meaningful conclusions from the little data that are available.

See supplementary <u>Table S6.10</u> for more information.

Summary of evidence	LE
Staged urethroplasty for bulbar strictures and for strictures involving the bulbar urethra yields patency rates of 33.3-90% depending upon patient and stricture characteristics and patient satisfaction is high with all types of staged urethroplasty.	3
Lichen sclerosus is a relative contraindication for staged urethroplasty in the literature with lower long-term urethral patency rates of 52.2% compared to urethral patency rates of 64.3% in non-lichen sclerosis patients.	3
Up to 45.5% of men elect not to proceed to 2 <sup>nd</sup> stage re-tubularisation after successful 1 <sup>st</sup> stage.	3
Up to 19% of men required revision of their 1 <sup>st</sup> stage urethroplasty.	3

Recommendations	Strength rating
Offer staged urethroplasty to men with complex anterior urethral stricture disease not	Weak
suitable for single stage urethroplasty and who are fit for reconstruction.	
Do not perform staged bulbar urethroplasty for lichen sclerosis if single stage urethroplasty	Weak
is possible.	
Consider staged procedure in patients unsure about perineal urethrostomy vs. urethral	Weak
reconstruction.	
Warn men that staged urethroplasty may comprise more than two stages.	Weak

# 6.3.2.4 Risk factors for adverse outcomes

In four series specifically dedicated to risk factors for failure after urethroplasty using multivariate analysis, there is conflicting evidence about several factors (aetiology, comorbidity, stricture length, prior therapy) that might be predictive for failure after urethroplasty (Table 6.6). Advanced age does not appear to be a risk factor for urethroplasty failure in the majority of studies, with the exception of Viers *et al.*, 2017 [354] retrospective case series which found that the risk for recurrence was significantly higher beyond the age of 60 (< 50 yrs 94%, > 70 yrs 74%) in 184 patients having a wide variety of urethroplasties. Previous radiation therapy was also found to be a risk factor for stricture recurrence in both Viers' [354] retrospective case series and Ahyai's 2015 series [355] – with only a 71% patency rate at a median follow-up of 29 months in those with previous radiotherapy. Based on these data, a clear and evidence-based recommendation cannot be formulated.

Table 6.6: Risk factors for failure after urethroplasty based on multivariable Cox regression analyses

Study	Ν	Population	Comorbidity	Length	Aetiology	Prior stricture therapy
			HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Breyer <i>et al.</i> 2010 [356]	443	Mixed	NS	NS	NS	Prior DVIU: 1.7 (1.0-3.0) Prior urethroplasty: 1.8 (1.1-3.1)
Kinnaird <i>et al.</i> 2014 [357]	604	Mixed	NS	≥ 5 cm: 2.3 (1.2- 4.5)	latrogenic: 3.4 (1.2-10.0) LS: 5.9 (2.1-16.5) Infectious: 7.3 (2.3-23.7)	NS
Chapman <i>et al.</i> 2017 [323]	596	Isolated bulbar strictures	Overall comorbidity: 2.4 (1.1-5.3) Obesity: 2.9 (1.3-6.5)	1.2 (1.1-1.3)	Infectious: 3.7 (1.3-10.6)	NS
Verla <i>et al.</i> 2020 [358]	474	Anterior strictures	NS	NS	NS	NS

CI = confidence interval; HR = hazard ratio; LS = lichen sclerosus; N = number of patients; NR = not reported NS = not significant.

# 6.3.2.5 Management of recurrence after bulbar urethroplasty

Kahokehr *et al.*, [328] followed nearly 400 patients after urethroplasty and found a recurrence rate of 6% (n=25). Ninety-two percent of the failed cases were treated successfully with DVIU and only 8% needed another open reconstruction. However, they did not mention characteristics of the recurrent cases nor the duration of follow-up.

Rosenbaum *et al.*, [359] and Javali *et al.*, [360] retrospectively analysed the outcomes of BMG FGU for ReDo urethroplasty in 51 and 21 patients, respectively, using the other cheek as donor side. Patency rates were 82-86%, which is in the range of primary cases.

Vetterlein *et al.*, [361] compared primary (no previous open urethroplasty) vs. ReDo (previous open urethroplasty with BMG) vs. secondary (previous open urethroplasty without use of BMG) cases in a retrospective series of 534 patients with BMG FGU. The patency rates in primary and ReDo cases were comparable (87%) whilst the outcome in secondary cases was worse (71%).

A small series (n=37) reported on the use of EPA for revision surgery after failed urethroplasty in strictures of 2.1 (range 1-3.5) cm length on average. Patency rates using EPA after failed primary EPA (51%) and after any other technique of urethroplasty (49%) were 95 and 94% respectively with a mean follow-up of 30 months [321].

#### Summary of evidence

Buccal mucosa free graft urethroplasty after failed urethroplasty achieves the same patency rates as primary cases.

#### Recommendation

Strength rating

LE

Use oral mucosa free graft urethroplasty for ReDo urethroplasty in case the of a long stricture. Strong

#### 6.3.3 Urethroplasty for penobulbar or panurethral strictures

The possibilities for reconstruction are various and often include combinations of different techniques or grafts other than OMG. The patency rates are usually lower than in shorter reconstructions (Table 6.7). Hussein *et al.*, [362] performed a RCT comparing skin grafts vs. skin flaps in strictures of mean length 15 cm and found no difference in patency rates (72% vs. 79%) or complications.

Warner *et al.*, [307] performed a multi-institutional review in 2015 including 466 patients with stricture length > 8 cm and found an overall patency rate of 77.5%.

As discussed previously, Kozinn *et al.*, [261] reported on the outcome of staged urethroplasty in a cohort of which 54.9% had panurethral strictures (Table 6.7).

Kulkarni *et al.*, [363] proposed a one-stage completely perineal approach with invagination of the penis and one-sided urethral dissection. After 59 months the overall patency rate was 83.7% in 117 men with a mean stricture length of 14 cm.

Another option in patients refusing or unfit for complex reconstructive surgery is PU (see section 6.3.4 Perineal urethrostomy).

Author	Study	Length in cm (min, mean, range)	Technique	N	FU months (mean, range)	Patency
Hussein <i>et al.</i> 2011 [362]	RCT	NR, 15, 9-21	Skin graft vs. flap	37	36, 12-60	72 vs. 79%
Hussein <i>et al.</i> 2016 [364]	Prospective	NR, 8, NR	BM vs. skin dorsal onlay	69	56, NR	90 vs. 84%
Warner <i>et al.</i> 2015 [307]	Retrospective review	> 8, 12.5, 8-24	BM/staged/skin	466	20, 12-344	77.5%
El Dahshoury <i>et al.</i> 2009 [365]	Retrospective	NR, 18, 15-20	Skin flap	30	24, NR	87%
Mathur <i>et al.</i> 2010 [366]	Retrospective	NR, 12, 8-16.5	Tunica albuginea graft	86	36, NR	89%
Meeks <i>et al.</i> 2010 [367]	Retrospective	NR, 11, 4-24	Abdominal skin graft	21	28, 11-52	81%
Kulkarni <i>et al</i> . 2012 [363]	Retrospective	NR, 14	BM dorsal onlay	117	59, NR	83.7%
Tabassi <i>et al.</i> 2014 [368]	Retrospective	NR, 14.4, NR	BM dorsal onlay	117(37)	19, NR	84%
Xu <i>et al.</i> 2017 [303]	Retrospective	> 8, 12, 8-20	BM/LM/combination	81	>12, 41, 15-86	83%
Alsagheer <i>et al.</i> 2018 [369]	Retrospective	> 8, 11.3	BM onlay vs. skin flap	50	NR, 16, NR	70 vs. 77%
Kozinn <i>et al.</i> 2013 [261]	Retrospective	NR, 9.6, 4-17	Staged urethroplasty	91	15, 12-69	90.1%

Table 6.7: Study characteristics and patency rates of series on penobulbar strictures

BM = buccal mucosa; LM = lingual mucosa; FU = follow-up; N = number of patients; NR = not reported; RCT = randomised controlled trial.

Summary of evidence	LE
Publications about panurethral urethroplasties generally come from high volume centres.	4
Different materials and techniques might be needed for reconstruction.	3

Recommendations	Strength rating
Offer panurethral urethroplasties in specialised centres because different techniques and	Weak
materials might be needed.	
Combine techniques to treat panurethral strictures if one technique is not able to treat the	Weak
whole extent of the stricture.	

# 6.3.4 Perineal urethrostomy

# 6.3.4.1 Indications

Perineal urethrostomy offers a permanent or temporary solution for restoration of voiding in men with complex urethral stricture disease in whom:

- there are no further options to restore urethral patency either due to multiple previous failed urethroplasties [307, 349] or multiple co-morbidities precluding a more expansive surgical undertaking after failed endoscopic management [370];
- there is a lack of certainty on behalf of the surgeon regarding the most appropriate form of urethroplasty for the patient;
- following urethrectomy and/or penectomy for cancer [371].

### 6.3.4.2 Types of perineal urethrostomy

Johanson described an inverted anterior scrotal funnel PU in 1953. This was later modified by Gil-Vernet and Blandy to utilise a posteriorly based scrotal flap. Both these techniques utilise an inverted U or lambda incision. The Gil-Vernet-Blandy PU has been further modified with the addition of dorsal and/or ventral free OMG augment to allow use of PU in men with strictures consequent to radiotherapy [372] or LS [263] and/or in men with PU stenosis or stricture extending into the proximal bulbar or membranous urethra ("augmented Blandy") [370].

More recently, the '7 flap' PU utilising a unilateral posteriorly based scrotal flap has been developed for use in the very obese, or in men of all BMI with stricture extension into the proximal bulbar or membranous urethra [373]. Initially this was performed with transection of the distal bulbar urethra but latterly the technique has been modified to a non-transection technique with loop mobilisation of the bulbar urethra ("loop PU") [374]. The "7-flap" utilises a midline incision – which has been shown to have a significantly reduced side-effect profile in terms of superficial wound infection (1.9% c.f. 18.6%) and superficial wound dehiscence (11.9% c.f. 23.3%) than the inverted U or lambda incision [375, 376] and may be associated with improved urethroplasty (and by inference PU) outcomes, at least in the short term (0% failure c.f. 6.2% failure at six months) [375]. Operative time is similar for all types of PU with mean operative time varying between 97.2 minutes to 112 minutes [371, 377].

The utilisation of PU is increasing [378] – constituting 4.5% of 403 procedures for complex urethral stricture disease in a tertiary centre in 2008 and 38.7% in 2017 [379]. Perineal urethrostomy patients are generally older than those having urethroplasty with a median of 62.6 years of age for men having PU in Fuchs *et al.*, 2018 series compared with a median of 53.2 years for men having anterior urethroplasty [379]. Between 18.7% and 73.4% of men having staged urethroplasty for complex anterior urethral stricture decline to proceed to 2<sup>nd</sup> stage re-tubularisation after a successful 1<sup>st</sup> stage and remain voiding from the PU of their 1<sup>st</sup> stage urethroplasty [261, 349, 352].

#### 6.3.4.3 Outcomes

#### 6.3.4.3.1 Patency rates

Patency rates of 70-95% at mean/median follow-up of 20–63 months have been described [307, 349, 354, 370-372, 374, 377, 379]. All reports are retrospective series – all of which are heterogenous in terms of indications and patients. There is consequently little data available to determine which is the best technique for PU.

McKibben *et al.*, reported a patency rate of 92.9% in 42 patients for "7-flap" PU at median follow-up of 53.6 months, whilst they had a 100% patency rate with loop PU in twenty patients at a median follow-up of thirteen months [374].

Lumen *et al.*, in 2015 reported a 74.3% patency rate for Johanson PU compared with an 87.5% patency rate for Gil-Vernet-Blandy PU (p=0.248), but with a significantly longer follow-up after Johanson PU (median 36 vs. nine months) [371]. Barbagli *et al.*, published the largest series of PU patients to date – including 173 men (all of whom had been planned to have a staged urethroplasty for their complex anterior urethral stricture disease and 127 (73.4%) of whom declined to proceed with 2<sup>nd</sup> stage re-tubularisation). The median follow-up in this series was 62 months and the patency rate was 70% - confirming that patency rates for PU (and indeed for all urethroplasty [274, 326]) reduce with time [349].

See supplementary <u>Table S6.11</u> for further information.

#### 6.3.4.3.2 Complications

Perineal urethrostomy complications occur in 2.5-11.4% and include superficial wound dehiscence, scrotal abscess, UTI and urosepsis, bleeding, and transient scrotal pain and numbness [307, 371, 380]. The majority of

complications are Clavien-Dindo grades 1 (2.9-18.8%) and 2 (0-2.9%). Grade 3 complications are rare and only occur in 5.7-6.2%. In the medium-term 22.2-30.8% of men with PU report post-micturition dribble [371].

# 6.3.4.3.3 Patient reported outcomes

Barbagli *et al.*, reported that 168/173 (97.1%) of men were satisfied or very satisfied with the outcome of their Gil-Vernet-Blandy PU and would have the procedure again at median 62 months follow-up. Of these, 166/173 (95.9%) felt they had excellent or good results from their Gil-Vernet-Blandy PU, 145/173 (85%) felt it caused them no problems and 141/173 (82%) felt it caused their partner no problems [349]. The Trauma and Urologic Reconstructive Network of Surgeons (TURNS) collaborative found no significant change in sexual function and a significant improvement in urinary symptoms following PU in a small group of patients [381], whilst Lumen *et al.*, found satisfactory or acceptable International Prostate Symptom Score (IPSS) outcomes in 26/32 (81.25%) of men with Johanson or Gil-Vernet-Blandy PU at a median follow-up of 32 months and nine months, respectively.

McKibben *et al.*, found a mean patient global impression of improvement (PGI-I) of 1.3 in nineteen patients with either loop PU or "7-flap" PU [374] at median 31 months follow-up.

# 6.3.4.3.4 Risk factors for patency failure of the perineal urethrostomy

Lichen sclerosus, trauma and infection urethral strictures have poorer outcomes from PU, with PU patency failure in 36.7-67% at a median 62 month follow-up [349, 380]. Worse outcomes were also observed in patients with previous failed urethroplasty and multiple previous endoscopic and open treatments [349, 371, 372].

Barbagli *et al.*, found that stricture length was inversely related to PU patency, as was patient age [349]. Conversely Viers *et al.*, found outcomes worsened with age, reporting patency rates of 100% in men < 50 years old compared with 83% in men aged 60-69 years old [354]. Lopez *et al.*, found increased risk of PU failure in men with ischaemic heart disease which makes sense and would be a putative explanation for the age-related worsening of outcomes noted by Viers *et al.* [380].

Failure of PU is most commonly treated with surgical revision of PU using V-Y plasty, augmentation or complete ReDo but can also be managed with periodic dilatation or urinary diversion [349, 370, 371].

For further information see supplementary Table S6.11.

Summary of evidence	LE
Perineal urethrostomy provides very good short- and long-term outcomes for men with complex	1a
urethral stricture disease.	
Perineal urethrostomy provides very good short and long-term outcomes for men who are unable to	2b
have complex reconstruction due to co-morbidities.	
All types of PU yield equivalent very good outcomes.	4
Augmented Gil-Vernet-Blandy or "7-flap" PU yield very good outcomes in men with extension of their	2
urethral stricture disease into the proximal bulbar or membranous urethra.	
"7-flap" PU yields very good results in obese men.	3

Recommendations	Strength rating
Offer perineal urethrostomy (PU) as a management option to men with complex anterior	Strong
urethral stricture disease.	
Offer PU to men with anterior urethral stricture disease who are not fit or not willing to	Weak
undergo formal reconstruction.	
Choose type of PU based on personal experience and patient characteristics.	Weak
Consider augmented Gil-Vernet-Blandy perineal urethrostomy or "7-flap" PU in men with	Weak
proximal bulbar or membranous urethral stricture disease.	
Consider "7-flap" urethroplasty in obese men.	Weak

# 6.3.5 Posterior urethra

# 6.3.5.1 Non-traumatic posterior urethral stenosis

6.3.5.1.1 Treatment of non-traumatic posterior urethral stenosis

Several treatment modalities including conservative management (see section 6.1 Conservative options), endoluminal, open or minimally invasive surgical procedures are currently available, depending on patient's goals and health status.

6.3.5.1.2 Endoluminal management of non-traumatic posterior urethral stenosis

6.3.5.1.2.1 Dilatation of non-traumatic posterior urethral stenosis

This can be done under loco-regional anaesthesia [382-386]. Dilatation is used for VUAS [382-387] or radiationinduced BMS [117, 388] and in the majority of reported cases, patients were not previously treated for their stricture (see supplementary <u>Table S6.12</u>). Patency rates vary widely between 0-89% [117, 382-388]. The risk of *de novo* UI was low (0-11%) and no other complications were reported. It is of note that most series report on visually controlled dilatation [382-386] in VUAS without complete obliteration.

#### 6.3.5.1.2.2 Endoscopic incision/resection of non-traumatic posterior urethral stenosis (Table 6.8)

Incisions can be performed at multiple locations according to surgeon's preference [389]. However, aggressive incisions at the six and twelve o'clock positions should be avoided because of the risk of, respectively, rectal injury and urosymphyseal fistulation [187, 390-392]. The risk of urosymphyseal fistulation is especially a concern after previous radiotherapy [393]. Direct vision internal urethrotomy is mainly performed in patients with primary or recalcitrant VUAS although one series performed it in a mix of patients with VUAS and BNS [394] and two series reported it for radiation-induced BMS [117, 388]. Direct vision internal urethrotomy/ dilatation for non-irradiated BMS are usually included in series reporting on anterior strictures (see section 6.2 Male endoluminal treatment of anterior urethral strictures). Patency after a 1<sup>st</sup> "cold/hot knife" DVIU ranges between 25-80% [382, 385, 387, 389, 394-399]. Laser incision yields a 69-100% patency rate [385, 387, 400, 401]. In a retrospective and unbalanced series, LaBossiere et al., found better patency rates for laser incision as compared to dilatation, "cold knife" DVIU and transurethral resection (TUR) [385]. Redshaw et al., reported inferior patency rates for "cold knife" incision vs. "hot knife" incision followed by MMC for BNS (50 vs. 63%; p=0.03) [240] (see supplementary Table S6.13). Urinary incontinence largely varies between 0 and 53% but some series have not assessed urinary continence before DVIU [395, 397]. In series where pre-DVIU continence data were available, de novo urinary continence after DVIU ranges between 0% and 10% [382, 387, 396, 398, 400]. Noteworthy, of 21 patients that were incontinent pre-DVIU in the series of Giannarini et al., eleven (52%) patients became continent, and eight (38%) patients experienced improvement after DVIU [396]. In the series of Lagerveld, 1/5 (20%) patients noticed improvement of UI after DVIU [400]. As most recurrences will occur early [396, 397], it is advised to wait for three to four months after DVIU [389, 397, 402] to proceed with incontinence surgery, if necessary, although others wait for twelve months [403]. The presence of recurrence must be ruled out by cystoscopy prior to incontinence surgery [389, 397, 402, 403].

Another option is to resect the stenosis. Popken *et al.*, reported a 47% patency rate with TUR for untreated VUAS and no patient suffered *de novo* SUI [398]. Kranz *et al.*, compared the results of TUR in 87 and 60 patients with, respectively, VUAS after RP and BNS after TURP. After a median follow-up of 27 (range: 1-98) months, patency rate was 40.2% for VUAS and 58.3% for BNS (p=0.031). The rate of *de novo* incontinence was significantly higher in patients treated for VUAS compared to BNS (13.8 vs. 1.7%; p=0.011) [404]. Kravchick *et al.*, reported a higher incontinence rate after TUR compared to "cold knife" DVIU and dilatation for VUAS (50% vs. 13% vs. 0%, respectively; p=0.005) [386]. However, the number of patients were small and a selection bias of more severe cases towards TUR might be possible [386]. Alternatively, thermal damage to the adjacent external sphincter during TUR (especially with monopolar current) might be the cause of incontinence [386]. Brodak *et al.*, compared TUR by bipolar resection (n=22) with holmium laser incision and vaporisation (n=17). After a mean follow-up of 42 months, two (9.1%) and four (23.5%) patients suffered a recurrence with bipolar resection respectively (p=0.37). After six months, patients treated with bipolar resection had a significant better Q<sub>max</sub> compared to laser treatment (13 vs. 6.1 ml/s; p < 0.001) [401]. Bipolar plasma vaporisation produced an 82% patency rate at a mean 24-month follow-up in 28 patients with VUAS who previously failed endoscopic treatment [405].

Cut-to-the-light technique for a complete obliterative stricture is not advised because of the very-low likelihood of durable patency and for the risk of false passage towards the rectum [402, 406, 407].

Repetitive DVIU was often able to stabilise the stricture [117, 382, 385, 388, 394-396, 404], but ultimately 6-10% required urinary diversion [397] or chronic suprapubic cystostomy [388, 394].

Transurethral resection can be performed for prostatic obstruction due to sloughing after high-energy treatments (HIFU, cryoablation) [101]. Transurethral resection for obstructive necrotic debris after radiotherapy is possible but is of limited role. Risk of recurrence is 50% and risk of *de novo* UI is 15-25% [101].

## Table 6.8: Results of endoluminal incision/resection for posterior non-traumatic stenosis

Study	Modality	Туре	N	Previous treatment (%)	FU (months)	Patency° (%)	Urinary incontinence (%)	Complications (%)
Merrick et al. [388]	Dilatation/ "Cold knife"	Radiation- induced	29	0	NR	69	NR	NR
	DVIU	BMS						
Sullivan <i>et al</i> . [117]	Dilatation (n=15) / "Cold knife" DVIU (n=20)	Radiation- induced BMS	39	0	16 (2-48)	51	11	NR
Brede <i>et al</i> . [397]	"Cold knife" DVIU	VUAS	63	Dilation 33 Incision 38 Both 29	11 (1-144)	73	52*	NR
Yurkanin	"Cold knife"	VUAS	61	Dilatation 100	31	87	12**	NR
<i>et al</i> . [395]	DVIU				(1-77)			
Giannarini	"Cold knife"	VUAS	43	0	48	74	0	NR
et al. [396]	DVIU				(23-80)			
Ramchandani et al. [382]	"Cold knife" DVIU	VUAS	10	0	NR	80	10	0
Hayashi et al. [387]	"Cold knife" DVIU	VUAS	6	Dilatation: 100	NR	50	NR	NR
	Holmium laser DVIU	VUAS	3	Dilatation + DVIU: 100	11-37	100	0	NR
Lagerveld <i>et al.</i> [400]	Holmium laser DVIU	VUAS	10	None: 40 Endoscopic (dilatation +/- DVIU +/- ISD): 60	18 (3-29)	100	0	0
Ramirez <i>et al</i> . [394]	"Hot knife" DVIU	VUAS: 74% BNS: 26%	50	None: 22	16	72	9	NR
Gousse et al. [399]	"Hot knife" DVIU	VUAS	15	None	15 (6-26)	80	100***	NR
Bang <i>et al.</i> [389]	"Hot knife" DVIU	VUAS	37	NR	13 (2-33)	65	100***	NR
Popken <i>et al</i> . [398]	"Cold knife" DVIU	VUAS	6	None	12-72	50	0	NR
	TUR	VUAS	15	None		47	0	NR
Kranz	TUR	VUAS	87	NR	27	40.2	13.8	NR
<i>et al</i> . [404]	TUR	VUAS	60	NR	(1-98)	58.3	1.7	NR
Brodak <i>et al</i> . [401]	TUR (bipolar)	BNS	22	DVIU 45	42 (14-72)	91	NR	NR
	Holmium laser DVIU	VUAS	17	DVIU: 12		76	NR	NR
Ozturk	TUR	VUAS	28	Dilatation: 75	24	82	0	0
et al. [402]	(bipolar)			DVIU: 25	(6-66)			
LaBossiere et al. [385]	Holmium laser DVIU	VUAS	70	NR	10	69	NR	NR
or al. [000]	"Cold knife" DVIU	VUAS	8	NR		25	NR	NR
	TUR	VUAS	36	NR		39	NR	NR

BNS = bladder neck stenosis; DVIU = direct vision internal urethrotomy; FU = follow-up; ISD = intermittent self-dilatation; NR = not reported; TUR = transurethral resection; VUAS = vesico-urethral anastomosis stricture.

°patency rate after 1<sup>st</sup> endoluminal treatment evaluated in the study.

\* requiring incontinence surgery (artificial urinary sphincter or male sling).

\*\* slightly problematic urinary incontinence by questionnaire post DVIU (no data on pre DVIU continence).

\*\*\*all incontinent pre-operatively.

# 6.3.5.1.2.3 Post-dilatation/direct vision internal urethrotomy strategies for non-traumatic posterior urethral stenosis

6.3.5.1.2.3.1 Intermittent self-dilatation for non-traumatic posterior urethral stenosis

As for anterior strictures, ISD can be offered to patients for recurrent posterior stenosis after dilation/DVIU to stabilise the stenosis. This is especially relevant for patients unfit/unwilling to undergo surgery or in patients with radiation-induced BMS [117, 385, 388, 408]. Although ISD may be acceptable to many urologists and patients, it usually is associated with a reduced QoL and poor patient compliance [35].

6.3.5.1.2.3.2 Intralesional injections for non-traumatic posterior urethral stenosis

In order to stabilise the luminal fibrosis and consequently to reduce the risk of recurrence, injection of antifibrotic agents at the time of endoluminal treatment has been proposed. The majority of patients in these studies were patients with recalcitrant/recurrent non-obliterative VUAS/BNS. Two series used corticosteroids [386, 402], whilst the others used MMC [245, 403, 406-409]. Patency rates with corticosteroid injections range between 50-100% [386, 402]. Patency rates with MMC vary between 50-79% [245, 403, 406-409]. No trials comparing endoluminal treatment with or without adjuvant intralesional injections were identified.

See supplementary <u>Table S6.13</u> for further information.

Complications are low across most studies, but all studies were retrospective in nature. Redshaw *et al.*, also reported grade 3 complications in four out of 55 (7%) patients, including osteitis pubis (n=2), bladder neck necrosis (n=1) and rectourethral fistula (n=1) in one multi-institutional study [245]. Three of these patients ultimately required urinary diversion with additional faecal diversion in one patient [245]. Given the severity of these complications, although rare, MMC should not be used outside the framework of a clinical trial [410].

#### 6.3.5.1.2.3.3 Urethral stent for non-traumatic posterior urethral stenosis

Stents have been used anecdotally in the posterior urethra [252, 253, 385]. Patency rates are relatively low (47-60%) [252, 253, 385] at the cost of a high-risk for UI (19-82%) [252, 253].

Summary of evidence	LE
For non-obliterative VUAS and radiation-induced BMS, visually controlled dilatation and DVIU yield a patency rate of respectively 0-89% and 25-100% with a low complication rate. It can be performed under loco-regional anaesthesia.	3
During DVIU, deep incision might provoke injury to the rectum at the six o' clock position and might provoke uro-symphyseal fistulation at the twelve o'clock position.	3
For BNS, TUR and "hot-knife" incision yield a patency rate of respectively 58.3 and 72% with a low complication rate.	3
Repetitive endoluminal treatments in non-obliterative VUAS, radiation-induced BMS or BNS can stabilise the posterior stenosis and are easy to perform compared to reconstructive surgery.	3
Any form of endoluminal treatment might be associated with <i>de novo</i> UI (up to 25%) or worsening of existing UI (up to 15%).	3
Vesico-urethral anastomosis stricture, BMS and BNS with complete obliteration are not included in present series and endoluminal treatment is unlikely to be successful.	3
Urethral stents at the posterior urethra have a rather low patency rate (47-60%) and incontinence rate (19-82%).	3

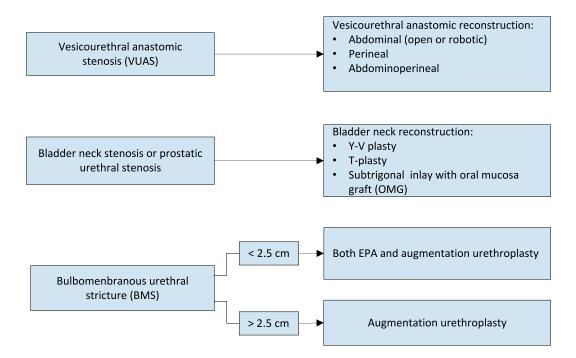
Recommendations	Strength rating
Perform visually controlled dilatation or direct vision internal urethrotomy (DVIU) as 1 <sup>st</sup> line-	Weak
treatment for a non-obliterative vesico-urethral anastomosis stricture (VUAS) or radiation-	
induced bulbomembranous strictures (BMS).	
Do not perform deep incisions at the six and twelve o' clock position during DVIU for VUAS	Strong
or radiation-induced BMS.	
Perform transurethral resection (TUR) or "hot-knife" DVIU as 1 <sup>st</sup> line-treatment for patients	Strong
with non-obliterative bladder neck stenosis (BNS) after surgery for benign prostatic	
obstruction.	
Perform repetitive endoluminal treatments in non-obliterative VUAS or BNS in an attempt to	Weak
stabilise the stricture.	
Warn patients about the risk of <i>de novo</i> urinary incontinence (UI) or exacerbation of existing	Weak
UI after endoluminal treatment.	

Do not perform endoluminal treatment in case of VL	IAS, BMS and BNS with complete	Strong
obliteration.		
Do not use stents for strictures at the posterior uret	nra.	Weak

6.3.5.1.3 Lower urinary tract reconstruction for non-traumatic posterior urethral stenosis

If endoluminal treatment (repeatedly) fails or in case of a completely obliterated posterior stenosis [406, 407, 411, 412], lower urinary tract (LUT) reconstruction may be considered in fit patients motivated to undergo surgery (Figure 6.1). The choice of LUT reconstruction will depend upon the length, location, calibre and aetiology of the stenosis, continence status, bladder function, previous radiotherapy, patient's preference, and surgeon's expertise.

# Figure 6.1: Options for lower urinary tract reconstruction of non-traumatic posterior urethral obstruction (stenosis/stricture)



6.3.5.1.3.1 Redo vesico-urethral anastomosis for vesico-urethral anastomotic stenosis after radical prostatectomy

After excision of the stenosis, ReDo vesico-urethral anastomosis (ReDo VUA) can be performed. This may be performed via a retropubic, perineal, combined abdominoperineal or robot-assisted approach. Nikolavsky *et al.*, proposes a retropubic approach for VUAS involving the bladder neck, a perineal approach for short VUAS with intact bladder neck and an abdominoperineal approach for long segment (> 3 cm) VUAS with bladder neck involvement [411]. The ReDo VUA must be performed in a tension-free fashion which can be achieved either by mobilisation of the bladder (retropubic approach), mobilisation of the bulbar urethra with corporal splitting and inferior pubectomy if necessary (perineal approach) or both (abdominoperineal approach) [411, 413]. Dinerman *et al.*, reported a robot-assisted abdominoperineal approach in a case with 4.5 cm long complete obliteration [414]. Kirshenbaum *et al.*, reported a pure robot-assisted abdominal approach. Regardless of the approach, the procedure is technically demanding due to the location deep under the pubic symphysis, and the proximity of the external sphincter [413]. As a consequence, surgical morbidity must be considered. As most patients with VUAS were healthy enough to undergo RP, most patients will likewise remain fit and eligible for VUAS surgical reconstruction [411, 413].

#### Table 6.9: Outcomes of redo vesico-urethral anastomosis

Study	Ν	Approach (%)	Previous	FU (months)	Length	Patency	Incontinence	Complications
			RT (%)		(cm)	(%)	(%)	(%)
Nikolavsky	12	Perineal: 25	25	76 (14-120)	2.5 (1-5)	67	58	Persistent
<i>et al</i> . [411]		Abdominal: 67						extravasation due
		Abdominoperineal:						to anastomotic
		17						dehiscence grade
								3b: 8.3 (prior RT)
Mundy	17	Transperineal	0	NR	NR	88	100	NR
<i>et al</i> . [413]	6		100	NR	NR	67	100	NR
Schuettfort	22	Transperineal	0	45 (4-77)	NR	91	100*	Rectal injury: 4
<i>et al</i> . [415]	1		100		NR	0	100*	Lower leg
								paresthesia: 4
Pfalzgraf	20	Retropubic	NR	63 (15-109)	NR	60	65**	UTI: 5
<i>et al</i> . [416]								Fever: 5
								Renal failure: 5
								(all grade 2)
Giudice	10	Perineal: 5	NR	30 (4-106)	NR	80	70	NR
<i>et al</i> . [417]		Abdominal: 4						
		Combined: 1						
Dinerman	1	Robot-assisted	0	12	4.5	100	0***	0
<i>et al</i> . [414]		abdominoperineal						
Kirshenbaum	5	Robot-assisted	0	14 (5-30-)	NR	60	0	Pubovesical
<i>et al</i> . [412]		abdominal						fistula: 20 grade 3b
		(±VY-plasty)						

*FU* = follow-up; *NR* = not reported; *RT* = radiotherapy; *UTI* = Urinary tract infection.

\* incontinent before ReDo VUA.

\*\* de novo incontinence in four out of eleven patients.

\*\*\*social continent (1 pad/day).

ReDo VUA in non-irradiated patients yields patency rates of 60-91% (Table 6.9) [411-413, 415-417]. Prior radiotherapy is a risk factor for failure [413, 415]. In addition, radiation-induced bladder toxicity might provoke reduced bladder capacity, low bladder compliance, bladder spasms and pain, and urethral necrosis making reconstruction futile (see below) [393, 413, 418]. ReDo VUA should only be done in patients with adequate bladder function and in the absence of (peri)-urethral pathology (urethral necrosis, calcification, fistulation). Flaps (gracilis flap, peritoneal flap) to support and protect the anastomosis may be beneficial in irradiated patients [411].

With the transperineal approach, UI is inevitable, as this approach disrupts the external sphincter [412, 413, 415, 417]. With the retropubic approach, Pfalzgraf *et al.* reported *de novo* incontinence in only four out of eleven (36%) patients [416]. In the series of Nikolavsky *et al.*, where a retropubic approach was predominantly used, incontinence rate was 58% [411]. Kirshenbaum *et al.*, reported no incontinence in five patients treated by robot-assisted retropubic approach [412]. Giudice *et al.*, reported incontinence in one out of four patients treated with the retropubic approach [417]. Therefore, some authors [101, 411, 412] have proposed a preference for the retropubic approach in patients with good pre-operative urinary continence, although both approaches have never been directly compared for UI. In addition, the lack of perineal dissection by a retropubic approach will preserve the perineal anatomy and vascularisation which makes subsequent artificial urinary sphincter (AUS) less demanding [412]. Artificial urinary sphincter implantation should be deferred because of the risk of VUAS recurrence and difficulty of treating any recurrent VUAS with the cuff of the AUS in place [397, 413]. The exact timing of AUS placement is not consensual in the literature but most advise waiting at least three to six months to ensure stability of the VUA patency [393, 410, 413, 415, 416].

Due to the complexity of this pathology the EAU Urethral Strictures Panel advises that VUAS reconstruction should be performed only in experienced high-volume centres, particularly after prior radiotherapy or other energy ablative treatments.

Summary of evidence	LE
ReDo VUA has patency rates of 60-91% in non-irradiated patients and 67% in irradiated patients with	3
obliterative VUAS or VUAS refractory to endoluminal treatment.	
Urinary incontinence is inevitable after transperineal ReDo VUA. Artificial urinary sphincter placement	3
can be offered after three to six months if patency of ReDo VUA is ensured.	
De novo incontinence with retropubic ReDo VUA is 0-58%.	3

Recommendations	Strength rating
Perform ReDo vesico-urethral anastomosis (VUA) in non-irradiated patients and irradiated	Weak
patients with adequate bladder function with obliterative vesico-urethral anastomosis	
stricture or vesico-urethral anastomosis stricture refractory to endoluminal treatment.	
Warn patient that urinary incontinence (UI) is inevitable after transperineal ReDo VUA and	Strong
that subsequent anti-UI surgery might be needed in a next stage, after at least three to six	
months.	
Offer ReDo VUA by retropubic approach if the patient is pre-operatively continent.	Weak

# 6.3.5.1.3.2 Posterior stenosis after surgery for benign prostatic obstruction

6.3.5.1.3.2.1 Bladder neck reconstruction for bladder neck stenosis after surgery for benign prostatic

#### obstruction

The bladder neck is augmented by advancement of local bladder flaps (Y-V or T-plasty) with or without resection of scar tissue. They are used for BNS refractory to endoscopic treatments [412, 419-421]. Patency rates vary between 83-100% with fourteen to 45 months follow-up [412, 419-421]. There is a trend to perform bladder neck reconstruction by minimally invasive approach (laparoscopic, robot-assisted) [412, 420, 421]. *De novo* incontinence rate ranges from 0-14% [412, 419-421]. Satisfaction among patient is high with 88.5% of patients stating that they are pleased with the surgery, with an improvement of QoL in 75% of patients [419, 421]. Recently, a robot-assisted augmentation technique with subtrigonal buccal mucosa inlay has been successfully reported in a case report, but this technique requires further investigation [422].

See supplementary <u>Table S6.14</u> for further information.

6.3.5.1.3.2.2 Bulbomembranous strictures after surgery for benign prostatic obstruction

Bulbomembranous urethral strictures (BMS) after TURP or simple prostatectomy are managed as bulbar strictures and can be treated by EPA or augmentation urethroplasty with a graft, taking into account the length and tightness of the stricture [84, 423]. As reconstruction is in the proximity of the external sphincter and the bladder neck was already damaged during BPO surgery, the risk of incontinence (up to 25%) is present [84].

Summary of evidence	LE
Bladder neck reconstruction with Y-V or T-plasty for treatment refractory BNS has patency rates of	3
83-100%.	
Incontinence occurs in up to 14% with bladder neck reconstruction and up to 25% after	3
reconstruction of BMS after previous surgery for BPO.	

Recommendations	Strength rating
Perform bladder neck reconstruction with Y-V or T-plasty for treatment refractory bladder	Weak
neck stenosis (BNS).	
Warn patients about de novo urinary incontinence after reconstruction for BNS or	Strong
bulbomembranous urethral strictures with previous benign prostatic obstruction surgery as	
aetiology.	

#### 6.3.5.1.3.3 Radiation/high-energy induced posterior strictures

6.3.5.1.3.3.1 Bulbomembranous strictures secondary to radiation/high energy sources

The major challenge in treating radiation-induced strictures is the consequent tissue damage with impaired healing capacity, involving not only the stricture itself but also the adjacent proximal and distal areas of the scar [413, 424]. Additionally, proximity of the stricture to the external sphincter can further complicate surgery [84]. Due to these challenges, patients with radiation-induced BMS have long been considered poor candidates for urethral reconstruction and have been treated with urinary diversion if endoscopic treatments failed or were not possible [413].

Most radiation-induced BMS are short and in these cases, EPA is possible [84, 189, 425, 426]. Reported patency rates vary between 67-95% [84, 189, 426, 427]. *De novo* UI was reported in 33-36% of cases [84, 189, 426, 427] and this seems to be higher compared to the rates reported for bulbar and traumatic-posterior strictures (see sections 6.3.2 and 6.3.5). Chung *et al.*, reported *de novo* incontinence in twelve out of 36 (33%) patients with EPA for radiation-induced BMS vs. four out of 33 (12%) patients with EPA for PFUI (p=0.05) [427].

Excision and primary anastomosis has the advantage of avoiding the use of a graft or a local flap in an area of poor vascular health. However, EPA will not be possible for BMS with a long bulbar segment and in these cases, augmentation urethroplasty will be necessary despite the aforementioned concerns [189, 426, 428, 429]. Glass *et al.*, used a cut-off of 2.5 cm to proceed with augmentation urethroplasty, whilst this was 2 cm by Meeks *et al.* [426, 429]. Some authors have even used augmentation urethroplasty as their standard technique for radiation-induced BMS [355]. Both dorsal [423, 428] and ventral onlay [355, 429] have been described to treat radiation-induced BMS. In the absence of a robust vascular graft bed, the support by a gracilis flap has been proposed during ventral onlay graft urethroplasty [429, 430]. Patency rates with augmentation urethroplasty vary between 50-83% [189, 355, 426, 428] with *de novo* incontinence ranging between 11-50% [189, 355, 428](see supplementary Table S6.15). Rourke *et al.*, reported a patency rate of 91% vs. 75% for EPA and augmentation urethroplasty, respectively, but this difference did not reach statistical significance (p=0.31) [428]. Of note, strictures treated with augmentation urethroplasty were significantly longer compared to those treated by EPA (respectively 6.1 vs. 2.1 cm; p < 0.001). They reported no significant differences in *de novo* UI (26 vs. 25%; p=1), new onset ED (35 vs. 0%; p=0.06) or other adverse events (30% vs. 33%; p=1) [428].

#### 6.3.5.1.3.3.2 Prostatic strictures secondary to radiation/high energy sources

Radiotherapy and high-energy modalities (cryoablation, HIFU) might provoke prostatic necrosis, sloughing and obstruction [101]. Cases refractory to TUR and with good bladder capacity might be salvaged by prostatectomy taking into account the morbidity associated with salvage RP (rectal injury, VUAS, incontinence) [101, 424]. Mundy *et al.*, treated nine patients with patency in six, (67%) and one (11%) needing an AUS for severe incontinence [413].

Cases with impaired bladder function, urethral necrosis and/or peri-urethral pathology should be considered for supravesical diversion, especially if a suprapubic catheter is not tolerated due to bladder pain or spasms [393, 410, 413, 418].

Recently, a "pull-through" procedure has been reported as an alternative to cutaneous diversion for reconstruction of the devastated posterior urethra associated with a defunctionalised bladder after radiation where tissue vascularity and quality is poor [431]. This novel technique of total LUT reconstruction combines salvage cystectomy, ileal neobladder formation and urethral pull-through. An AUS was implanted in a 2<sup>nd</sup> stage. All eight patients maintained a patent posterior urethra after a median follow-up of 58 (range 16-84) months. Five patients experienced low-grade complications after the 1<sup>st</sup> stage, but no high-grade complications were reported. Four out of eight (50%) patients experienced cuff erosion with need for removal and subsequent reimplantation. After a median of two revision surgeries (range 0 to 4), all patients achieved social continence enhancing QoL [431]. This technique requires further validation before its use can be recommended.

Summary of evidence	LE
Patency rates with EPA and augmentation urethroplasty are respectively 67-95% and 50-83% in case	3
of radiation-induced BMS.	
Radiation-induced BMS longer than 2-2.5 cm are rarely amenable for EPA.	3
De novo incontinence and new onset ED after urethral surgery for radiation-induced BMS are reported	3
in respectively 11-50% and 0-35% of cases.	
Salvage prostatectomy can achieve patency in 67% of patients for prostatic strictures after irradiation	4
or high-energy treatments but morbidity is substantial.	

Recommendations	Strength rating
Use either excision and primary anastomosis or augmentation urethroplasty for short (<	Weak
2.5 cm) radiation-induced bulbomembranous strictures (BMS) refractory to endoscopic	
treatment depending on surgeon's experience.	
Perform augmentation urethroplasty for long (> 2.5 cm) radiation-induced BMS.	Weak

Warn patients about the risk of <i>de novo</i> incontinence and new onset erectile dysfunction	Strong
after urethroplasty for radiation-induced BMS.	
Offer salvage prostatectomy in motivated and fit patients with adequate bladder function in	Weak
case of a prostatic stricture due to irradiation or high-energy treatment.	

6.3.5.1.4 Extirpative surgery and urinary diversion for non-traumatic posterior urethral stenosis

In complex and/or recurrent cases [411], LUT reconstruction is not possible or not indicated due to severe necrosis, calcification and significant morbidity, especially severe pain [410]. Intractable haematuria or fistulation might be other reasons to abandon the urethral outlet. Typically, the patient has a history of pelvic irradiation or high energy prostate cancer treatment and several previous attempts to achieve cure. Moreover, and equally important, any of the options used to deal with a devastated posterior urethra are dependent upon good bladder capacity, compliance and function allowing for bladder preservation as well as healthy distal ureters [393, 410]. The last resort therapeutic option is urinary diversion (continent or incontinent) with or without cystectomy [413, 418]. Different techniques have been described and the choice between them largely depends on the bladder capacity, presence of local symptoms, performance status and expectations of the patient. Cystectomy during urinary diversion is able to palliate symptoms of intractable bladder pain, spasms and haematuria which are especially prevalent after pelvic radiotherapy [432-435]. The satisfaction rate was reported to be 100% and the overwhelming majority of patients would have undergone this extirpative surgery an average of thirteen months sooner in a study of fifteen patients by Sack *et al.* [436]. In a report by Faris *et al.*, 27% of the patients also required bowel diversion due to intractable gastrointestinal morbidity, highlighting the complexity of this pathology [418].

Summary of evidence	LE
Urinary diversion can improve QoL in patients with a devastated LUT with a high satisfaction rate.	3
Cystectomy is able to palliate symptoms of intractable bladder pain, spasms, and haematuria.	3

Recommendations	Strength rating
Perform urinary diversion in recurrent or complex cases with loss of bladder capacity and/or	Weak
incapacitating local symptoms.	
Perform cystectomy during urinary diversion in case of intractable bladder pain, spasms	Weak
and/or haematuria.	

# 6.3.5.2 Post-traumatic posterior stenosis

The acute and early management of PFUIs is discussed in the EAU Guidelines on Urological Trauma. A nonobliterative stenosis is the result of a partial injury at the membranous urethra or occurs after unsuccessful early realignment of a partial or complete injury. An obliterative stenosis is the consequence of a complete injury with a distraction defect between the ruptured urethral ends. The gap between these ends fills up with dense fibrotic tissue [11].

The deferred management of PFUI is at earliest three months after the trauma. After that period, the pelvic haematoma has nearly always resolved, the prostate has descended into a more normal position, the scar tissue has stabilised [437] and the patient is clinically stable and able to lie down in the lithotomy position [437, 438].

# 6.3.5.2.1 Endoluminal treatment for post-traumatic posterior stenosis

6.3.5.2.1.1 Endoluminal treatment as primary treatment for post-traumatic posterior stenosis

Endoluminal treatment (dilation, DVIU) of an obliterative stenosis using the cut-to-the light principle will not be successful [48] and has a risk of creating a false passage towards the bladder base or rectum [439]. For a non-obliterative, short ( $\leq 1.5$  cm) stenosis, one attempt of endoluminal treatment (endoscopic incision or dilation) can be performed. Kulkarni *et al.*, reported a 92.3% and 96.5% stricture-free rate with "cold knife" and holmium laser urethrotomy, respectively (median follow-up respectively 61 and 57 months) [440]. These results are challenged by Barbagli *et al.*, who reported a 51% stricture-free rate with holmium laser urethrotomy but with no data on length of follow-up available [441]. Cai *et al.*, compared patient outcomes between bipolar plasma vaporisation and "cold knife" DVIU in 53 patients with posterior traumatic (80%) and iatrogenic (20%) urethral strictures with significantly different stricture-free rates of 81.5% vs. 53.8% at a mean follow-up of 13.9 months, respectively [442]. No severe complications were reported in either group. A statistically significant shorter operative time was found in the bipolar group [442]. Barratt *et al.*, calculated a composite stricture-free rate of 20% after all types of endoscopic treatments (but with a mix of obliterative and non-obliterative

stenoses) [48]. *De novo* UI was reported in 4% of cases [48]. Repetitive endoluminal treatments are unlikely to be curative and must be discouraged as this delays the time to definitive cure and can lead to more complications [443, 444].

6.3.5.2.1.2 Endoluminal treatment after failed urethroplasty for post-traumatic posterior stenosis

In case of a non-obliterative and short ( $\leq 1$  cm) recurrence after failed urethroplasty, endoluminal treatment can be performed [445, 446]. Although a 1<sup>st</sup> and 2<sup>nd</sup> DVIU can be successful with a stricture-free rate of 22.9-77.3% and 0-60% respectively, three or more incisions are never successful (see supplementary <u>Table S6.16</u>) [445-449]. Therefore, repetitive endoluminal treatments (dilations and/or endoscopic incisions) can only be considered as a palliative option [446, 450].

Summary of evidence	LE
Endoluminal treatment of obliterative stenoses is not successful and may create false passages	3
towards bladder or rectum.	
Endoluminal treatment of short, non-obliterative, stenoses has a 20-96.5% stricture-free rate.	3
A 1 <sup>st</sup> DVIU has stricture-free rates of 22.9-77.3% for a short and non-obliterative recurrence after	3
excision and primary anastomosis.	

Recommendations	Strength rating
Do not perform endoscopic treatment for an obliterative stenosis.	Strong
Perform one attempt at endoluminal treatment for a short, non-obliterative stenosis.	Weak
Do not perform more than two direct vision internal urethrotomies and/or dilatations for a	Weak
short and non-obliterative recurrence after excision and primary anastomosis for a traumatic	
posterior stenosis if long-term urethral patency is the desired intent.	

### 6.3.5.2.2 Urethroplasty for post-traumatic posterior stenosis

In view of the complexity and difficulty of urethroplasty and the fact that the best results are obtained with its first attempt, this surgery must be performed in high-volume centres [451-453]. It has been calculated that to achieve and maintain sufficient experience in the reconstruction of PFUI, one centre per twelve million inhabitants is sufficient (for well-resourced countries) [452].

#### 6.3.5.2.2.1 First urethroplasty for post-traumatic posterior stenosis

6.3.5.2.2.1.1 Indication and technique of urethroplasty for post-traumatic posterior stenosis Progressive perineal EPA is the standard treatment for an obliterative stenosis and for a non-obliterative stenosis as first attempt, or after failure of primary endoluminal treatment [48, 454].

Although both a midline and inverted U-incision are possible to gain access to the posterior urethra, a midline incision is associated with a significant reduction in trauma to the superficial perineal and posterior scrotal nerves and vessels, in the rate of surgical site infections (3.1% vs. 16.4%) and reduced length of hospitalisation [376].

A combined transpubic abdomino-perineal approach is only necessary in complicated cases such as those with associated para-urethral bladder base fistula, trauma-related recto-urethral fistula, and bladder neck injury [439]. Total pubectomy during transpubic abdomino-perineal reconstruction has a higher complication rate (bleeding, pelvic instability, dead space) compared to partial (superior or inferior) pubectomy with no gain in surgical exposure [455]. Although also considered complex situations, iatrogenic recto-urethral fistula (after misdirected endoscopic treatment), traumatic recto-urethral fistula < 5 cm from the anus, UCF and urinoma cavity can usually be corrected by a progressive perineal approach only [439, 456].

# 6.3.5.2.2.1.2 Patency rate after urethroplasty for post-traumatic posterior stenosis

The overall patency rate after deferred EPA is 85.7% [48]. Complete excision of scar tissue is a strong predictor for freedom of stricture whereas number (3-5 vs. 6-7) and size (3.0 vs. 4.0 cm) of sutures are not [457]. One retrospective cohort study showed a significantly improved patency rate if dorsal anterior urethral spatulation was performed compared to ventral anterior urethral spatulation [458]. Another retrospective study showed an improved patency rate after eversion of the urethral mucosa of both urethral ends before anastomosis ("valgus urethral mucosa anastomosis") [459]. The findings of both studies have yet to be confirmed in a prospective fashion.

To preserve the antegrade arterial inflow of the bulbar urethra and reduce the surgical trauma of "classic" deferred EPA, bulbar artery sparing EPA has been described [460]. Initial patency rates vary between 88.5-100% with 20-45 months of follow-up (see supplementary <u>Table S6.17</u>) [460-462]. Xie *et al.*, only used this technique for distraction defects less than 2.5 cm [462]. No evidence exists to date whether bulbar artery sparing EPA is superior to the "classic" EPA in terms of patency rate and potency and continence rates.

In case of a very deep location of the proximal urethral end that makes anastomotic suturing impossible, Badenoch described a pull-through technique which has a 33.3-96.5% patency rate after 43-126 months of follow-up (see supplementary <u>Table S6.18</u> for further information) [440, 463, 464]. With the aim to reduce stricture recurrence, Wong *et al.*, advise a 1.5 cm segment overlap of the bulbar stump within the prostatic urethra during the pull-through technique [463]. To facilitate the suturing at the proximal part of the urethra located deep under the pubic bone, the robotic approach is under exploration but there is no evidence so far of improved outcome with this approach [465].

Patency rate in children varies between 75-89.8% (Table 6.10). The statement that EPA in children is associated with poorer results [466] cannot therefore be generally accepted [467].

Study	N	Follow-up	patency rate	Erectile	Incontinence	Abdomino-perineal
		(months)		dysfunction		
Podesta et al. [468]	49	78 (60-264)	44 (89.8%)	3 (6.1%)	9 (18.4%)	21 (43%)
Waterloos et al. [469]	7	57 (8-198)	6 (85.7%)	2 (28.6%)	1 (14.3%)	1 (14.3%)
Singh et al. [466]	5	26 (12-42)	4 (80%)	NA	0 (0%)	0 (0%)
Singla et al. [470]	28	36 (3-58)	21 (75%)	-	1 (3.6%)	1 (3.6%)
Voelzke et al. [471]	18	13 (1-71)	16 (88.9%)	-	-	1 (5.6%)

### Table 6.10: Outcomes of EPA in children

N = number of patients; NA = not applicable.

# 6.3.5.2.2.1.3 Sexual function, urinary continence, and rectal injury after urethroplasty for post-traumatic posterior stenosis

Regarding erectile function, a prospective study by Hosseini *et al.*, found no significant difference before, and three or six months after EPA for posterior traumatic stenosis [472]. Another prospective study by Tang *et al.*, also demonstrated no significant overall change in ED after urethroplasty. However, in the subgroup of patients with pre-operative non-vascular ED, a significant post-operative increase in ED was observed [473]. A meta-analysis of retrospective studies showed a significant decline of the rate of ED from 43.27% before to 24.01% after posterior urethroplasty (p < 0.001) [474]. Assessment of erectile function and its definitive treatment (e.g., penile prosthesis) should be performed two years after the trauma because of the potential return of normal erectile function within that time [475, 476].

After deferred EPA, antegrade ejaculation is present in 98.3-100% of cases [477, 478]. Decreased ejaculatory volume and/or diminished ejaculatory force were reported in 17.2-18.7% of cases but it cannot be assessed whether this is due to the trauma or due to the surgery [477, 478].

Continence after PFUI and urethroplasty is generally attributed to a competent bladder neck [48]. On the other hand, as most ruptures occur at the bulbomembranous junction just below the external sphincteric mechanism, at least a part of the external sphincter mechanism can be spared during urethroplasty [479]. Therefore, incontinence is rare with deferred EPA (6.8%) and is usually due to incompetence of the bladder neck although an incompetent bladder neck will not necessarily result in incontinence after urethroplasty [48, 479].

Rectal injury is a relatively rare (0-10.2%) but severe complication after deferred EPA (see supplementary Table S6.19) [437, 449, 455, 458, 480-484]. The risk of rectal injury tends to be higher in complicated cases or cases with previous urethral manipulations [437, 480, 485].

# 6.3.5.2.2.2 ReDo-urethroplasty for post-traumatic posterior stenosis

In case of a recurrent stenosis, a repeat ("ReDo") urethroplasty is possible. In the majority of cases, especially if not all consecutive length-gaining manoeuvres have been used during the 1<sup>st</sup> EPA, another EPA can be performed [468, 480, 481, 486, 487]. The Badenoch pull-through technique is again an option if no adequate mucosa-to-mucosa suturing is possible (See supplementary <u>Table S6.18</u>) [463, 464]. In case of excessive dead space after resection of the fibrosis, gracilis muscle [485] or omental flaps (laparoscopically harvested if urethroplasty was performed using perineal approach only) [439, 483] have been advised to fill up this space

and support the anastomosis. These flaps, or alternatively bulbospongious muscle or local subcutaneous dartos flaps, are also useful to separate the suture lines in case of a concomitant recto-urethral fistula [439, 451, 456, 485]. If the urethra cannot be anastomosed in a tension-free fashion, despite the aforementioned manoeuvres, or in cases of ischemic narrowing/necrosis of the bulbar urethra, options are a tubed preputial island flap, staged BMG urethroplasty with flap, staged buccal mucosa dartos flap, radial forearm free flap urethroplasty or entero-urethroplasty [451, 481, 486, 488]. In case of entero-urethroplasty, the sigmoid colon is preferred above ileum (which is in turn better than stomach) because of the proximity of the vascular pedicle to the perineum. Entero-urethroplasty should only be done in the presence of a competent bladder neck because subsequent implantation of an AUS is nearly impossible [488].

Patency rate of different types of ReDo-urethroplasty varies between 37.5-100% (Table 6.11) [446, 451, 453, 480, 481, 483, 486-488]. An alternative is to abandon the normal urinary outlet and opt for Mitrofanoff-vesicostomy, PU (if local perineoscrotal skin is suitable) or permanent suprapubic diversion [481, 488].

Study	Туре	Ν	Follow-up	Patency rate
			(months)	
Bhagat <i>et al</i> . [486]	Progressive perineal EPA	28	29 (12-108)	36 (83,72%)
	Transpubic EPA	12		
	Tubed preputial flap	1		
	Staged BMG + local flap	2		
Fu <i>et al</i> . [480]	Progressive perineal EPA	55	36 (18-47)	33 (60%)
Garg et al. [481]	Progressive perineal EPA	40	31 ± 11	30 (75%)
	Transpubic EPA	2	25	2 (100%)
	Tubed preputial flap	1	25	1 (100%)
	Staged BMG + local flap	2	17	1 (50%)
	Radial forearm free flap	1	15	1 (100%)
Gupta et al. [487]	Progressive perineal EPA	52	54 (10-144)	42 (80.8%)
Koraitim M. [446]	Progressive perineal EPA	4	168 (12-300)	4 (100%)
	Transpubic EPA	5		5 (100%)
Kulkarni <i>et al</i> . [483]	Progressive perineal EPA	15	18 (6-24)	14 (93.3%)
Kulkarni <i>et al</i> . [451]	Progressive perineal EPA	541	68 (12-240)	412 (79.1%)
	Tubed preputial flap	37		30 (81%)
	Staged BMG flap	10		6 (60%)
	Staged BMG + local flap	15		13 (86.6%)
	Entero-urethroplasty	2		2 (100%)
	Radial forearm free flap	3		3 (100%)
	Pedicled anterolateral thigh flap	1		1 (100%)
Mundy et al. [488]	Entero-urethroplasty	11	NA	7 (63.6%)
Podesta et al. [468]	Transpubic EPA	4	120 (72-204)	4 (100%)
Singh <i>et al</i> . [453]	Progressive perineal EPA	8	31 (13-90)	3 (37.5%)
Singh <i>et al</i> . [466]	Progressive perineal EPA	37	26 (12-42)	32 (86.5%)
Singla et al. [470]	Progressive perineal EPA	1	NA	1 (100%)
	Tubed preputial flap	2	NA	2 (100%)

# Table 6.11: Outcome of different types of ReDo-urethroplasty

BMG = buccal mucosa graft; EPA = excision and primary anastomosis; N = number of patients; NA = not applicable.

Summary of evidence	LE
The best results are obtained after the 1 <sup>st</sup> urethroplasty.	4
The overall stricture-free rate after EPA is 85.7%. By using the progressive perineal approach, a	3
combined transpubic abdomino-perineal approach is usually not needed.	
After failed endoluminal treatment, EPA is the standard treatment for a non-obliterative stenosis.	3
Both a midline and inverted U perineal incision equally gain access to the posterior urethra, but a	2b
midline incision is associated with less anatomical damage to local vessels and nerves, reduced risk	
of surgical site infection and hospital stay.	

Total pubectomy during transpubic abdomino-perineal reconstruction has a higher complication rate	4
(bleeding, pelvic instability, dead space) compared to partial (superior or inferior) pubectomy with no	
gain in surgical exposure.	
By using the progressive perineal approach, a combined transpubic abdomino-perineal approach	3
is usually not needed except for very long distraction defects and in case of complicated situations,	
which include associated para-urethral bladder base fistula, trauma-related recto-urethral fistula, and	
bladder neck injury.	
If the urethra cannot be anastomosed in a tension-free fashion or in case of ischaemic narrowing/	3
necrosis of the bulbar urethra, options are a tubed preputial island flap, staged buccal mucosa graft	
urethroplasty with flap, staged buccal mucosa dartos flap, radial forearm free flap urethroplasty or	
entero-urethroplasty.	
In case of excessive dead space after resection of the fibrosis, local flaps have been advised to fill up	3
this space and support the anastomosis. These flaps are also useful to separate the suture lines in	
case of a concomitant recto-urethral fistula.	

Recommendations	Strength rating
Perform open reconstruction for post-traumatic posterior stenosis only in high-volume	Weak
centres.	
Perform progressive perineal excision and primary anastomosis (EPA) for obliterative	Strong
stenosis.	
Perform progressive perineal EPA for non-obliterative stenosis after failed endoluminal	Strong
treatment.	
Perform a midline perineal incision to gain access to the posterior urethra.	Strong
Do not perform total pubectomy during abdomino-perineal reconstruction.	Strong
Reserve abdomino-perineal reconstruction for complicated situations including very long	Weak
distraction defect, para-urethral bladder base fistula, trauma-related recto-urethral fistula,	
and bladder neck injury.	
Perform another urethroplasty after 1 <sup>st</sup> failed urethroplasty in motivated patients not willing	Weak
to accept palliative endoluminal treatments or urinary diversion.	
Use a local tissue flap to fill up excessive dead space or after correction of a concomitant	Weak
recto-urethral fistula.	

# 7. DISEASE MANAGEMENT IN FEMALES

# 7.1 Signs and symptoms of female urethral strictures

The symptoms of female urethral strictures are non-specific and therefore generally non-diagnostic. Female urethral stricture presents with mixed filling and voiding symptoms with frequency in 60.2%, urgency in 51%, poor flow in 42%, incomplete emptying in 42%, UI in 36% (stress, urge or mixed), nocturia in 26%, UTI in 20% and straining to void in 16%. It very rarely presents with urethral pain (3%), terminal dribble (1%), haematuria (1%) or renal failure (1%) (see supplementary <u>Table S7.1</u>) [15, 23, 124, 126, 127, 132, 134, 136, 138, 489-492]. There is often a significant delay in diagnosis of FUS from time of development of symptoms with mean delays of 4.3-12 years described (range 1-30 years) [129, 136].

# 7.2 Diagnosis of female urethral strictures

Twenty-four studies detail investigations leading to a diagnosis of FUS (see supplementary <u>Table S7.2</u>) [13, 15, 124-127, 130-136, 138, 491-500]. In all cases a full history was taken, and a detailed pelvic examination was performed to assess for prolapse, masses, scars and vulval dermatological disorders such as LS, lichen planus or vulvo-vaginal atrophy. Flow rate and US PVR assessment was evaluated in eighteen (75%) and seventeen (71%) studies, respectively. Lateral VCUG was performed routinely in fifteen studies (63%) and as required in one study (4%). Cystourethroscopy was performed routinely in thirteen studies (54%) and as required in two studies (8%). Urodynamics (UDS) were performed routinely in four studies (17%) and as required in seven studies (30%) whilst video-urodynamics (VUDS) were performed routinely in three studies (13%) and urethral calibration (to < 14 Fr) also in three studies (13%). Pelvic MRI was performed as required in four series (17%) whilst transrectal US (TRUS) and renal US were each performed routinely in two series (8%) and intravenous urography (IVU) in ten (4%).

Flow rate and PVR assessment make inherent sense as initial non-invasive screening tools and allow for simple monitoring of effect of treatment. Voiding cystourethrography and/or VUDS will permit diagnosis of BOO [23, 499], visualisation of ballooning above the proximal end of the FUS [134], and delineation of alternate or co-existent diagnoses such as detrusor overactivity (DO) and SUI [127], although VCUG, VUDS and UDS require the ability to insert a 6 Fr catheter and may not be possible without preliminary urethral dilatation in all cases of FUS [492]. Likewise, passage of a cystourethroscopy will require a preliminary dilation in the majority of cases even when a paediatric uretero-renoscope is utilised [125]. Cystourethroscopy will allow for formal identification of the distal end of the FUS and will also allow for exclusion of a functional cause of BOO [134]. Magnetic resonance imaging is performed mainly to exclude alternate pathology such as urethral diverticulum and urethral carcinoma and also allows assessment of the degree of urethral fibrosis associated with FUS [492, 501]. Proponents of TRUS utilise it in lieu of MRI and for visualisation of the dilated urethra above the proximal end of the FUS [502].

# 7.3 Treatment of female urethral strictures

#### 7.3.1 Minimally invasive techniques for treatment of female urethral strictures

Several minimally invasive treatments have been reported; these include urethrotomy, dilatation, meatotomy and meatoplasty. Meatotomy and meatoplasty are essentially the same procedure in the female urethra and the term 'meatoplasty' will be used throughout this document.

#### 7.3.1.1 Urethrotomy for treatment of female urethral strictures

No papers were found detailing the use and outcomes of urethrotomy specifically for the management of FUS. Internal urethrotomy or dilation was used by Massey and Abrams [503] to treat a variety of pathologies, including FUS, causing symptoms of obstructed voiding, and resulted in symptomatic improvement in 80% of patients. As this study included women with a variety of complaints and did not assess urodynamic parameters, the results in the patient subset with true urethral stricture are unclear. If utilised, urethrotomy in the female urethra involves incisions at three, nine and occasionally twelve o'clock [503].

#### 7.3.1.2 Urethral dilatation for treatment of female urethral strictures

With this treatment, the urethra is dilated to between 30 Fr and 41 Fr Some patients will continue with ISD. Romman *et al.*, 2012 [491] and Popat & Zimmern [492] also described suture plication of bleeding areas of the meatus if required post-urethral dilatation.

Four studies described the results after twelve to 59 months follow-up of, in total, 183 patients having dilatation only. Patency rates ranges from 7.5-51% (see Table 7.1) [127, 128, 491, 492]. In another four studies that included, in total, 31 patients that continued to perform ISD, stabilisation of the stricture with "patency" was obtained in 37.3-100% of cases at twelve to 21 months of follow-up (see Table 7.1) [13, 132, 135, 497].

New onset SUI (0.8%) and other complications are very rare after dilation (see supplementary <u>Table</u> <u>S7.3</u>). Due to the low complication rate, the minimally invasive nature of the technique and the reasonable success rate, it is acceptable to start with urethral dilation as a first-line treatment for an uncomplicated FUS.

#### 7.3.1.3 Meatoplasty for treatment of female urethral strictures

Meatal stenosis is extremely rare, with only 2/58 (3%) of females evaluated for voiding dysfunction found to have true meatal stenosis [504]. Only three meatoplasty papers were identified containing 60 patients (see supplementary <u>Table S7.4</u>): one [505] detailed meatoplasty outcomes in a series of 58 girls whilst the 2<sup>nd</sup> was from a study analysing outcomes of various forms of FUS treatment that included one case of meatoplasty [506], and the third was a case report [132]. The patency rate of meatoplasty in girls is excellent with 97% of the 58 girls in Hesing's series having a successful outcome with no reported side effects at twelve months. Forty-eight of 50 patients experienced resolution of their recurrent UTIs and improved voiding symptoms one year after meatoplasty [505]. None of these studies reported incontinence or other acute complications. For short meatal strictures, meatoplasty is the first-line treatment option.

#### 7.3.2 Urethroplasty for treatment of female urethral strictures

Twenty-five papers report the outcomes of urethroplasty for FUS disease in 231 patients in total after the scope search of the Panel. The Panel have analysed the outcomes of these urethroplasty according to flap or graft type as: vaginal graft, vaginal flap, labial/vestibular graft, labial/vestibular flap and buccal or lingual graft.

In female urethroplasty, a dorsal approach is via a stricturotomy at twelve o'clock, a ventral approach is via a stricturotomy at six o'clock and circumferential is a full circumference reconstruction.

#### 7.3.2.1 Vaginal graft augmentation urethroplasty for treatment of female urethral strictures

There were four studies reporting vaginal graft urethroplasty including 37 patients [15, 495, 500, 507]. All

37 vaginal graft urethroplasties were performed via a dorsal approach in women with a mean/median age of 47.5-60.6 years (range 35-70). In these studies, patency rates of 73-100% were reported after 22-27 months follow-up (Table 7.1). No complications and no new onset UI were reported.

See supplementary <u>Table S7.5</u> for further information.

## 7.3.2.2 Vaginal flap augmentation urethroplasty for treatment of female urethral strictures

Vaginal flap urethroplasty was reported in 70 women and was always via a ventral approach, utilising an inverted U vaginal flap inlay in five studies (n=52) [126, 127, 130, 489, 490], a lateral C vaginal flap in three studies (n=17) [124, 132, 136] and one vaginal island flap urethroplasty in one patient [130]. At a mean/median follow-up time of 30-80.7 months, patency rates of 67-100% were reported (Table 7.1). Eight (11.4%) patients had a simultaneous pubo-vaginal sling (PVS), four (5.7%) had a simultaneous Martius fat pad flap interposition and one (1.4%) had a simultaneous excision of urethral diverticulum. Five (7.1%) patients developed new onset UI, two (2.9%) developed UTIs and two (2.9%) described temporary intravaginal direction of their urinary stream.

See supplementary <u>Table S7.6</u> for further information.

### 7.3.2.3 Labial/vestibular graft augmentation urethroplasty for treatment of female urethral strictures

There were four papers detailing the outcomes of 31 patients having labial or vestibular graft urethroplasty (see supplementary <u>Table S7.7</u>); nineteen had ventral labial minora graft [131, 138, 494] and twelve had dorsal labial graft [135]. At a mean follow-up of fifteen to 24 months, patency rates of 75-100% were reported with ventral grafting whilst this was 100% with dorsal grafting at six to fifteen months follow-up (Table 7.1). One (5.2%) ventral graft patient developed a UTI post-surgery. There were no other complications (including UI).

### 7.3.2.4 Labial/vestibular flap urethroplasty for treatment of female urethral strictures

There were two papers detailing the outcomes of nineteen patients having labial/vestibular flap urethroplasty: two had a ventral labia minora flap [508] and seventeen had a dorsal vestibular flap [16]. At a follow-up of 24 months the two ventral flap patients (100%) remained stricture-free whilst fifteen (88%) dorsal flap patients remained stricture-free at a mean of twelve months follow-up (Table 7.1 and supplementary <u>Table S7.8</u>). There were no adverse short- or long-term effects reported in either group.

# 7.3.2.5 Buccal and lingual mucosal graft augmentation urethroplasty for treatment of female urethral strictures

There were twelve papers detailing the outcomes of 73 patients, all treated with BMG except in the series of Sharma *et al.*, who used lingual mucosa graft (LMG) in fifteen patients at the dorsal urethra [125]; 44 patients with dorsal onlay oral (buccal or lingual) mucosa graft (DOOMG) [125-127, 130, 133, 493, 499, 507, 509]; 27 with ventral onlay BMG (VOBMG) [126, 134, 510, 511] and two with circumferential BMG urethroplasty [126]. At a mean/median follow-up of six to 28 months, 62.5-100% of DOOMG urethroplasty patients were stricture-free whilst 50-100% of VOBMG patients were stricture-free at a mean of ten to 24 months follow-up. Both circumferential BMG patients were stricture-free at a mean of 21 months follow-up (Table 7.1). Seven (15.9%) DOOMG patients suffered a low-grade short-term adverse effect and no patients in any subgroup developed sustained new onset UI.

For further information see supplementary Tables S7.9, S7.10 and S7.11.

# 7.3.2.6 Anastomotic urethroplasty

Anastomotic urethroplasty has only been described in two cases in the literature – both in women with very short mid-urethral stricture and both of whom were stricture-free at four and 24-months follow-up respectively. None of them suffered from UI post-operatively [126, 496] (see supplementary <u>Table S7.12</u>).

# Table 7.1: Summary of available evidence on treatment of female urethral strictures

Treatment	No. of	N	Patency rate	UI (%)	Mean/Median	Refs
	studies		(%)		FU Months	
Urethral Dilatation	4	183	7.5-51	0	12-59	[127, 128, 491, 492]
Urethral Dilatation + ISD/	4	31	37.3-100	1.9	12-21	[13, 132, 135, 497]
planned repeat dilatation						
Dorsal Vaginal graft	4	37	73-100	0	22.4-27	[15, 495, 500, 507]
urethroplasty						
Ventral Vaginal flap	8	70	67-100	7	30-80.7	[124, 126, 127, 130,
urethroplasty						132, 136, 489, 490]
Ventral Labial/Vestibular	3	19	75-100	0	15-24	[131, 138, 494]
graft urethroplasty						
Dorsal Labial/Vestibular	1	12	100	0	6-15	[135]
graft urethroplasty						
Ventral Labial/Vestibular	1	2	100	0	24	[508]
flap urethroplasty						
Dorsal Labial/ Vestibular	1	15	88	0	12	[16]
flap urethroplasty						
Dorsal BMG urethroplasty	9	44	62.5-100	0	6-28	[125-127, 130, 133,
						493, 499, 507, 509]
Ventral BMG urethroplasty	4	27	50-100	0	10-24	[126, 134, 510, 511]

FU = follow-up; ISD = intermittent self-dilatation; N = number of patients; UI= urinary incontinence.

Summary of evidence	LE				
Female urethral stricture symptoms are long standing and non-specific, the most commonly reported are frequency, urgency, poor flow, incomplete emptying, and UI. It is important to exclude FUS in female patients with LUTS.					
Urethral dilatation alone to 30-41 Fr provides low stricture-free rates of mean 35% at mean follow-up 36.3 months.	3				
Urethral dilatation and ISC or planned repeat dilatation provides stricture-free rates of 75%.	3				
Urethroplasty provides stricture-free rates of 81-92%. No one particular type of urethroplasty is superior to another.	3				
Meatotomy/meatoplasty for short meatal strictures has a success rate of 95% at twelve months follow-up.	3				

Recommendations	Strength rating
Perform flow rate, post-void residual and voiding cystourethrogram or video-urodynamics in	Strong
all women with refractory lower urinary tract symptoms.	
Perform urethral dilatation to 30-41 Fr as initial treatment of female urethral stricture (FUS).	Weak
Perform repeat urethral dilatation and start planned weekly intermittent self-dilatation (ISD)	Weak
with a 16-18 Fr catheter for the 1 <sup>st</sup> recurrence of FUS.	
Perform urethroplasty in women with a 2 <sup>nd</sup> recurrence of FUS and who cannot perform ISD	Strong
or wish definitive treatment. The technique for urethroplasty should be determined by the	
surgeon's experience, availability and quality of graft/flap material and quality of the ventral	
vs. dorsal urethra.	
Treat meatal strictures by meatotomy/meatoplasty.	Weak

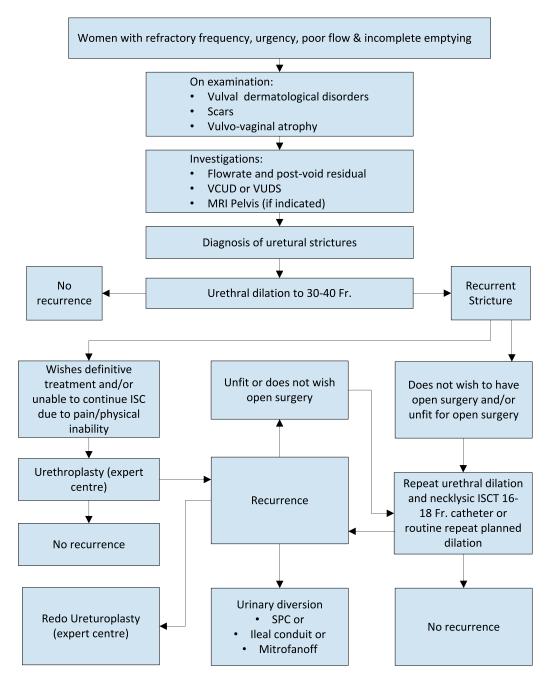


Figure 7.1: Women with refractory frequency, urgency, poor flow and incomplete emptying

ISC = intermittent self-catheterisation; MRI = magnetic resonance imaging; VUDS = video-urodynamics.

# 8. DISEASE MANAGEMENT IN TRANSGENDER PATIENTS

# 8.1 Treatment of strictures in trans men

In trans men, stricture treatment depends on the time after neophallic reconstruction, stricture location, stricture length and quality of local tissues [512].

# 8.1.1 Management of 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 six months [32, 145]. Endoscopic incision for short (< 3 cm)

urethral strictures has been performed, mainly at the anastomotic site, with a maximum stricture-free rate of only 16.7% when performed within six months after neophallic reconstruction [513]. Insertion of a suprapubic catheter is the first-line treatment in cases of obstructive symptoms severely affecting the patient's QoL, recurrent UTI or retention. The alternative is perineostomy, which is a specialist procedure and should be performed by a urologist familiar with transgender urethral anatomy. The perineostomy may be closed at the time of formal urethral reconstruction [145].

## 8.1.2 Treatment of meatal stenosis in trans men

Intermittent urethral dilatation is an option, as palliative treatment, for low-grade meatal stenosis with the interval of dilatation depending on the interval of stricture recurrence. Patients with high-grade meatal stenosis, those who refuse ISD, or those who want a durable solution should be offered simple meatotomy. Patency is 75% (mean follow-up 39 months) but the drawback is that the meatus will be in a hypospadiac position [145]. Alternatively, a staged urethroplasty can be offered [145].

# 8.1.3 Treatment of 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 (34% patency rate after median follow-up of 51 months) [513].

Single-stage graft urethroplasty is only possible if the graft can be supported and covered by the healthy surrounding fatty tissue of the neophallus. Experience is very limited and reported patency rate is 50% after a mean follow-up of 102 months [145].

The standard treatment for these strictures is staged urethroplasty with or without graft augmentation [145, 512] (BMG or full thickness SG) [32, 145]. A patency rate of 69.7% has been described with these techniques (mean follow-up: 25 months) [145].

For complex (e.g., fully obliterated) or recurrent strictures at the neophallic urethra, a 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 a part of the neoscrotum or by a gracilis flap have been successfully reported in a very limited number of patients [512].

## 8.1.4 Treatment of strictures at the anastomosis neophallic urethra-fixed part of the urethra

Short, non-obliterative, strictures can be treated by endoscopic incision. A first endoscopic incision has a 45.5% patency rate, but this dropped to 0% in case of three or more attempts (median follow-up of 51 months) [513]. 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 reporting a 57.9% patency rate after a mean follow-up of 44 months [145].

If endoscopic incision fails or if the stricture is nearly or completely obliterative, options are EPA or graft augmentation urethroplasty. In case of short (< 2-3 cm) strictures, EPA yields a 57.1% patency rate (mean follow-up of 35 months) [32, 145]. If EPA is not possible, usually for strictures longer than 2 cm, a ventral onlay BMG urethroplasty demonstrated a 50% patency rate (median follow-up of 9.5 months) [514]. In case of insufficient ventral tissue during graft urethroplasty, it is advised to support this graft by a local fasciocutaneous flap [515]. An alternative (especially after failure of the previous techniques) can be a staged approach, but no data are currently available [514].

# 8.1.5 Treatment of strictures at the fixed part of the urethra

This 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, single-stage dorsal inlay graft urethroplasty is possible for strictures at this site. Experience however is very limited [145, 512].

Staged repair with or without a dorsal graft is a reliable treatment for these rare strictures [145].

#### 8.1.6 **Definitive perineostomy in trans men**

The vast majority of trans men have a strong desire to void in a standing position [512]. Therefore, definitive perineostomy should only be offered to those with refractory strictures or to patients with strictures who do not wish to have complex reconstructive surgery [32, 145].

# 8.2 Peri-operative care after treatment of strictures in trans men

Anecdotally, after endoscopic incision and urethroplasty, the urethral catheter is maintained for two to three weeks [513, 514]. Peri-catheter urethrography is advised before catheter removal as it might be challenging to reinsert the urethral catheter in case of urinary extravasation [514].

# 8.3 Strictures in trans women

It is acceptable to start with dilation of a short and non-obliterative stricture in trans women although no longterm data about the effectiveness are available [33, 516]. If this is not possible or if it fails, a short (< 1 cm) meatal stricture can be treated by Y-V meatoplasty with an 85% stricture-free rate [517]. Somewhat longer (1-2 cm) meatal strictures can be treated by a neovaginal advancement flap (inverted U or "7-flap") with no recurrence observed after 37 months median follow-up [518].

Summary of evidence	LE
After neophallic reconstruction, local tissues go through the different stages of wound healing and	3
stable wound healing is usually achieved after six months.	
After two attempts, endoscopic incision is no longer successful in trans men.	3
Two-stage urethroplasty for strictures at the neophallic urethra has a stricture-free rate of 69.7%.	3
Y-V meatoplasty for short (< 1 cm) meatal stenosis in trans women has a stricture-free rate of 85%.	3

Recommendations	Strength rating
Do not perform endoscopic incision or urethroplasty within six months after neophalloplasty.	Strong
Do not perform more than two endoscopic incisions for strictures in trans men unless with	Strong
palliative intent.	
Perform staged urethroplasty for strictures at the neophallic urethra if open reconstruction is	Weak
indicated.	
Perform Y-V meatoplasty for short (< 1 cm) meatal stenosis in trans women if open	Weak
reconstruction is indicated.	

# 9. TISSUE TRANSFER

# 9.1 Comparison of grafts with flaps

One small RCT (LS excluded) comparing OMG with PSF found no significant difference in urethral patency rate [519]. Penile skin flaps had a higher urogenital morbidity (superficial penile skin necrosis, penile torsion, penile hypoesthesia, and post-void dribbling) and longer operation time compared to OMG. Furthermore, patient dissatisfaction was significantly higher with penile flaps [519]. Another small RCT (LS excluded) comparing penile skin necrosis in the group of the flaps whereas the urethral patency rate was similar between both groups [362]. Several retrospective series also found a comparable urethral patency rate between PSF and grafts [273, 275, 280, 520] (Table 9.1).

Study	Type of study	LS	Follow-up		Flap		Graft	
			(months)	Туре	Urethral	type	Urethral	
					patency		patency	
Barbagli	Retrospective	Excl.	55	LIF	12/18	OMG/PSG	36/45	0.32
<i>et al.</i> [273]					(67%)		(80%)	
Dubey	RCT	Excl.	22-24	LIF	22/26	BMG	24/27	0.70
<i>et al</i> . [519]					(84.6%)		(88.9%)	
Fu	Retrospective	Excl.	>12	All types	166/199	LMG	80/94	0.71
<i>et al.</i> [275]					(83.4%)		(85.1%)	
Hussein	RCT	Excl.	36	TIF	15/19	PSG	13/18	0.25
<i>et al.</i> [362]					(78.9%)		(72.2%)	
Lumen	Retrospective	NR	42-43	All types	23/29	OMG/PSG	63/75	0.57
<i>et al</i> . [280]					(79.3%)		(84%)	

# Table 9.1: Comparative studies of grafts vs. flaps used in urethroplasty for anterior urethral strictures

Sa	Retrospective	Excl.	28 (18-60)	TIF	28/34	BMG	67/82	0.851
et al. [520]					(82.3%)		(81.7%)	

BMG = buccal mucosa graft; Excl. = excluded; LIF = longitudinal island flap; LMG = lingual mucosa graft; LS = lichen sclerosus; mo = months; NR = not reported; OMG = oral mucosa graft; PSG = penile skin graft; TIF = transverse island flap; RCT = randomized controlled trial.

\* if not reported: recalculated by EAU Urethral Strictures Panel with chi2-statistics.

Due to their robust vascular pedicle, flaps can be used as a tube as well as a patch in a single-stage approach [451]. Castagnetti *et al.*, showed that grafts used as a tube have significantly higher complication rates as compared to onlay grafts (OR: 5.86; 95% CI: 1.5-23.4) [521]. A review by Patterson *et al.*, also reported high (circa 50%) complication and recurrence rates for tubularised grafts [522]. Iqbal *et al.*, have shown an encouraging 87% stricture-free rate in 23 patients who were offered single-stage circumferential skin flap urethroplasty [284]. Therefore, if there is a need to reconstruct a complete urethral segment with a tissue-transfer tube in a one-stage operation, flaps are usually the preferred option. As flaps carry their own vascular supply to the reconstruction site, they do not rely on the local vascularisation of the recipient site. Therefore, they need to be considered in case of poor urethral vascularisation (e.g., after irradiation or dense scarring after previous urethroplasty) [280, 523]. In addition, flaps survive well in the presence of active urinary infection [524].

Grafts and flaps should not be considered competitors in urethral surgery. A combination of a flap with a graft is possible for complex, multifocal or penobulbar strictures [280, 525, 526].

Summary of evidence	LE
Flaps have a higher urogenital morbidity, but a comparable patency rate compared to grafts.	1b
Grafts have a significantly higher complication rate compared to flaps when complete tubularisation in	1b
a single-stage approach is needed.	
Flaps do not rely on the local vascularisation of the recipient site.	3

Recommendations	Strength rating
Use a graft above a flap when both options are equally indicated.	Strong
Do not use grafts in a tubularised fashion in a single-stage approach.	Strong
Use flaps in case of poor vascularisation of the urethral bed.	Weak

# 9.2 Comparison of different types of flaps

Different local flaps have been described. Penile skin flaps are generally hairless, although the ventral penile skin can be hair-bearing around the raphe in some ethnic groups/phenotypes. They can be harvested as a transverse preputial skin flap [527], a transverse distal PSF [365, 524, 528, 529] or as a longitudinal island flap [530]. Urethral patency rates vary between 74.2-100% [275, 365, 524, 527-530]. Complications include skin necrosis (0-3.8%), fistula (0-7%), penile deformity (0-7%), post-void dribbling (0-79%) and sacculation (0-16.5%) (see supplementary Table S9.1). As there are no direct comparative series available about these flaps it is not possible to determine which performs better.

Hair-bearing perineal and scrotal flaps have been described as well. Fu *et al.*, demonstrated that PSF had a significantly better urethral patency rate compared to scrotal and perineal skin flaps (respectively 87.7%, 69% and 66.7%) [275]. The hair-bearing perineal and scrotal skin flaps are associated with hairball formation and chronic infection which may cause failure of the repair. A study of Blandy with long-term follow-up, reports 3% revision for calculi and 3% revision for diverticula [531].

An alternative is to epilate the needed scrotal skin prior to tissue transfer [532, 533] or to patch an OMG to the underlying dartos tissue of the scrotum after incision of the scrotal skin and use this patch as a flap in a second attempt [451].

Summary of evidence	LE
Hair-bearing flaps have a lower urethral patency rate compared to non-hair-bearing flaps.	3
Train-bearing haps have a lower diethral patency rate compared to non-hair-bearing haps.	0

Recommendation	Strength rating
Do not use hair-bearing perineal or scrotal flaps unless no other option is feasible.	Strong

## 9.3 Comparison of different types of grafts

Buccal mucosa is at present the most commonly used graft. Urethral patency rates of buccal mucosa vary between 75.6% and 91.7% with 16-75 months of follow-up (see supplementary <u>Table S9.2</u>) [534-540].

Penile skin is another popular graft, especially in uncircumcised men where the foreskin is an abundant source of graft material.

In case of LS, Trivedi *et al.*, demonstrated a significantly higher urethral patency rate when using non-genital mucosal grafts for reconstruction (82.6%) compared to genital skin grafts (4%) [541]; therefore, the use of genital skin in LS cases is not indicated.

There is no RCT comparing buccal mucosa with penile skin. A secondary analysis of a meta-analysis comparing dorsal with ventral onlay graft urethroplasty found a superior urethral patency rate for buccal mucosa compared to penile skin (88.1% vs. 79%; p < 0.001). In this secondary analysis, no data were available about the stricture aetiology, stricture length, follow-up duration or other potential confounders between both groups [542]. A pooled analysis of non-RCTs comparing buccal mucosa (n=483) with penile skin (n=428) found a better urethral patency rate for buccal mucosa (respectively 85.9% vs. 81.8%). However, the results might be biased because of the longer follow-up time and longer stricture length in the penile skin group [543]. Lengthy skin grafts (up to 20 cm) can be taken from the foreskin in a spiroid fashion which is clearly more difficult with OMG.

The main disadvantage of BMG harvesting is the oral morbidity and because of this morbidity, lingual mucosa has been proposed as alternative. A SR and meta-analysis of comparative studies comparing LMG with BMG (four prospective, two retrospective studies) showed no significant differences in urethral patency rate and overall long-term complication rate [544-546]. These studies revealed that LMG was associated with more difficulties in eating/drinking, speaking, tongue protrusion and dysgeusia [544, 545]. In 13.8-20%, speaking problems remained after six months [544, 545]. A retrospective study of Xu et al., reported difficulties in tongue movements, numbress over the donor site and speaking difficulties in 6.2%, 4.9% and 2.5% of patients, respectively after twelve months [303]. On the other hand, BMG harvesting provoked more oral tightness which was present in up to 24% of patients after six months [544, 545]. Chauhan et al., showed that immediate and early donor site complications were more common in the BMG group, except for bleeding being more common in the LMG group. Numbness (61%), difficulty in chewing (54%), swelling (48%) and articulation (40%) were the most common problems during the first week. Late donor site complications were rare [547]. Pal et al., describes more short-term complications (difficulty in tongue movement and slurring of speech) in the LMG group, compared to the BMG group. Long-term complications (after three months) at the donor site (persistent pain, perioral numbress, tightness of mouth, salivary disturbance, scarring of the cheeks) were only seen in the BMG group [548]. For long strictures, buccal mucosa can be combined with lingual mucosa [303].

The use of lower lip mucosa was described, especially when smaller grafts are needed, and has similar qualities to lingual mucosa. However, a narrative review based on the experience from retrospective series showed that these grafts have a higher post-operative donor site morbidity and can lead to permanent sequelae (persistent discomfort, neurosensory deficits, salivary flow changes and important aesthetic changes) at the donor site, which have not been described with lingual mucosa [549].

Beyond the oral mucosa and penile skin graft, a multitude of other autologous grafts have been described. These include: postauricular skin [526, 550], abdominal skin [367], split-thickness mesh graft from the thigh [351], inguinal skin [302] and colonic mucosa [551] (Table 9.2). Manoj *et al.*, only used the postauricular skin when both genital skin and oral mucosa were not usable [550]. Marchal *et al.*, used postauricular skin in addition to oral mucosa to reconstruct lengthy strictures [526]. Meeks *et al.*, reported the use of abdominal skin graft mainly in patients with lengthy strictures where OMG harvesting would be insufficient, in case of prior OMG urethroplasty or if OMG was refused by the patient [367]. Pfalzgraf *et al.*, reported a comparable urethral patency rate for split-thickness mesh graft and BMG (respectively 84 and 83%), but more penile deviation (9% vs. 0%) and lower satisfaction (83.3% vs. 96.7%) with split-thickness mesh graft [351]. Xu *et al.*, used colonic mucosa for lengthy (> 10 cm) strictures. Urethral patency rate was 85.7% but graft harvest requires an abdominal procedure, and 1/35 (2.9%) patient developed a colonic-abdominal fistula [551]. Due to the limited experience with grafts other than oral mucosa and penile skin, they should only be considered if oral mucosa and penile skin are not available, indicated, or desired.

## Table 9.2: Outcome of case series of other autologous grafts

Study	Type of graft	pe of graft N Follow-up Stricture		Stricture	Urethral	
			(months)	length (cm)	patency (%)	
Bastian et al. 2012 [302]	Inguinal skin	34	70 (3-86)	8 (1.5-14)	91	
Manoj et al. 2009 [550]	Postauricular skin	35	22 (3-48)	8.9 (3-15)	89	
Meeks et al. 2010 [367]	Abdominal wall skin	21	28 (11-52)	11 (4-24)	81	
Pfalzgraf et al. 2010 [351]	Split thickness skin graft	57/68	32	NR	84	
Xu et al. 2009 [551]	Colonic mucosa	35	53.6 (26-94)	15.1 (10-20)	85.7	

N = number of patients; NR = not reported.

Summary of evidence	LE
Patency rates of buccal mucosa and lingual mucosa are comparable.	1a
Different types of oral grafts have distinct types of oral morbidity and some of the oral complications might last in the long-term.	1a
Patency rates with penile skin grafts are 79-81.8% vs. 85.9-88.1% with buccal mucosa.	3
In LS related strictures, the use of genital skin graft is associated with poor patency rates (4%).	3

Recommendations	Strength rating
Use buccal or lingual mucosa if a graft is needed and these grafts are available.	Weak
Inform the patient about the potential complications of the different types of oral grafting	Strong
(buccal vs. lingual vs. lower lip) when an oral graft is proposed.	
Use penile skin if buccal/lingual mucosa is not available, suitable, or accepted by the	Weak
patient for reconstruction.	
Do not use genital skin graft in case of lichen sclerosus.	Strong

# 9.4 Tissue engineered grafts

# 9.4.1 Cell-free tissue engineered grafts

These grafts are derived from cadaveric or animal sources (e.g., porcine small intestine submucosa [SIS], acellular bladder matrix, acellular dermal matrix), are completely cell-free and serve as a scaffold for host cell ingrowth [552]. The main advantage suggested for their use is the off-shelf availability [552].

A small RCT (n=30) comparing acellular bladder matrix with BMG reported a urethral patency rate of respectively 66.6% and 100%. The poorer results of acellular bladder matrix were the most apparent in cases of an unhealthy urethral bed [553]. Palminteri *et al.*, reported a global urethral patency rate with SIS graft in 19/25 (76%) cases [554]. In this series SIS graft urethroplasty failed in all cases with a stricture length > 4 cm [554]. On the other hand, Xu *et al.*, reported adequate urethral patency in 26/28 patients (92.8%) after a median follow-up of 25 months. Of note, only one patient in this series underwent previous urethroplasty suggesting only minor spongiofibrosis in the remaining patients [555]. Other series have included only a limited number of patients with short follow-up. In these series, urethral patency rates vary between 20-100% [552].

#### Summary of evidence

Patency rate of cell-free tissue engineered grafts decreases with large stricture length and unhealthy urethral bed.

Recommendation	Strength rating
Do not use cell-free tissue engineered grafts in case of extensive spongiofibrosis, after	Weak
failed previous urethroplasty or stricture length > 4 cm.	

# 9.4.2 Autologous tissue engineered oral mucosa grafts

These grafts contain a matrix seeded with autologous oral mucosa cells. Production requires a small oral mucosa biopsy (@ 0.5 cm<sup>2</sup>) and the graft is further manufactured in the lab. The main advantage suggested is the reduction of oral donor site morbidity whereas the main disadvantages are costs and the strict time frame between manufacturing and implantation of the graft [552].

LE

The clinical use of autologous tissue-engineered OMG was evaluated in a prospective, multicentre study including 99 patients [556]. Estimated twelve- and 24-months urethral patency rate was 67.3 and 58.2%, respectively. Oral adverse events were minimal. No comparative studies with acellular grafts or native OMGs are available nor are there any data about the cost-effectiveness [552].

Summary of evidence	LE
Safety, patency rate and cost-effectiveness of autologous tissue-engineered grafts is currently under	3
research.	

#### Recommendation

Do not use autologous tissue-engineered oral mucosa grafts outside the frame of a clinical trial. Strong

# 9.5 Management of oral cavity after buccal mucosa harvesting

The post-operative morbidity of closure vs. non-closure of the buccal mucosa harvesting site has been evaluated by a number of prospective RCTs.

The results are summarised in Table 9.3. Based on these findings, no clear recommendation can be provided as to whether or not to close the harvesting site and the decision can be left to the treating physician.

Oral rinsing with chamomile [557] or chlorhexidine [545, 558] solution has been suggested in the first postoperative days without any evidence that this reduces pain or other oral complications.

Table 9.3: Effect of non-closure compared to closure on oral morbidit	y after buccal mucosa harvesting
-----------------------------------------------------------------------	----------------------------------

Study	Early oral pain	Eating/ drinking problems	Altered taste	Altered salivation	Oral tightness	Perioral numbness	Oral bleeding	Slurred speech
Soave et al. [557]	=	=	=	=	=	=	=	=
Rourke et al. [559]	=	↓ I	NR	NR	↓	V	=	NR
Muruganandam et al. [560]	V	=	NR	=	=	=	=	NR
Wong et al. [558]	=	1	NR	NR	=	=	=	NR
Lumen et al. [545]	1	NR	NR	NR	NR	NR	NR	NR

 $\downarrow$  = less morbidity with non-closure;  $\uparrow$  = more morbidity with non-closure; = = no significant difference; NR = not reported.

# 10. PERI-OPERATIVE CARE OF URETHRAL SURGERY

#### 10.1 Urethral rest

After any form of urethral manipulation (urethral catheter, ISD, dilatation, DVIU), a period of urethral rest is necessary in order to allow tissue recovery and stricture "maturation" before considering urethroplasty. This improves the ability to identify the true extent of the fibrotic segments during subsequent surgery. If the patient develops incapacitating obstructive symptoms or urinary retention, a suprapubic catheter should be inserted. Terlecki *et al.*, propose diagnostic evaluation after two months and urethroplasty after three months of urethral rest. These timings are based on the general principles of wound healing [561]. In their study, it has been shown that these periods allow for reliable stricture evaluation during urethrography which is, in turn, important to ensure selection of the most appropriate urethroplasty technique [561]. Utilising this strategy, similar outcomes were obtained compared to patients with stable previously unmanipulated strictures [561]. However, the optimal duration of urethral rest for all patients is not known and the degree of associated infection and inflammation should be taken into account as well, with longer periods of rest in those with greater degrees of infection and inflammation.

Strength rating

Summary of evidence	LE
After any form of urethral manipulation, a minimum period of three months urethral rest is necessary to	3
allow for tissue healing before performing urethroplasty.	

Recommendation	Strength rating
Do not perform urethroplasty within three months of any form of urethral manipulation.	Weak

# 10.2 Antibiotics

Post-operative wound infection and UTI are common post-operative complications and infection at the site of reconstruction may contribute to failure of urethroplasty. The vast majority of reconstructive urologists perform urine culture one to two weeks prior to surgery [562]. Urine culture is superior to urine-analysis which can be omitted in the pre-operative evaluation [562]. If infection or colonisation is present, a therapeutic course with antibiotics is recommended pre-operatively. In case of an indwelling catheter general principles would suggest at least an attempt to suppress the colonisation with pre-operative antibiotics [562]. These practices are in accordance with the strong recommendations of the EAU Guidelines on Urological Infections:

- "Screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa."
- "Treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions."

An intra-operative prophylactic regimen with antibiotics (according to local antibiotic resistance profiles) is effective in reducing the rate of post-operative surgical site and UTIs [562]. Although most urologists continue with post-operative antibiotics upon and even beyond catheter removal, there is no evidence that such a prolonged administration would reduce the infective complication rate [562]. The EAU Guidelines on Urological Infections do not routinely recommend the use of antibiotic prophylaxis to prevent clinical UTI after urethral catheter removal. There is no evidence that this recommendation would not apply to catheter removal after urethral surgery.

Summary of evidence	LE
An intra-operative prophylactic regimen with antibiotics is effective in reducing the rate of	4
postoperative surgical site and urinary tract infections.	

Recommendation	Strength rating
Administer an intra-operative prophylactic regimen with antibiotics at time of urethral	Strong
surgery.	

# 10.3 Catheter management

After uncomplicated DVIU, there is no advantage in maintaining the catheter for a prolonged period and it should be removed within 72 hours [563].

After one-stage urethroplasty and closure of the urethral plate after staged urethroplasty, urinary extravasation at the site of reconstruction must be avoided [564]. For this purpose, urinary diversion by either transurethral catheter or suprapubic catheter with urethral stent can be used. With respect to the type of catheter material, a prospective randomised (but underpowered) trial comparing silicone vs. hydrogel coated latex transurethral catheters showed no significant difference in the time to stricture recurrence nor in the overall recurrence rate [564]. The size of the urethral catheter utilised usually varies between 14 Fr and 20 Fr [565, 566]. Systematic use of anticholinergic drugs has not shown a significant reduction in the rate of involuntary pericatheter voiding whilst catheterised [567].

After urethroplasty an indwelling catheter is commonly left *in situ* for two to three weeks [566, 568]. After three weeks of urethral catheterisation, an extravasation rate of 2.2-11.5% at urethrography has been reported after different types of urethroplasty [568-571]. However, success with early catheter removal under three weeks has also been reported. A study after EPA for non-complicated anterior strictures demonstrated no significant difference in extravasation (6.8% vs. 4.5%) and recurrence rates (4.9% vs. 5.2%) between catheter removal at one or two weeks respectively [572]. Poelaert *et al.*, reported an extravasation rate of 3.5% vs. 8.3%, when the catheter was removed  $\leq$  10 days or > 10 days respectively after all types of urethroplasty (n=219) (p=0.158) [565]. Importantly, patients who had a duration of catheterisation of > 10 days had longer and more complex strictures [565].

Prior to catheter removal after urethroplasty, it is important to assess for urinary extravasation to avoid ensuing complications including peri-urethral inflammation, abscess formation and fistulation [568, 570]. Importantly, some authors have identified urinary extravasation as a predictive factor for stricture recurrence [565, 573]. Other series, however, could not confirm the prognostic significance of urinary extravasation but they included any form of extravasation (including minor leaks) [570, 571]. Grossgold *et al.*, found that high-grade leaks (defined as length  $\geq$  1.03 cm and width  $\geq$  0.32 cm) were significantly associated with higher restricture rates. This study also found length of extravasation > 1.03 cm alone to be an independent predictor of restricture [573]. In cases of persistent and significant urinary extravasation, the catheter should be maintained or reinserted and the examination repeated after one week [568]. However, low-grade ("wisp-like") extravasation does not appear to affect long-term restricture rate and the catheter can be removed in these cases without subsequent urethrogram [570, 573]. In case of any doubt about the significance of extravasation, it is safe to keep the catheter in for an additional week and ReDo the assessment.

The assessment of urinary extravasation is achieved by either pericatheter retrograde urethrography (pcRUG), classic RUG or VCUG [568]. Voiding cystourethrography (after catheter removal) is the most physiologic examination as it shows the urethra under normal intra-urethral pressures and using this test residual urethral narrowing is most accurately identified. This has been found to be a strong prognostic factor for failure in a series evaluating bulbar FGU [571]. In contrast, pcRUG is associated with supraphysiological intra-urethral pressures and a potentially higher chance of false positive results [568, 573]. Although there is no evidence that one imaging modality is superior to the other, pcRUG should be performed if there is a high-risk of leakage as it avoids the need for catheter reinsertion through a recently reconstructed urethra in case of a positive exam. High risk of leakage depends on the complexity of urethroplasty (e.g., stricture length > 10 cm, panurethral repair) [570, 573]. External clinical signs of impaired wound healing (e.g., abscess formation, wound dehiscence) are also associated with a high risk (71.4%) of leakage [565]. In cases of attempted VCUG where the patient is not able to void during fluoroscopy after catheter removal, RUG should be performed [573].

Although limited evidence for urethroplasty care in trans men exists, one study advised a three-week period of transurethral catheterisation with pcRUG upon catheter removal [514].

After perineostomy or the 1<sup>st</sup> stage of staged urethroplasty, the catheter can be removed without need for urethrography after three to five days [349, 570].

Summary of evidence	LE
Prior to catheter removal after urethroplasty, it is important to assess for urinary extravasation with urethrography to avoid ensuing complications including peri-urethral inflammation, abscess formation and fistulation.	2b
After uncomplicated DVIU, there is no advantage in maintaining the catheter for a prolonged period.	3
Early catheter removal may be appropriate for a subset of patients with short, uncomplicated, strictures.	3

Recommendations	Strength rating
Perform a form of validated urethrography after urethroplasty to assess for urinary	Strong
extravasation prior to catheter removal.	
Remove the catheter within 72 hours after uncomplicated direct vision internal urethrotomy	Weak
or urethral dilatation.	
Consider 1 <sup>st</sup> urethrography seven to ten days after uncomplicated urethroplasty to assess	Weak
whether catheter removal is possible, especially in patients with bother from their urethral	
catheter.	

# 11. FOLLOW-UP

# 11.1 Rationale for follow-up after urethral surgery

The rationale for following-up patients after urethral stricture surgery is to detect and manage any complication or recurrence. As with any surgical procedure, following urethroplasty some patients will present with complications at short to medium follow-up: approximately 38% with bulbar urethroplasties [322] and up to 54% for all anterior urethroplasties [574]. Most of these complications (92%) would be classified as Clavien

grade 1 or 2 [322]. Even though urethroplasty techniques provide the highest chances for successful treatment of urethral strictures, some patients will experience recurrence [326]. For further details on particular outcomes in each urethral segment, please review the individual chapters of this Guideline.

Summary of evidence	LE
After urethroplasty surgery, recurrent strictures appear with different frequency depending on stricture	3
features and urethroplasty techniques.	

Recommendation	Strength rating
Offer follow-up to all patients after urethroplasty surgery.	Strong

# 11.2 Definition of success after urethroplasty surgery

The "traditional academic" definition of post-operative success after urethroplasty has been considered as "The lack of any post-operative intervention for restricture" [575]. This definition, despite being widely used [307, 322] is problematic as it ignores asymptomatic or even symptomatic recurrences in patients not willing to undergo further surgeries [575]. There is some variation as to what is considered intervention with some groups accepting endoscopic treatments as success, while considering failure only as the requirement for a ReDo urethroplasty [308].

A more objective definition of success is the "anatomic success", defined as "Normal urethral lumen during RUG or cystoscopy, regardless of patient symptoms". Using this definition, stricture recurrence or anatomical failure is considered by some groups as urethral narrowing found to be endoscopically impassable – without force – with a 16 Fr flexible endoscope [143, 576]. This definition is certainly stricter, with up to 35% of cystoscopic recurrences after bulbar urethroplasty remaining asymptomatic, and thus would have been considered as successful if a "lack of further intervention" definition was used [143]. Other groups consider cystoscopic recurrence as any stricture that is visible on post-operative cystoscopy, even the so-called "large calibre re-strictures" (> 17 Fr) [141]. Not all anatomic recurrent strictures would need further treatment [575]. It was suggested to intervene when the anatomic recurrence is associated with recurrence of symptoms, stricture-related high post-void residuals or a stricture calibre of < 14 Fr – even if these are asymptomatic [575].

Over the last ten years, the evaluation of urethral surgery outcomes has shifted towards a "patient-reported definition of success". The aim of any urethral intervention is to allow patients to return to a normal state of voiding while maintaining QoL [577] or to minimise symptoms, reduce disability, and improve HRQoL by restoring normal urinary function [578]. Even if the surgeon reconstructed a wide and patent urethra, if patients experience pain, sexual dysfunction or perceive their urinary function as not improved, they will not rate their outcome as successful [575]. On a multivariate analysis including both patient-reported and clinical parameters, urine flowmetry parameters failed to demonstrate significant contribution to satisfaction [579]. Kessler et al., reported that only 78.3% of patients with clinical success described themselves as (very) satisfied. More dissatisfaction significantly appeared with penile curvature, penile shortening, worsening of erectile function and impairment of sexual life [580]. Conversely, 80% of patients defined as clinical failures considered themselves as (very) satisfied with their outcomes [580]. Regardless of anatomic success after urethroplasty, post-operative pain, sexual dysfunction and persistent LUTS were independent predictors of patient dissatisfaction [579]. Improvement in voiding function (i.e., statistical improvement on IPSS) alone does not predict patient satisfaction after urethroplasty [581]. On a multivariate analysis including both patientreported and clinical parameters, after adjusting for disease recurrence and age, persistence in voiding symptoms (weak stream), genitourinary pain, and post-operative sexual function alterations were the greatest independent drivers of post-operative dissatisfaction [579]. In addition, penile shortening (OR: 2.26; 95% CI: 1.39-3.69) and chordee (OR: 2.26; 95% CI: 1.44-4.19) were independent predictors of patient dissatisfaction after urethroplasty [581] (Table 11.1).

# Table 11.1: Predictors of patient dissatisfaction after urethral surgery

Predictor/Symptoms	Measure of effect	Authors
Weak/very weak urinary stream	< 0.001	Kessler TM et al.
Penile curvature	0.001	J Urol 2002 [580]
Penile shortening	0.001	
Worsening of erectile function	0.001	
Impairment of sexual life	< 0.001	
Sexual activity alteration	OR: 4.36 (1.54 – 12.37)*	Bertrand LA et al.
Erection confidence (SHIM)	OR: 1.53 (1.12 – 2.07)*	J Urol 2016 [579]
Inability to ejaculate (MSHQ)	OR: 1.52 (1.15 – 2.01)*	
Urethral pain	OR: 1.71 (1.05 - 2.77)*	
Bladder pain	OR: 2.74 (1.12 – 6.69)*	
Urinary strain (CLSS)	OR: 3.23 (1.74 – 6.01)*	
Hesitancy (IPSS)	OR: 2.01 (1.29 – 3.13)*	
Voiding quality of life (IPSS)	OR: 1.96 (1.42 – 2.72)*	
Penile shortening	OR: 2.26 (1.39-3.69)**	Maciejewski CC et al.
Chordee	OR: 2.26 (1.44 – 4.19)**	Urology 2017 [581]

\* *p* < 0.05; \*\* *p* < 0.001.

SHIM = Sexual Heath Inventory for Men; MSHQ = Male Sexual Health Questionnaire;

CLSS = Core Lower Urinary Tract Symptom Score; IPSS = International Prostate Symptoms Score.

Due to this evident discrepancy between surgeon's assessment and patient assessment, PROMs have been developed for the follow-up after urethroplasty [158, 578].

A complete approach for urethral surgery outcomes would combine both anatomic, endoscopic, and patientreported success [324, 575]. The Panel suggest using a functional definition of success in clinical practice, namely "lack of symptoms and/or need for further interventions".

Collecting standardised documentation of the patient's subjective assessment of their symptoms and objective anatomic outcomes would be limited for academic purposes, in order to allow comparison of surgical outcomes among reconstructive urologic surgeons and centres. Those objective and subjective outcomes measures should therefore be assessed and reported (simultaneously but separately) when evaluating urethroplasty results [575].

# 11.3 Follow-up tools after urethral surgery

# 11.3.1 Diagnostic tools for follow-up after urethral surgery

# 11.3.1.1 Calibration during follow-up after urethral surgery

The difference between calibration and urethral dilatation is usually subjective as soft strictures may be dilated during calibration [582]; therefore, urethral calibration should be used with caution for follow-up after urethroplasty. Dedicated calibration bougies should be used and not dilatators.

# 11.3.1.2 Urethrocystoscopy during follow-up after urethral surgery

Urethrocystoscopy has been considered the most useful tool to confirm the presence or absence of a recurrent stricture [141, 583], as up to 35% of patients with re-strictures remain asymptomatic [143]. Also, the cystoscope could be a measure to calibrate the strictured lumen, bearing in mind the most commonly used endoscopes: 15.7 Fr (5 mm diameter) or 17.3 Fr (5.5 mm diameter) [583]. Urethrocystoscopy allows differentiation of recurrences as diaphragm/cross-bridging – responding to simple intervention, or significant urethral restrictures – requiring repeated interventions or ReDo surgeries [584]. Endoscopic assessment at three months after anterior urethroplasty can predict the risk for further re-intervention at one year. Compared to normal endoscopy, large calibre (> 17 Fr) restrictures have a HR of 3.1 (1.35-7.29) for repeat intervention while small calibre (< 17 Fr) restrictures have a 23.7 HR (12.44-45.15) adjusted for age, stricture length, location, and aetiology [141]. The main problem with using urethrocystoscopy for routine follow-up is the low compliance of patients as only 54% of patients underwent endoscopy at one year after urethroplasty, even when it was a part of a study protocol [143].

11.3.1.3 Retrograde urethrogram and voiding cystourethrogram during follow-up after urethral surgery Retrograde urethrogram combined with VCUG are commonly used to confirm suspected recurrence [585, 586] or as part of a routine protocol to assess post-operative urethral patency [587, 588]. 11.3.1.4 Urethral ultrasound – Sonourethrography during follow-up after urethral surgery

The use of SUG as a follow-up tool is not very common. It would be a reliable tool for diagnostic recurrent strictures [585].

#### 11.3.2 Screening tools for follow-up after urethral surgery

These tools are used to assess whether there is suspicion of stricture recurrence and need for subsequent diagnostic evaluation (see section 5. Diagnostic evaluation).

#### 11.3.2.1 Flow-rate analysis during follow-up after urethral surgery

Evaluating the  $Q_{max}$  is the commonest follow-up tool. Different cut-off points from  $Q_{max}$  15 ml/s or 12 ml/s were suggested to consider the intervention as a failure or to trigger a confirmatory test for recurrence [587]. There is no clear threshold, and 19% of patients with  $Q_{max} < 14$  ml/s would still have a patent urethra, allowing passage of 15 Fr cystoscope [144].

Flow rates may be affected by operator error, BPO/LUTS, bladder dysfunction, and variations in bladder capacity. Further limitations of uroflowmetry include the need for a minimum voided volume of 125-150 ml to reach a voided flow rate that reliably predicts an abnormality [582]. Even in controlled settings, the percentage of patients with adequate pre- and post-operative uroflowmetry analysis is only 31% [588]. Comparing both pre- and post-operative  $Q_{max}$  levels was suggested, and a difference in  $Q_{max}$  of 10 ml/s or less is found to be a reliable screen tool for recurrence (sensitivity 92%, specificity 78%). This measure also has strong reproducibility (R=0.52) [588]. Unfortunately, this improvement after urethroplasty is significantly different between age groups, with less than 10 ml/s average change in those over 65 years old, probably affected by BPO and/or bladder dysfunction [589]. Another parameter to consider is the shape of the voiding curve, recording it as flat (obstructed) or bell-shaped [590]. An obstructive voiding curve demonstrated 93% sensitivity to predict recurrent strictures, while a combination of urinary symptoms and obstructive voiding curve achieved 99% sensitivity and 99% NPV [590].

#### 11.3.2.2 Post-void residual ultrasound measure during follow-up after urethral surgery

Post-void residual US measure is significantly increased in patients with recurrent strictures compared with those without recurrences [585]. Unfortunately, PVR measurement is affected by abdominal ascites, bladder diverticula and/or poor bladder function [582], with some studies reporting inconsistent correlation with obstruction in the presence of BPO. Also, US measures of PVR are user dependent, showing high interobserver variability. Combined with other tests – uroflowmetry, IPSS, and SUG – PVR achieves adequate predictive values [585], but currently there is no literature to support its solo use, to assess urethral stricture recurrence [591].

#### 11.3.2.3 Symptom questionnaires during follow-up after urethral surgery

The IPSS questionnaire, despite being designed for BPO, showed significant improvement after successful urethroplasty and inverse significant correlation with  $Q_{max}$  [581, 582]. The mean improvement of IPSS is around -11 points (range -19 to -5) [589].

Author	Ν	Mean pre-	Mean post-	Change	Significancy
		operative value	operative value		
Morey AF et al.	50	26.9	4.4	NR	p < 0.0001
1998 [592]					
DeLong J et al.	110	NR	NR	-11 (IQR -195)	p < 0.001
2013 [589]					
Maciejewski CC et al.	94	18.7 (+/- 9)	5.8 (+/- 5)	NR	p < 0.0001
2017 [581]					

#### Table 11.2: Post-urethroplasty changes in IPSS values

N = number of patients; NR = not reported; IPSS = International Prostate Symptoms Score; IQR = interquartile range.

Combination of IPSS and  $Q_{max}$  analysis was suggested to diagnose recurrences. Using an IPSS cut-off point of 10 points associated with  $Q_{max} > 15$  ml/s would prevent further invasive studies in 34% of patients, while only 4.3% of strictures < 14 Fr would have been missed. Using an IPSS cut-off point of 15 points associated with  $Q_{max} > 15$  ml/s would prevent further invasive studies in 37% of cases, while 6% of strictures < 14 Fr would have been missed [593].

The Visual Prostate Symptom Score (VPSS) was also used to diagnose recurrent urethral strictures, offering a significantly shorter time to completion compared with IPSS, especially in cases of illiteracy or limited education. Visual Prostate Symptom Score showed a good correlation with IPSS,  $Q_{max}$  and urethral diameter. A combination of VPSS > 8 with  $Q_{max} < 15$  ml/s had a NPV of 89% and a PPV of 87% for recurrent urethral strictures [594].

Post-micturition dribble, assessed by the specific question of the USS-PROM questionnaire, was present in 73% of patients pre-operatively and 40% after anterior urethroplasty, while only 6.3% was *de novo*. Incidence was not predicted by stricture location nor urethroplasty type [148].

# 11.3.3 Quality of life assessment, including disease specific questionnaires during follow-up after urethral surgery

Urethral stricture affects QoL evaluated by EQ-5D-3L questionnaire. Pre-operative anxiety and depression was found in 29% of patients. *De novo* AD after urethroplasty is uncommon (10%) and has two predictors: decreased sexual function and poor reported image of overall health [595]. A more recommended approach is the assessment of the condition-related QoL [596]. The USS-PROM proved useful to assess outcomes in anterior urethroplasty patients [578]. Its use also received criticism, as some of the individual generic QoL questions do not improve after successful urethroplasty, as they are not condition-specific [597]. Currently, there is another version of PROM, being developed and validated by a North American collaborative group, including questions related to the sexual consequences of urethral stricture disease [159]. PROM questionnaires should be implemented in each visit to check for functional success, as they are able to show improvement over time.

The Core Lower Urinary Tract Symptom Score (CLSS) questionnaire was used to assess pre- and posturethroplasty pain in the bladder, penis/urethra, and perineum/scrotum. Most of the parameters improved after urethroplasty, but up to 29% of patients reported worsening of perineal pain after surgery [598].

Sexual function should be evaluated by validated tools if not assessed in a PROM. The international index on erectile function (IIEF), SHIM, O'Leary Brief Male Sexual Function Inventory (BMFSI), SLQQ (Sexual Life Quality Questionnaire), Male Sexual Health Questionnaire (MSHQ) have all been used after urethroplasties for evaluation of erectile and ejaculatory functions. Other non-validated tools were suggested such as the Post-Urethroplasty Sexual Questionnaire (PUSQ) [599] or specific questionnaires for genital appearance (length, curvature) or sensitivity [600].

Summary of evidence	LE
Retrograde urethrography and urethrocystoscopy are able to identify anatomical success after a urethroplasty.	2a
	0-
A significant gap was demonstrated between objective and subjective outcomes after urethroplasties.	2a
PROM questionnaires are specific tools to assess subjective outcomes and patient satisfaction after	
urethroplasty surgeries.	-
Validated questionnaires proved useful to assess the consequences of urethral surgery on sexual	2a
function.	

Recommendations	Strength rating
Use cystoscopy or retrograde urethrography to assess anatomic success after urethroplasty	Weak
surgery.	
Use patient reported outcome measure questionnaires to assess subjective outcomes and	Strong
patient satisfaction.	
Use validated questionnaires to evaluate sexual function after urethral stricture surgeries.	Strong

#### 11.4 Ideal follow-up interval after urethral surgery

The optimal follow-up strategy must allow for an objective determination of anatomic and functional outcomes to assess surgical success whilst avoiding excessive invasive testing that leads to unnecessary cost, discomfort, anxiety, and risk [575].

After anterior urethroplasty, 21% of recurrences are clinically evident, and cystoscopically confirmed, after three months [601] and 96% after one year [584]. Early recurrences are more frequent in patients with LS and older age, in longer strictures and when skin grafts were used [601].

#### 11.5 Length of follow-up after urethral surgery

The median time of recurrence after bulbar urethroplasty is approximately ten months [328]. In case series, between 55.4% [601] and 96% [584, 587] of all recurrences are detected during the first year of follow-up after urethral surgery. Twenty-three percent of bulbar stricture recurrences are detected during the second year of follow-up, and the percentage of recurrences decreases after the second year [326].

On the other hand, long-term follow-up studies highlighted the role of length of follow-up as a predictor for stricture recurrence after bulbar urethroplasty [326, 603]. Late recurrences – later than five years after urethroplasty – could be observed in up to 15% of cases [144, 326]. This should be considered mainly after augmentation urethroplasties, especially in case skin grafts were used [586]. Certainly, patients should be instructed to seek urological evaluation if they experience late recurrent symptoms [603].

#### 11.6 Risk-stratified proposals during follow-up after urethral surgery

Cost of follow-up after urethroplasty is higher in the first year after the procedure [602]. In a literature review it ranged between 205 to 1,784 US Dollars, with higher costs associated to posterior urethral repairs [602]. As the risk of recurrence and side effects are related to the type of stricture and urethroplasty, a different follow-up schedule was proposed and shown to be cost-effective in the USA, potentially saving up to 85% of costs after five years [576]:

- Urethroplasties with a low risk of recurrence (EPA urethroplasty without history of radiotherapy, hypospadias, or LS features) could be safely followed up based on monitoring of symptoms, using self-administered IPSS questionnaire, every three months for one year, and annually thereafter.
- Urethroplasties with standard risk of recurrence (urethroplasty using grafts, flaps, and/or post-irradiation, hypospadias and/or LS patients) could combine IPSS questionnaire + flowmetry every three months for one year, and annually thereafter. Additionally, RUG at three and twelve months should be performed.

In this protocol, urethrocystoscopy is only performed if required [576]. Another suggested follow-up protocol includes urethrocystoscopy or RUG/VCUG at three months post-operatively, in order to rule out early failures, especially in case of graft use. If there is evidence of good anatomical outcome in these tests, flowmetry and questionnaire results at three months should be considered as the new baseline. Thereafter, follow-up could be safely and routinely performed with non-invasive tests (flowmetry – evaluating  $Q_{max}$  and the shape of curve – and questionnaires). Any deterioration should be further investigated with a urethrocystoscopy [591].

A recently suggested protocol also included assessment of LUTS, sexual function (erectile and ejaculatory), and LUT pain, that need to be compared with pre-operative findings which should include a PROM questionnaire [575]. Cystoscopy and flowmetry should be performed between three to six months postoperatively, and flowmetry findings should be considered as the new baseline for longitudinal follow-up. Future significant decline (25-30%) in  $Q_{max}$  or  $Q_{max}$  - (average flow rate) should trigger new cystoscopy to rule out anatomic recurrence, even in patients who are symptom-free [575]. A routine cystoscopy at twelve to fifteen months should be performed at the surgeon's discretion, based on risk assessment of three aspects: higher-risk patients, evidence of partial urethral narrowing at three-month assessment, low-volume surgeons [575].

Summary of evidence	LE
The higher percentage of recurrences presents during the first twelve months, after urethroplasty	2a
surgery.	
Risk-adjusted follow-up protocols are cost-effective and safe for the patients.	3

Recommendations	Strength rating
Offer a routine follow-up of at least one year after urethroplasty.	Strong
Adopt a risk-adjusted follow-up protocol.	Weak

#### 11.7 Follow-up protocol proposal after urethroplasty

#### 11.7.1 Surgeries with low risk of recurrence

 Anastomotic urethroplasties in the bulbar/(bulbo)membranous segment with no history of radiotherapy, hypospadias, or balanitis xerotica obliterans (BXO)/LS features.

#### Table 11.3: Follow-up protocol for urethroplasty with low risk of recurrence

Surgery	3 months	12 months	24 months*
Uroflowmetry	+	+	+
PROM (incl. sexual function)	+	+	+
Anatomic evaluation: (Urethrocystoscopy/	+**	On indication	On indication
RUG-VCUG)			

\*Follow-up could be discontinued after two years, advising the patient to seek urological evaluation if symptoms worsen. Academic centres could increase the length of follow-up for research purposes. \*\*The Panel suggests performing an anatomic assessment at three months.

#### 11.7.2 Surgical management options with standard risk of recurrence

- Anastomotic urethroplasties in the bulbar segment with prior history of radiotherapy, hypospadias, or BXO/LS features;
- Penile urethroplasties;
- Non-traumatic posterior urethroplasties;
- Graft or/and flap substitution urethroplasties.

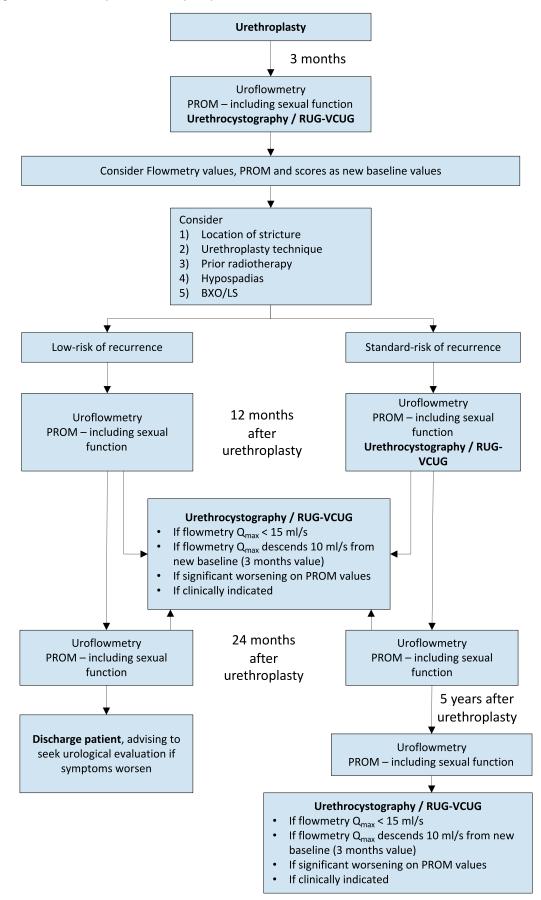
#### Table 11.4: Follow-up protocol for urethroplasty with standard risk of recurrence

Surgery	3 months	12 months	24 months	5 years *
Uroflowmetry	+	+	+	+
PROM (incl. sexual function)	+	+	+	+
Anatomic evaluation:	+	+	+	On indication
(Urethrocystoscopy/ RUG-VCUG)				

\* Follow-up could be discontinued after five years, advising the patient to seek urological evaluation if symptoms worsen. A longer follow-up period should be considered after penile and substitution urethroplasties. Academic centres could increase the length of follow-up for research purposes.

Please see Figure 11.1 for further guidance.

Figure 11.1: Follow-up after urethroplasty



BXO = balanitis xerotica obliterans; LS = lichen sclerosus; PROM = patient reported outcome measure;  $Q_{max} =$  maximum flow rate; RUG = retrograde urethrography; VCUG = voiding cystourethrography.

# 12. REFERENCES

1. Guyatt, G.H., *et al.* What is "quality of evidence" and why is it important to clinicians? BMJ, 2008. 336: 995.

https://pubmed.ncbi.nlm.nih.gov/18456631/

- Guyatt, G.H., *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, 2008. 336: 924. <u>https://pubmed.ncbi.nlm.nih.gov/18436948/</u>
- 3. Philips, C.B. Modified from Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009). 2014:Updated Jeremy Howick March 2009.

https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-basedmedicine-levels-of-evidence-march-2009

- 4. Guyatt, G.H., *et al.* Going from evidence to recommendations. BMJ, 2008. 336: 1049. <u>https://pubmed.ncbi.nlm.nih.gov/18467413/</u>
- 5. Hoebeke, P., *et al.* [Principles of wound healing as applied to urethra surgery]. Ann Urol (Paris), 1993. 27: 209.
- https://pubmed.ncbi.nlm.nih.gov/8239546/
- 6. Esperto, F., *et al.* What is the role of single-stage oral mucosa graft urethroplasty in the surgical management of lichen sclerosus-related stricture disease in men? A systematic review. World J Urol, 2021.

https://pubmed.ncbi.nlm.nih.gov/34448008/

- Barratt, R., *et al.* Free Graft Augmentation Urethroplasty for Bulbar Urethral Strictures: Which Technique Is Best? A Systematic Review. Eur Urol, 2021. 80: 57. <u>https://pubmed.ncbi.nlm.nih.gov/33875306/</u>
- Lumen, N., et al. European Association of Urology Guidelines on Urethral Stricture Disease (Part 1): Management of Male Urethral Stricture Disease. Eur Urol, 2021. 80: 190. https://pubmed.ncbi.nlm.nih.gov/34059397/
- 9. Campos-Juanatey, F., *et al.* European Association of Urology Guidelines on Urethral Stricture Disease (Part 2): Diagnosis, Perioperative Management, and Follow-up in Males. Eur Urol, 2021. 80: 201. https://pubmed.ncbi.nlm.nih.gov/34103180/
- Riechardt, S., *et al.* European Association of Urology Guidelines on Urethral Stricture Disease Part 3: Management of Strictures in Females and Transgender Patients. Eur Urol Focus, 2021. <u>https://pubmed.ncbi.nlm.nih.gov/34393082/</u>
- 11. Mundy, A.R., *et al.* Urethral trauma. Part I: introduction, history, anatomy, pathology, assessment and emergency management. BJU Int, 2011. 108: 310. https://pubmed.ncbi.nlm.nih.gov/21771241/
- 12. Latini, J.M., *et al.* SIU/ICUD Consultation On Urethral Strictures: Epidemiology, etiology, anatomy, and nomenclature of urethral stenoses, strictures, and pelvic fracture urethral disruption injuries. Urology, 2014. 83: S1.
  - https://pubmed.ncbi.nlm.nih.gov/24210733/
- 13. Smith, A.L., *et al.* Female urethral strictures: successful management with long-term clean intermittent catheterization after urethral dilatation. BJU Int, 2006. 98: 96. https://pubmed.ncbi.nlm.nih.gov/16831151/
- 14. Osman, N.I., *et al.* A systematic review of surgical techniques used in the treatment of female urethral stricture. Eur Urol, 2013. 64: 965.

https://pubmed.ncbi.nlm.nih.gov/23937829/

15. Singh, M., *et al.* Dorsal onlay vaginal graft urethroplasty for female urethral stricture. Indian J Urol, 2013. 29: 124.

https://pubmed.ncbi.nlm.nih.gov/23956514/

- 16. Montorsi, F., *et al.* Vestibular flap urethroplasty for strictures of the female urethra. Impact on symptoms and flow patterns. Urol Int, 2002. 69: 12.
- https://pubmed.ncbi.nlm.nih.gov/12119432/
  17. Alwaal, A., *et al.* Epidemiology of urethral strictures. Transl Androl Urol, 2014. 3: 209. https://pubmed.ncbi.nlm.nih.gov/26813256/
- 18. Palminteri, E., *et al.* Contemporary urethral stricture characteristics in the developed world. Urology, 2013. 81: 191.
  - https://pubmed.ncbi.nlm.nih.gov/23153951/
- 19. Groutz, A., *et al.* Bladder outlet obstruction in women: definition and characteristics. Neurourol Urodyn, 2000. 19: 213.

https://pubmed.ncbi.nlm.nih.gov/10797578/

- 20. Chuang, F.C., *et al.* Lower Urinary Tract Symptoms and Video-Urodynamic Characteristics of Women with Clinically Unsuspected Bladder Outlet Obstruction. Low Urin Tract Symptoms, 2013. 5: 23. https://pubmed.ncbi.nlm.nih.gov/26663244/
- Malde, S., *et al.* Female bladder outlet obstruction: Common symptoms masking an uncommon cause. Low Urin Tract Symptoms, 2019. 11: 72. https://pubmed.ncbi.nlm.nih.gov/28990728/
- 22. Nitti, V.W., *et al.* Diagnosing bladder outlet obstruction in women. J Urol, 1999. 161: 1535. https://pubmed.ncbi.nlm.nih.gov/10210391/
- Kuo, H.C. Videourodynamic characteristics and lower urinary tract symptoms of female bladder outlet obstruction. Urology, 2005. 66: 1005. <u>https://pubmed.ncbi.nlm.nih.gov/16286113/</u>
- 24. Santucci, R.A., *et al.* Office dilation of the female urethra: a quality of care problem in the field of urology. J Urol, 2008. 180: 2068.
- https://pubmed.ncbi.nlm.nih.gov/18804232/
- 25. Vetterlein, M.W., *et al.* Anterior Urethral Strictures in Children: Disease Etiology and Comparative Effectiveness of Endoscopic Treatment vs. Open Surgical Reconstruction. Front Pediatr, 2019. 7. https://www.frontiersin.org/articles/10.3389/fped.2019.00005/full
- 26. Snodgrass, W.T., *et al.* Management of Urethral Strictures After Hypospadias Repair. Urol Clin North Am, 2017. 44: 105.
  - https://pubmed.ncbi.nlm.nih.gov/27908364/
- 27. Stein, D.M., *et al.* A geographic analysis of male urethral stricture aetiology and location. BJU Int, 2013. 112: 830.
  - https://pubmed.ncbi.nlm.nih.gov/23253867/
- 28. Dielubanza, E.J., *et al.* Distal urethroplasty for fossa navicularis and meatal strictures. Transl Androl Urol, 2014. 3: 163.

https://pubmed.ncbi.nlm.nih.gov/26816765/

- 29. Mangera, A., *et al*. Urethral stricture disease. Surgery (Oxford), 2011. 29: 272. <u>https://www.sciencedirect.com/science/article/abs/pii/S0263931911000603</u>
- Daneshvar, M., et al. Surgical Management of Fossa Navicularis and Distal Urethral Strictures. Curr Urol Rep, 2018. 19: 43. <u>https://pubmed.ncbi.nlm.nih.gov/29667080/</u>
- Tonkin, J.B., *et al.* Management of distal anterior urethral strictures. Nat Rev Urol, 2009. 6: 533. <u>https://pubmed.ncbi.nlm.nih.gov/19736550/</u>
- Santucci, R.A. Urethral Complications After Transgender Phalloplasty: Strategies to Treat Them and Minimize Their Occurrence. Clin Anat, 2018. 31: 187. https://pubmed.ncbi.nlm.nih.gov/29178533/
- Dreher, P.C., *et al.* Complications of the neovagina in male-to-female transgender surgery: A systematic review and meta-analysis with discussion of management. Clin Anat, 2018. 31: 191. https://pubmed.ncbi.nlm.nih.gov/29057562/
- 34. Bertrand, L.A., et al. Lower urinary tract pain and anterior urethral stricture disease: prevalence and effects of urethral reconstruction. J Urol, 2015. 193: 184. <u>https://pubmed.ncbi.nlm.nih.gov/25046621/</u>
- Lubahn, J.D., *et al.* Poor quality of life in patients with urethral stricture treated with intermittent selfdilation. J Urol, 2014. 191: 143.
  - https://pubmed.ncbi.nlm.nih.gov/23820057/
- 36. Greenwell, T.J., et al. Repeat urethrotomy and dilation for the treatment of urethral stricture are neither clinically effective nor cost-effective. J Urol, 2004. 172: 275. <u>https://pubmed.ncbi.nlm.nih.gov/15201793/</u>
- Santucci, R.A., *et al.* Male urethral stricture disease. J Urol, 2007. 177: 1667. https://pubmed.ncbi.nlm.nih.gov/17437780/
- 38. Lumen, N., *et al.* Etiology of urethral stricture disease in the 21st century. J Urol, 2009. 182: 983. https://pubmed.ncbi.nlm.nih.gov/19616805/
- 39. Lazzeri, M.S., *et al.* Incidence, Causes, and Complications of Urethral Stricture Disease. Eur Urol Suppl, 2016. 15: 2.

https://www.sciencedirect.com/science/article/abs/pii/S1569905615000652

- 40. Heyns, C., *et al.* A. Etiology of male urethral strictures-Evaluation of temporal changes at a single center, and review of the literature. African J Urol, 2012. 18: 4. https://www.sciencedirect.com/science/article/pii/S1110570412000100
- Depasquale, I., *et al.* The treatment of balanitis xerotica obliterans. BJU Int, 2000. 86: 459. https://pubmed.ncbi.nlm.nih.gov/10971272/

- 42. Regauer, S. Immune dysregulation in lichen sclerosus. Eur J Cell Biol, 2005. 84: 273. https://pubmed.ncbi.nlm.nih.gov/15819407/
- 43. Mallon, E., *et al*. Circumcision and genital dermatoses. Arch Dermatol, 2000. 136: 350. <u>https://pubmed.ncbi.nlm.nih.gov/10724196/</u>
- 44. Hofer, M.D., *et al.* Lichen sclerosus in men is associated with elevated body mass index, diabetes mellitus, coronary artery disease and smoking. World J Urol, 2014. 32: 105. https://pubmed.ncbi.nlm.nih.gov/23633127/
- 45. Erickson, B.A., *et al.* Understanding the Relationship between Chronic Systemic Disease and Lichen Sclerosus Urethral Strictures. J Urol, 2016. 195: 363. https://pubmed.ncbi.nlm.nih.gov/26343349/
- 46. Bjekic, M., *et al.* Risk factors for genital lichen sclerosus in men. Br J Dermatol, 2011. 164: 325. https://pubmed.ncbi.nlm.nih.gov/20973765/
- 47. Falcone, M., *et al.* Current Management of Penile Fracture: An Up-to-Date Systematic Review. Sex Med Rev, 2018. 6: 253.

https://pubmed.ncbi.nlm.nih.gov/28874325/

- Barratt, R.C., *et al.* Pelvic fracture urethral injury in males-mechanisms of injury, management options and outcomes. Transl Androl Urol, 2018. 7: S29. https://pubmed.ncbi.nlm.nih.gov/29644168/
- 49. Tausch, T.J., *et al.* Gunshot wound injuries of the prostate and posterior urethra: reconstructive armamentarium. J Urol, 2007. 178: 1346.
- https://pubmed.ncbi.nlm.nih.gov/17706720/
- 50. Fenton, A.S., *et al.* Anterior urethral strictures: etiology and characteristics. Urology, 2005. 65: 1055. <u>https://pubmed.ncbi.nlm.nih.gov/15913734/</u>
- 51. Sunay, M., *et al.* Single-institution outcomes of open reconstruction techniques for management of pediatric and adolescent post-traumatic urethral strictures. Urology, 2011. 77: 706. <u>https://pubmed.ncbi.nlm.nih.gov/20970838/</u>
- 52. Hollingsworth, J.M., *et al.* Determining the noninfectious complications of indwelling urethral catheters: a systematic review and meta-analysis. Ann Intern Med, 2013. 159: 401. https://pubmed.ncbi.nlm.nih.gov/24042368/
- 53. Davis, N.F., *et al.* Long-term outcomes of urethral catheterisation injuries: a prospective multiinstitutional study. World J Urol, 2020. 38: 473. https://pubmed.ncbi.nlm.nih.gov/31020421/
- 54. Kashefi, C., *et al.* Incidence and prevention of iatrogenic urethral injuries. J Urol, 2008. 179: 2254. https://pubmed.ncbi.nlm.nih.gov/18423712/
- 55. Davis, N.F., *et al.* Incidence, Cost, Complications and Clinical Outcomes of latrogenic Urethral Catheterization Injuries: A Prospective Multi-Institutional Study. J Urol, 2016. 196: 1473. https://pubmed.ncbi.nlm.nih.gov/27317985/
- 56. Daneshgari, F., *et al.* Evidence-based multidisciplinary practice: improving the safety and standards of male bladder catheterization. Medsurg Nurs, 2002. 11: 236. https://pubmed.ncbi.nlm.nih.gov/12830746/
- 57. Ghaffary, C., *et al*. A practical approach to difficult urinary catheterizations. Curr Urol Rep, 2013. 14: 565.
  - https://pubmed.ncbi.nlm.nih.gov/23959835/
- 58. Davoodian, P., *et al.* Inappropriate use of urinary catheters and its common complications in different hospital wards. Saudi J Kidney Dis Transpl, 2012. 23: 63. https://pubmed.ncbi.nlm.nih.gov/22237221/
- 59. Fernandez-Ruiz, M., *et al.* Inappropriate use of urinary catheters in patients admitted to medical wards in a university hospital. Enferm Infecc Microbiol Clin, 2013. 31: 523. https://pubmed.ncbi.nlm.nih.gov/23601704/
- 60. Fakih, M.G., *et al.* Effect of establishing guidelines on appropriate urinary catheter placement. Acad Emerg Med, 2010. 17: 337.
  - https://pubmed.ncbi.nlm.nih.gov/20370769/
- 61. Fakih, M.G., *et al.* Avoiding potential harm by improving appropriateness of urinary catheter use in 18 emergency departments. Ann Emerg Med, 2014. 63: 761.
- 62. <u>https://pubmed.ncbi.nlm.nih.gov/24656760/</u> 63. Shimoni, Z., *et al.* Will more restrictive indications decrease ra
- Shimoni, Z., et al. Will more restrictive indications decrease rates of urinary catheterisation? An historical comparative study. BMJ Open, 2012. 2: e000473. https://pubmed.ncbi.nlm.nih.gov/22403341/

- 63. Thomas, A.Z., *et al.* Avoidable iatrogenic complications of urethral catheterization and inadequate intern training in a tertiary-care teaching hospital. BJU Int, 2009. 104: 1109. <u>https://pubmed.ncbi.nlm.nih.gov/19338562/</u>
- 64. Manalo, M., Jr., *et al.* Medical interns' knowledge and training regarding urethral catheter insertion and insertion-related urethral injury in male patients. BMC Med Educ, 2011. 11: 73. https://pubmed.ncbi.nlm.nih.gov/21951692/
- 65. Davis, N.F., *et al.* Preventing Urethral Trauma from Inadvertent Inflation of Catheter Balloon in the Urethra during Catheterization: Evaluation of a Novel Safety Syringe after Correlating Trauma with Urethral Distension and Catheter Balloon Pressure. J Urol, 2015. 194: 1138. https://pubmed.ncbi.nlm.nih.gov/25711195/
- 66. Davis, N.F., *et al.* Clinical Evaluation of a Safety-device to Prevent Urinary Catheter Inflation Related Injuries. Urology, 2018. 115: 179.
- https://pubmed.ncbi.nlm.nih.gov/29501711/
   Bugeja, S., et al. A new urethral catheterisation device (UCD) to manage difficult urethral catheterisation. World J Urol, 2019. 37: 595. https://pubmed.ncbi.nlm.nih.gov/30251050/
- 68. Yuminaga, Y., *et al.* Multi-centre, prospective evaluation of the Seldinger technique for difficult male urethral catheter insertions by non-urology trained doctors. BJU Int, 2017. 120 Suppl 3: 21. <a href="https://pubmed.ncbi.nlm.nih.gov/28872750/">https://pubmed.ncbi.nlm.nih.gov/28872750/</a>
- 69. Yuruk, E., *et al.* Catheter dwell time and diameter affect the recurrence rates after internal urethrotomy. Turk J Urol, 2016. 42: 184. https://pubmed.ncbi.nlm.nih.gov/27635294/
- 70. Liss, M.A., *et al.* Preventing perioperative complications of robotic-assisted radical prostatectomy. Urology, 2013. 81: 319.
  - https://pubmed.ncbi.nlm.nih.gov/23374792/
- 71. Ferrie, B.G., *et al.* Comparison of silicone and latex catheters in the development of urethral stricture after cardiac surgery. Br J Urol, 1986. 58: 549. https://pubmed.ncbi.nlm.nih.gov/3490896/
- 72. Nacey, J.N., *et al.* Catheter-induced urethritis: a comparison between latex and silicone catheters in a prospective clinical trial. Br J Urol, 1985. 57: 325. https://pubmed.ncbi.nlm.nih.gov/3891005/
- 73. Lam, T.B., *et al.* Types of indwelling urethral catheters for short-term catheterisation in hospitalised adults. Cochrane Database Syst Rev, 2014: CD004013. https://pubmed.ncbi.nlm.nih.gov/25248140/
- 74. Robertson, G.S., *et al.* Effect of catheter material on the incidence of urethral strictures. Br J Urol, 1991. 68: 612.
  - https://pubmed.ncbi.nlm.nih.gov/1773292/
- 75. Goodwin, M.I., *et al.* Meatal strictures after transurethral prostatectomy using latex or polyvinyl chloride three-way catheters. Ann R Coll Surg Engl, 1990. 72: 125. https://pubmed.ncbi.nlm.nih.gov/2185681/
- 76. Hart, A.J., *et al.* Incidence of urethral stricture after transurethral resection of prostate. Effects of urinary infection, urethral flora, and catheter material and size. Urology, 1981. 18: 588. https://pubmed.ncbi.nlm.nih.gov/7314361/
- 77. Lawrence, E.L., *et al.* Materials for urinary catheters: a review of their history and development in the UK. Med Eng Phys, 2005. 27: 443.
  - https://pubmed.ncbi.nlm.nih.gov/15990061/
- 78. Cornu, J.N., et al. A Systematic Review and Meta-analysis of Functional Outcomes and Complications Following Transurethral Procedures for Lower Urinary Tract Symptoms Resulting from Benign Prostatic Obstruction: An Update. Eur Urol, 2015. 67: 1066. <u>https://pubmed.ncbi.nlm.nih.gov/24972732/</u>
- 79. Chen, M.L., *et al.* Urethral Strictures and Stenoses Caused by Prostate Therapy. Rev Urol, 2016. 18: 90.
  - https://pubmed.ncbi.nlm.nih.gov/27601967/
- Michielsen, D.P., *et al.* Urethral strictures and bipolar transurethral resection in saline of the prostate: fact or fiction? J Endourol, 2010. 24: 1333. <u>https://pubmed.ncbi.nlm.nih.gov/20583960/</u>
- 81. Balbay, M.D., *et al.* Development of urethral stricture after transurethral prostatectomy: a retrospective study. Int Urol Nephrol, 1992. 24: 49. <u>https://pubmed.ncbi.nlm.nih.gov/1378047/</u>

- 82. Rassweiler, J., *et al.* Complications of transurethral resection of the prostate (TURP)--incidence, management, and prevention. Eur Urol, 2006. 50: 969. https://pubmed.ncbi.nlm.nih.gov/16469429/
- Robinson, H.P., *et al.* Postoperative contracture of the vesical neck. II. Experimental production of contractures in dogs: transurethral series. J Urol, 1962. 87: 610. https://pubmed.ncbi.nlm.nih.gov/14492908/
- 84. Lumen, N., *et al.* Challenging non-traumatic posterior urethral strictures treated with urethroplasty: a preliminary report. Int Braz J Urol, 2009. 35: 442. https://pubmed.ncbi.nlm.nih.gov/19719860/
- 85. Doluoglu, O.G., *et al.* Impact of asymptomatic prostatitis on re-operations due to urethral stricture or bladder neck contracture developed after TUR-P. Int Urol Nephrol, 2012. 44: 1085. https://pubmed.ncbi.nlm.nih.gov/22252218/
- 86. Tao, H., *et al.* Analysis of risk factors leading to postoperative urethral stricture and bladder neck contracture following transurethral resection of prostate. Int Braz J Urol, 2016. 42: 302. https://pubmed.ncbi.nlm.nih.gov/27256185/
- 87. Tan, G.H., *et al.* Urethral strictures after bipolar transurethral resection of prostate may be linked to slow resection rate. Investig Clin Urol, 2017. 58: 186. https://pubmed.ncbi.nlm.nih.gov/28480344/
- 88. Gunes, M., *et al.* Does resectoscope size play a role in formation of urethral stricture following transurethral prostate resection? Int Braz J Urol, 2015. 41: 744. https://pubmed.ncbi.nlm.nih.gov/26401868/
- 89. Park, J.K., *et al.* Is warm temperature necessary to prevent urethral stricture in combined transurethral resection and vaporization of prostate? Urology, 2009. 74: 125. https://pubmed.ncbi.nlm.nih.gov/19395006/
- 90. Varkarakis, J., *et al.* Long-term morbidity and mortality of transurethral prostatectomy: a 10-year follow-up. Prostate, 2004. 58: 248.
- https://pubmed.ncbi.nlm.nih.gov/14743463/
- 91. Lee, Y.H., *et al.* Comprehensive study of bladder neck contracture after transurethral resection of prostate. Urology, 2005. 65: 498.
- https://pubmed.ncbi.nlm.nih.gov/15780363/
- 92. Lan, Y., *et al.* Thulium (Tm:YAG) laser vaporesection of prostate and bipolar transurethral resection of prostate in patients with benign prostate hyperplasia: a systematic review and meta-analysis. Lasers Med Sci, 2018. 33: 1411.

https://pubmed.ncbi.nlm.nih.gov/29947009/

- 93. Sciarra, A., *et al.* Use of cyclooxygenase-2 inhibitor for prevention of urethral strictures secondary to transurethral resection of the prostate. Urology, 2005. 66: 1218. <u>https://pubmed.ncbi.nlm.nih.gov/16360446/</u>
- 94. Bailey, M.J., *et al.* The role of internal urethrotomy in the prevention of urethral stricture following transurethral resection of prostate. Br J Urol, 1979. 51: 28. https://pubmed.ncbi.nlm.nih.gov/465957/
- 95. Steenfos, H.H., *et al.* The importance of internal urethrotomy a.m. Otis for the incidence of urethral stricture following transurethral prostatectomy. Int Urol Nephrol, 1988. 20: 55. https://pubmed.ncbi.nlm.nih.gov/3360588/
- 96. Schultz, A., *et al.* Prevention of urethral stricture formation after transurethral resection of the prostate: a controlled randomized study of Otis urethrotomy versus urethral dilation and the use of the polytetrafluoroethylene coated versus the uninsulated metal sheath. J Urol, 1989. 141: 73. https://pubmed.ncbi.nlm.nih.gov/2642313/
- 97. Nielsen, K.K., *et al.* Does internal urethrotomy prevent urethral stricture after transurethral prostatectomy. Early and late results. Eur Urol, 1989. 16: 258. https://pubmed.ncbi.nlm.nih.gov/2670580/
- 98. Nielsen, K.K., *et al.* Urethral stricture following transurethral prostatectomy. Urology, 1990. 35: 18. https://pubmed.ncbi.nlm.nih.gov/2404365/
- 99. Faul, P. Video TUR: raising the gold standard. New aspects, techniques and tendencies to minimize invasiveness. Eur Urol, 1993. 24: 256.
- https://pubmed.ncbi.nlm.nih.gov/8375449/
   100. Rocco, N.R., *et al.* An update on best practice in the diagnosis and management of post-prostatectomy anastomotic strictures. Ther Adv Urol, 2017. 9: 99. https://pubmed.ncbi.nlm.nih.gov/28588647/

- 101. Browne, B.M., *et al.* Management of Urethral Stricture and Bladder Neck Contracture Following Primary and Salvage Treatment of Prostate Cancer. Curr Urol Rep, 2017. 18: 76. <u>https://pubmed.ncbi.nlm.nih.gov/28776126/</u>
- 102. Herschorn, S., et al. SIU/ICUD Consultation on Urethral Strictures: Posterior urethral stenosis after treatment of prostate cancer. Urology, 2014. 83: S59. https://pubmed.ncbi.nlm.nih.gov/24361008/
- 103. Tewari, A., *et al.* Positive surgical margin and perioperative complication rates of primary surgical treatments for prostate cancer: a systematic review and meta-analysis comparing retropubic, laparoscopic, and robotic prostatectomy. Eur Urol, 2012. 62: 1. https://pubmed.ncbi.nlm.nih.gov/22405509/
- 104. Sujenthiran, A., *et al.* National cohort study comparing severe medium-term urinary complications after robot-assisted vs laparoscopic vs retropubic open radical prostatectomy. BJU Int, 2018. 121: 445.
  - https://pubmed.ncbi.nlm.nih.gov/29032582/
- 105. Hu, J.C., *et al.* Comparative effectiveness of minimally invasive vs open radical prostatectomy. JAMA, 2009. 302: 1557.
  - https://pubmed.ncbi.nlm.nih.gov/19826025/
- 106. Almatar, A., *et al.* Effect of radical prostatectomy surgeon volume on complication rates from a large population-based cohort. Can Urol Assoc J, 2016. 10: 45. <u>https://pubmed.ncbi.nlm.nih.gov/26977206/</u>
- 107. Patel, V.R., *et al.* Robotic radical prostatectomy in the community setting--the learning curve and beyond: initial 200 cases. J Urol, 2005. 174: 269. https://pubmed.ncbi.nlm.nih.gov/15947662/
- 108. Spector, B.L., *et al.* Bladder Neck Contracture Following Radical Retropubic versus Robotic-Assisted Laparoscopic Prostatectomy. Curr Urol, 2017. 10: 145. <u>https://pubmed.ncbi.nlm.nih.gov/28878598/</u>
- 109. Gillitzer, R., *et al.* Single center comparison of anastomotic strictures after radical perineal and radical retropubic prostatectomy. Urology, 2010. 76: 417. https://pubmed.ncbi.nlm.nih.gov/19969328/
- 110.
   Hu, J.C., et al. Role of surgeon volume in radical prostatectomy outcomes. J Clin Oncol, 2003. 21: 401.

   <u>https://pubmed.ncbi.nlm.nih.gov/12560426/</u>
- Srougi, M., *et al.* The influence of bladder neck mucosal eversion and early urinary extravasation on patient outcome after radical retropubic prostatectomy: a prospective controlled trial. BJU Int, 2005. 95: 757.
  - https://pubmed.ncbi.nlm.nih.gov/15794777/
- 112. Kowalewski, K.F., *et al.* Interrupted versus Continuous Suturing for Vesicourethral Anastomosis During Radical Prostatectomy: A Systematic Review and Meta-analysis. Eur Urol Focus, 2019. 5: 980. <u>https://pubmed.ncbi.nlm.nih.gov/29907547/</u>
- Bai, Y., et al. Assessing the Impact of Barbed Suture on Vesicourethral Anastomosis During Minimally Invasive Radical Prostatectomy: A Systematic Review and Meta-analysis. Urology, 2015. 85: 1368.
  - https://pubmed.ncbi.nlm.nih.gov/25868736/
- 114. Awad, M.A., *et al.* Prostate cancer radiation and urethral strictures: a systematic review and metaanalysis. Prostate Cancer Prostatic Dis, 2018. 21: 168. <u>https://pubmed.ncbi.nlm.nih.gov/29296018/</u>
- 115. Moltzahn, F., *et al.* Urethral strictures after radiation therapy for prostate cancer. Investig Clin Urol, 2016. 57: 309.
  - https://pubmed.ncbi.nlm.nih.gov/27617311/
- 116. Hofer, M.D., *et al.* Treatment of Radiation-Induced Urethral Strictures. Urol Clin North Am, 2017. 44: 87.
  - https://pubmed.ncbi.nlm.nih.gov/27908375/
- 117. Sullivan, L., *et al.* Urethral stricture following high dose rate brachytherapy for prostate cancer. Radiother Oncol, 2009. 91: 232.
- https://pubmed.ncbi.nlm.nih.gov/19097660/118.Hindson, B.R., *et al.* Urethral strictures following high-dose-rate brachytherapy for prostate cancer:
  - analysis of risk factors. Brachytherapy, 2013. 12: 50. https://pubmed.ncbi.nlm.nih.gov/22561217/
- 119. Kowalczyk, K.J., *et al.* Optimal timing of early versus delayed adjuvant radiotherapy following radical prostatectomy for locally advanced prostate cancer. Urol Oncol, 2014. 32: 303. <u>https://pubmed.ncbi.nlm.nih.gov/24321259/</u>

- 120. Seppenwoolde, Y., *et al.* HDR prostate monotherapy: dosimetric effects of implant deformation due to posture change between TRUS- and CT-imaging. Radiother Oncol, 2008. 86: 114. <u>https://pubmed.ncbi.nlm.nih.gov/18054101/</u>
- 121. Mohammed, N., *et al.* Comparison of acute and late toxicities for three modern high-dose radiation treatment techniques for localized prostate cancer. Int J Radiat Oncol Biol Phys, 2012. 82: 204. https://pubmed.ncbi.nlm.nih.gov/21167653/
- 122. Lumen, N., *et al.* Urethroplasty for failed hypospadias repair: a matched cohort analysis. J Pediatr Urol, 2011. 7: 170.

https://pubmed.ncbi.nlm.nih.gov/20965140/

- 123. Cotter, K.J., *et al.* Trends in Urethral Stricture Disease Etiology and Urethroplasty Technique From a Multi-institutional Surgical Outcomes Research Group. Urology, 2019. 130: 167. https://pubmed.ncbi.nlm.nih.gov/30880075/
- 124. Simonato, A., *et al.* Vaginal flap urethroplasty for wide female stricture disease. J Urol, 2010. 184: 1381. https://pubmed.ncbi.nlm.nih.gov/20727538/
- 125. Sharma, G.K., *et al.* Dorsal onlay lingual mucosal graft urethroplasty for urethral strictures in women. BJU Int, 2010. 105: 1309.

https://pubmed.ncbi.nlm.nih.gov/19874307/

- 126. Onol, F.F., *et al.* Techniques and results of urethroplasty for female urethral strictures: our experience with 17 patients. Urology, 2011. 77: 1318.
- https://pubmed.ncbi.nlm.nih.gov/21459417/
- 127. Blaivas, J.G., *et al.* Management of urethral stricture in women. J Urol, 2012. 188: 1778. <u>https://pubmed.ncbi.nlm.nih.gov/22998912/</u>
- 128. Rijal, A., *et al.* Bladder outflow problems in females. Nepal Med Coll J, 2013. 15: 46. <u>https://pubmed.ncbi.nlm.nih.gov/24592794/</u>
- 129. Xu, Y.M., *et al.* A rationale for procedure selection to repair female urethral stricture associated with urethrovaginal fistulas. J Urol, 2013. 189: 176. https://pubmed.ncbi.nlm.nih.gov/23174242/
- 130. Kowalik, C., *et al.* Intermediate outcomes after female urethral reconstruction: graft vs flap. Urology, 2014. 83: 1181.

https://pubmed.ncbi.nlm.nih.gov/24674113/

131. Onol, F.F., *et al.* Ventral inlay labia minora graft urethroplasty for the management of female urethral strictures. Urology, 2014. 83: 460.

https://pubmed.ncbi.nlm.nih.gov/24210559/

- 132. Spilotros, M., *et al.* Female urethral stricture: a contemporary series. World J Urol, 2017. 35: 991. <u>https://pubmed.ncbi.nlm.nih.gov/27704202/</u>
- 133. Powell, C.R., *et al.* Dorsal Onlay Buccal Urethroplasty in the Female is Associated with High Quality of Life Using Validated Lower Urinary Tract Symptom Instruments. Urol Pract, 2017. 4: 48. https://www.auajournals.org/doi/abs/10.1016/j.urpr.2016.02.002
- 134. Mukhtar, B.M.B., *et al.* Ventral-onlay buccal mucosa graft substitution urethroplasty for urethral stricture in women. BJU Int, 2017. 120: 710. https://pubmed.ncbi.nlm.nih.gov/28749039/
- 135. Tao, T.T., *et al.* Novel surgical technique for female distal urethral stricture disease: an evaluation of efficacy and safety compared with urethral dilatation. Int J Clin Exp Med, 2018. 11: 12002. <a href="http://www.ijcem.com/files/ijcem0080490.pdf">http://www.ijcem.com/files/ijcem0080490.pdf</a>
- 136. Romero-Maroto, J., *et al.* Lateral-based Anterior Vaginal Wall Flap in the Treatment of Female Urethral Stricture: Efficacy and Safety. Eur Urol, 2018. 73: 123. https://pubmed.ncbi.nlm.nih.gov/27692474/
- 137. West, C., *et al.* Female urethroplasty: contemporary thinking. World J Urol, 2019. 37: 619. https://pubmed.ncbi.nlm.nih.gov/30456711/
- 138. Rehder, P., *et al.* Dorsal urethroplasty with labia minora skin graft for female urethral strictures. BJU Int, 2010. 106: 1211.

https://pubmed.ncbi.nlm.nih.gov/20230383/

- 139.
   Wood, D.N., et al. Peritoneal and perineal anatomy and surgical approaches. BJU Int, 2004. 94: 719.

   <u>https://pubmed.ncbi.nlm.nih.gov/15329090/</u>
- 140.
   Terlecki, R.P., et al. Grafts are unnecessary for proximal bulbar reconstruction. J Urol, 2010. 184: 2395.

   <u>https://pubmed.ncbi.nlm.nih.gov/20952000/</u>
- 141. Baradaran, N., et al. Clinical significance of cystoscopic urethral stricture recurrence after anterior urethroplasty: a multi-institution analysis from Trauma and Urologic Reconstructive Network of Surgeons (TURNS). World J Urol, 2019. <u>https://pubmed.ncbi.nlm.nih.gov/30712091/</u>

- 142. Purohit, R.S., *et al.* Natural History of Low-stage Urethral Strictures. Urology, 2017. 108: 180. https://pubmed.ncbi.nlm.nih.gov/28552818/
- 143. Erickson, B.A., *et al.* Multi-institutional 1-year bulbar urethroplasty outcomes using a standardized prospective cystoscopic follow-up protocol. Urology, 2014. 84: 213. <u>https://pubmed.ncbi.nlm.nih.gov/24837453/</u>
- 144. Palminteri, E., *et al.* Two-sided dorsal plus ventral oral graft bulbar urethroplasty: long-term results and predictive factors. Urology, 2015. 85: 942. https://pubmed.ncbi.nlm.nih.gov/25817122/
- 145. Lumen, N., *et al.* Urethroplasty for strictures after phallic reconstruction: a single-institution experience. Eur Urol, 2011. 60: 150. https://pubmed.ncbi.nlm.nih.gov/21145648/
- 146. Rourke, K., *et al.* The clinical spectrum of the presenting signs and symptoms of anterior urethral stricture: detailed analysis of a single institutional cohort. Urology, 2012. 79: 1163. <a href="https://pubmed.ncbi.nlm.nih.gov/22446349/">https://pubmed.ncbi.nlm.nih.gov/22446349/</a>
- 147. Nuss, G.R., *et al.* Presenting symptoms of anterior urethral stricture disease: a disease specific, patient reported questionnaire to measure outcomes. J Urol, 2012. 187: 559. https://pubmed.ncbi.nlm.nih.gov/22177165/
- 148. Cotter, K.J., *et al.* Prevalence of Post-Micturition Incontinence before and after Anterior Urethroplasty. J Urol, 2018. 200: 843.
- https://pubmed.ncbi.nlm.nih.gov/29654804/

   149.
   Anwar M.S., et al. To find out the Incidence of Erectile Dysfunction among patients of Stricture

   Number of the incidence of the incincidence of the incidence of the incidence of the inc
  - Urethra. Pak J Med Hlth Sci 2018. 12: 746. https://pjmhsonline.com/2018/april\_june/pdf/746.pdf
- Mondal, S., *et al.* Erectile dysfunction in anterior urethral strictures after urethroplasty with reference to vascular parameters. Med J Armed Forces India, 2016. 72: 344.
   <a href="https://pubmed.ncbi.nlm.nih.gov/27843181/">https://pubmed.ncbi.nlm.nih.gov/27843181/</a>
- 151. Blaschko, S.D., *et al.* De novo erectile dysfunction after anterior urethroplasty: a systematic review and meta-analysis. BJU Int, 2013. 112: 655. https://pubmed.ncbi.nlm.nih.gov/23924424/
- 152. Kaluzny, A., *et al.* Ejaculatory Disorders in Men With Urethral Stricture and Impact of Urethroplasty on the Ejaculatory Function: A Systematic Review. J Sex Med, 2018. 15: 974. https://pubmed.ncbi.nlm.nih.gov/29960631/
- 153. Browne, B.M., *et al.* Use of Alternative Techniques and Grafts in Urethroplasty. Urol Clin North Am, 2017. 44: 127.
  - https://pubmed.ncbi.nlm.nih.gov/27908367/
- 154. Gelman, J., *et al.* Posterior Urethral Strictures. Adv Urol, 2015. 2015: 628107. https://pubmed.ncbi.nlm.nih.gov/26691883/
- 155. Potts, B.A., *et al.* Intraurethral Steroids are a Safe and Effective Treatment for Stricture Disease in Patients with Biopsy Proven Lichen Sclerosus. J Urol, 2016. 195: 1790. https://pubmed.ncbi.nlm.nih.gov/26707511/
- 156. Anderson, K.M., *et al.* Management of the devastated posterior urethra and bladder neck: refractory incontinence and stenosis. Transl Androl Urol, 2015. 4: 60. https://pubmed.ncbi.nlm.nih.gov/26816811/
- 157. Simms, M.S., *et al.* Well leg compartment syndrome after pelvic and perineal surgery in the lithotomy position. Postgrad Med J, 2005. 81: 534. https://pubmed.ncbi.nlm.nih.gov/16085748/
- Jackson, M.J., *et al.* Defining a patient-reported outcome measure for urethral stricture surgery. Eur Urol, 2011. 60: 60.
  - https://pubmed.ncbi.nlm.nih.gov/21419566/
- 159. Breyer, B.N., *et al.* Comprehensive Qualitative Assessment of Urethral Stricture Disease: Toward the Development of a Patient Centered Outcome Measure. J Urol, 2017. 198: 1113. <u>https://pubmed.ncbi.nlm.nih.gov/28559007/</u>
- 160. Bonkat G, *et al.* Urological Infections, in EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2022., The European Association of Urology: Arnhem, The Netherlands. https://uroweb.org/guideline/urological-infections/
- 161. Lambert, E., *et al.* Validated uroflowmetry-based predictive model for the primary diagnosis of urethral stricture disease in men. Int J Urol, 2018. 25: 792. https://pubmed.ncbi.nlm.nih.gov/30021245/

162. Bishara S., et al. Can urodynamics distinguish betweenurethral strictures and Benign Prostatic Hyperplasia (BPH)?. J Clin Urol, 2015. 8: 274. https://journals.sagepub.com/doi/abs/10.1177/2051415814565371 163. Rosenbaum, C.M., et al. Management of Anterior Urethral Strictures in Adults: A Survey of Contemporary Practice in Germany. Urol Int, 2017. 99: 43. https://pubmed.ncbi.nlm.nih.gov/28601862/ Mahmud, S.M., et al. Is ascending urethrogram mandatory for all urethral strictures? J Pak Med 164. Assoc, 2008. 58: 429. https://pubmed.ncbi.nlm.nih.gov/18822639/ 165. Krukowski, J., et al. Comparison between cystourethrography and sonourethrography in preoperative diagnostic management of patients with anterior urethral strictures. Med Ultrason, 2018. 20: 436. https://pubmed.ncbi.nlm.nih.gov/30534649/ 166. Kalabhavi S., et al. Role of Sonourethrogram in Evaluation of Anterior Urethral Stricture and its Correlation with Retrograde Urethrogram and Intraoperative Findings-A Prospective Study. J Clin Diag Res, 2018. 12: PC01. https://www.researchgate.net/publication/326945990 167. Bach, P., et al. Independently interpreted retrograde urethrography does not accurately diagnose and stage anterior urethral stricture: the importance of urologist-performed urethrography. Urology, 2014. 83: 1190. https://pubmed.ncbi.nlm.nih.gov/24767528/ 168. Goel, A., et al. Antegrade urethrogram: A technique to visualize the proximal bulbous urethral segment in anterior urethral stricture. Indian J Urol, 2009. 25: 415. https://pubmed.ncbi.nlm.nih.gov/19881146/ 169. Sung, D.J., et al. Obliterative urethral stricture: MR urethrography versus conventional retrograde urethrography with voiding cystourethrography. Radiology, 2006. 240: 842. https://pubmed.ncbi.nlm.nih.gov/16857977/ 170. Kathpalia, R., et al. Effect of phallic stretch on length of bulbous urethral stricture during retrograde urethrography. Urol Int, 2014. 93: 63. https://pubmed.ncbi.nlm.nih.gov/24080710/ Buckley, J.C., et al. Impact of urethral ultrasonography on decision-making in anterior urethroplasty. 171. BJU Int, 2012. 109: 438. https://pubmed.ncbi.nlm.nih.gov/21615851/ 172. Bansal, A., et al. Urethro-venous intravasation: a rare complication of retrograde urethrogram. BMJ Case Rep, 2016. 2016. https://pubmed.ncbi.nlm.nih.gov/27045054/ Berna-Mestre, J.D., et al. Optimisation of sonourethrography: the clamp method. Eur Radiol, 2018. 173. 28: 1961. https://pubmed.ncbi.nlm.nih.gov/29247355/ 174. Shahrour, W., et al. The Benefits of Using a Small Caliber Ureteroscope in Evaluation and Management of Urethral Stricture. Adv Urol, 2018. 2018: 9137892. https://pubmed.ncbi.nlm.nih.gov/30584423/ 175. Bircan, M.K., et al. Diagnosis of urethral strictures: is retrograde urethrography still necessary? Int Urol Nephrol, 1996. 28: 801. https://pubmed.ncbi.nlm.nih.gov/9089050/ 176. Li, X., et al. Flexible cystoscope for evaluating pelvic fracture urethral distraction defects. Urol Int, 2012.89:402. https://pubmed.ncbi.nlm.nih.gov/23221433/ 177. Bryk, D.J., et al. Outpatient Ultrasound Urethrogram for Assessment of Anterior Urethral Stricture: Early Experience. Urology, 2016. 93: 203. https://pubmed.ncbi.nlm.nih.gov/26993351/ 178. Ravikumar, B.R., et al. A comparative study of ascending urethrogram and sono-urethrogram in the evaluation of stricture urethra. Int Braz J Urol, 2015. 41: 388. https://pubmed.ncbi.nlm.nih.gov/26005985/ 179. Talreja, S.M., et al. Comparison of sonoelastography with sonourethrography and retrograde urethrography in the evaluation of male anterior urethral strictures. Turk J Urol, 2016. 42: 84. https://pubmed.ncbi.nlm.nih.gov/27274893/ 180. Talreja, S.M., et al. 'Real-time sonoelastography' in anterior urethral strictures: A novel technique for assessment of spongiofibrosis. Cent Eur J Urol, 2016. 69: 417.

https://pubmed.ncbi.nlm.nih.gov/28127461/

181. Chen, L., et al. Three-Dimensional Computerized Model Based on the Sonourethrogram: A Novel Technique to Evaluate Anterior Urethral Stricture. J Urol, 2018. 199: 568. https://pubmed.ncbi.nlm.nih.gov/28866465/ Murugesan V.K., et al. Role of Magnetic Resonance Urethrography in Evaluation of Male Urethral 182. Stricture Against Conventional Retrograde Urethrography. J Clin Diagn Res, 2018. 12: 7. https://www.researchgate.net/publication/325867037 183. Fath El-Bab, T.K., et al. Magnetic resonance urethrography versus conventional retrograde urethrography in the evaluation of urethral stricture Comparison with surgical findings. Egypt J Radiol Nucl Med, 2015. 46: 199. https://www.researchgate.net/publication/276316898 184. El-Ghar, M.A., et al. MR urethrogram versus combined retrograde urethrogram and sonourethrography in diagnosis of urethral stricture. Eur J Radiol, 2010. 74: e193. https://pubmed.ncbi.nlm.nih.gov/19608363/ Oh, M.M., et al. Magnetic resonance urethrography to assess obliterative posterior urethral stricture: 185. comparison to conventional retrograde urethrography with voiding cystourethrography. J Urol, 2010. 183: 603. https://pubmed.ncbi.nlm.nih.gov/20018323/ 186. Horiguchi, A., et al. Pubourethral Stump Angle Measured on Preoperative Magnetic Resonance Imaging Predicts Urethroplasty Type for Pelvic Fracture Urethral Injury Repair. Urology, 2018. 112: 198. https://pubmed.ncbi.nlm.nih.gov/29158171/ 187. Bugeja, S., et al. Fistulation into the Pubic Symphysis after Treatment of Prostate Cancer: An Important and Surgically Correctable Complication. J Urol, 2016. 195: 391. https://pubmed.ncbi.nlm.nih.gov/26301787/ 188. Whybrow, P., et al. How Men Manage Bulbar Urethral Stricture by Concealing Urinary Symptoms. Qual Health Res, 2015. 25: 1435. https://pubmed.ncbi.nlm.nih.gov/25711843/ 189. Hofer, M.D., et al. Outcomes after urethroplasty for radiotherapy induced bulbomembranous urethral stricture disease. J Urol, 2014. 191: 1307. https://pubmed.ncbi.nlm.nih.gov/24333513/ 190. Fuchs, J.S., et al. Role of Chronic Suprapubic Tube in the Management of Radiation Induced Urethral Strictures. Urol Pract, 2017. 4: 479. https://www.auajournals.org/doi/10.1016/j.urpr.2016.10.004 191. Harrison, S.C., et al. British Association of Urological Surgeons' suprapubic catheter practice guidelines. BJU Int, 2011. 107: 77. https://pubmed.ncbi.nlm.nih.gov/21054755/ 192. Ferguson G.G., et al. Minimally invasive methods for bulbar urethral strictures: a survey of members of the American Urological Association. Urology, 2011. 78: 701. https://pubmed.ncbi.nlm.nih.gov/21762965/ 193. Ather M.H., et al. The Safety and Efficacy of Optical Urethrotomy Using a Spongiosum Block With Sedation: A Comparative Nonrandomized Study. J Urol, 2009. 181: 2134. https://pubmed.ncbi.nlm.nih.gov/19296978/ 194. Munks D.G., et al. Optical urethrotomy under local anaesthesia is a feasible option in urethral stricture disease. Trop Doct, 2010. 40: 31. https://pubmed.ncbi.nlm.nih.gov/19850602/ 195. Uzun H., et al. Internal Urethrotomy Under Local Urethral Anaesthesia Is Feasible With Sedation and Analgesia. Nephro-Urol Mon, 2012. 4: 636. https://pubmed.ncbi.nlm.nih.gov/23573506/ 196. Steenkamp J.W., et al. Internal Urethrotomy versus dilatation as treatment for male urethral strictures: a prospective, randomised comparison. J Urol 1997. 157: 98. https://pubmed.ncbi.nlm.nih.gov/8976225/ 197. Wong, S.S., et al. Simple urethral dilatation, endoscopic urethrotomy, and urethroplasty for urethral stricture disease in adult men. The Cochrane database of systematic reviews, 2012. 12: CD006934. https://pubmed.ncbi.nlm.nih.gov/23235635/ 198. Stephenson, R., et al. Open urethroplasty versus endoscopic urethrotomy -- clarifying the management of men with recurrent urethral stricture (the OPEN trial): study protocol for a randomised controlled trial. Trials, 2015. 16: 600. https://pubmed.ncbi.nlm.nih.gov/26718754/ 199. Diamond, D.A., et al. What is the optimal surgical strategy for bulbous urethral stricture in boys? J Urol, 2009. 182: 1755. https://pubmed.ncbi.nlm.nih.gov/19692008/

200.	Santucci R., et al. Urethrotomy Has a Much Lower Success Rate Than Previously Reported. J Urol,
	2010. 183: 1859.
	https://pubmed.ncbi.nlm.nih.gov/20303110/
201.	Pansadoro V., et al. Internal urethrotomy in the management of anterior urethral strictures: long term
	follow-up. J Urol, 1996. 156: 73.
	https://pubmed.ncbi.nlm.nih.gov/8648841/
202.	Kluth L.A., et al. Direct Vision Internal Urethrotomy for Short Anterior Urethral Strictures and Beyond:
202.	
	Success Rates, Predictors of Treatment Failure, and Recurrence Management. Urology, 2017.
	106: 210.
	https://pubmed.ncbi.nlm.nih.gov/28479479/
203.	Barbagli G., et al. Focus on Internal Urethrotomy as Primary Treatment for Untreated Bulbar Urethral
	Strictures: Results from a Multivariable Analysis. Eur Urol Focus, 2020. 6: 164.
	https://pubmed.ncbi.nlm.nih.gov/30409684/
204.	Al Taweel W., et al. Visual Internal Urethrotomy for Adult Male Urethral Stricture Has Poor Long-Term
	Results. Adv Urol, 2015: 1.
	https://pubmed.ncbi.nlm.nih.gov/26494995/
205.	Pal D.K., <i>et al.</i> Direct visual internal urethrotomy: Is it a durable treatment option? Urol Ann, 2017. 9: 18.
	https://pubmed.ncbi.nlm.nih.gov/28216923/
206.	Launonen, E., et al. Role of visual internal urethrotomy in pediatric urethral strictures. J Pediatr Urol,
200.	2014. 10: 545.
	https://pubmed.ncbi.nlm.nih.gov/24388665/
007	Redon-Galvez, L., et al. Predictors of urethral stricture recurrence after endoscopic urethrotomy.
207.	
	Actas Urol Esp, 2016. 40: 529.
	https://pubmed.ncbi.nlm.nih.gov/27207599/
208.	Harraz A.M., et al. Is there a way to predict failure after direct vision internal urethrotomy for single
	and short bulbar urethral strictures? Arab J Urol, 2015. 13: 277.
	https://pubmed.ncbi.nlm.nih.gov/26609447/
209.	Goulao, B., et al. Surgical Treatment for Recurrent Bulbar Urethral Stricture: A Randomised Open-
	label Superiority Trial of Open Urethroplasty Versus Endoscopic Urethrotomy (the OPEN Trial). Eur
	Urol, 2020.
	https://pubmed.ncbi.nlm.nih.gov/32636099/
210.	Brown, E.T., et al. Direct visual internal urethrotomy for isolated, post-urethroplasty strictures: a
	retrospective analysis. Ther Adv Urol, 2017. 9: 39.
	https://pubmed.ncbi.nlm.nih.gov/28203286/
211.	Rosenbaum, C.M., et al. Internal urethrotomy in patients with recurrent urethral stricture after buccal
	mucosa graft urethroplasty. World J Urol, 2015. 33: 1337.
	https://pubmed.ncbi.nlm.nih.gov/25428791/
212.	Farrell, M.R., et al. Internal Urethrotomy With Intralesional Mitomycin C: An Effective Option for
212.	Endoscopic Management of Recurrent Bulbar and Bulbomembranous Urethral Strictures. Urology,
	2017. 110: 223.
	https://pubmed.ncbi.nlm.nih.gov/28735714/
213.	Jin, T., et al. Safety and efficacy of laser and cold knife urethrotomy for urethral stricture. Chin Med
	J (Engl), 2010. 123: 1589.
	https://pubmed.ncbi.nlm.nih.gov/20819517/
214.	Heyns, C.F., et al. Treatment of male urethral strictures: is repeated dilation or internal urethrotomy
	useful? J Urol, 1998. 160: 356.
	https://pubmed.ncbi.nlm.nih.gov/9679876/
215.	Cotta, B.H., et al. Endoscopic Treatment of Urethral Stenosis. The Urologic clinics of North America,
	2017. 44: 19.
	https://pubmed.ncbi.nlm.nih.gov/27908368/
216.	Buckley, J.C., et al. SIU/ICUD Consultation on Urethral Strictures: Dilation, internal urethrotomy, and
	stenting of male anterior urethral strictures. Urology, 2014. 83: S18.
	https://pubmed.ncbi.nlm.nih.gov/24286602/
017	
217.	Shaw, N.M., et al. Endoscopic Management of Urethral Stricture: Review and Practice Algorithm for
	Management of Male Urethral Stricture Disease. Curr Urol Rep , 2018. 19: 19.
040	https://pubmed.ncbi.nlm.nih.gov/29479640/
218.	Torres Castellanos, L., et al. Evaluation of the Efficacy and Safety of Laser versus Cold Knife
	Urethrotomy in the Management of Patients with Urethral Strictures: A Systematic Review and
	Meta-Analysis of Randomized Clinical Trials. Urol Int, 2017. 99: 453.
	https://pubmed.pebi.plm.pib.gov/28607506/

https://pubmed.ncbi.nlm.nih.gov/28697506/

219.	Chen, J., et al. Comparison of holmium laser combined ureteroscopy and cold knife urethrotomy in
	treatment of simple urethral stricture: a 5 year follow-up study. Int J Clin Exp Med 2018. 11: 13792.
	http://www.ijcem.com/files/ijcem0079991.pdf
220.	Yenice, M.G., et al. Comparison of cold-knife optical internal urethrotomy and holmium: YAG laser
	internal urethrotomy in bulbar urethral strictures. Cent Eur J Urol, 2018. 71: 114.
	https://pubmed.ncbi.nlm.nih.gov/29732217/
221.	Holzhauer, C., et al. Is the laser mightier than the sword? A comparative study for the urethrotomy.
	World J Urol, 2018. 36: 663.
	https://pubmed.ncbi.nlm.nih.gov/29332261/
222.	Cecen, K., et al. PlasmaKinetic versus cold knife internal urethrotomy in terms of recurrence rates: a
	prospective randomized study. Urol Int, 2014. 93: 460.
000	https://pubmed.ncbi.nlm.nih.gov/25138990/
223.	Ozcan, L., et al. Internal urethrotomy versus plasmakinetic energy for surgical treatment of urethral
	stricture. Arch Ital Urol Androl, 2015. 87: 161.
	https://pubmed.ncbi.nlm.nih.gov/26150037/
224.	Basok, E.K., et al. Can bipolar vaporization be considered an alternative energy source in the
	endoscopic treatment of urethral strictures and bladder neck contracture? Int Braz J Urol, 2008.
	34: 577.
	https://pubmed.ncbi.nlm.nih.gov/18986561/
225.	Graversen, P.H., et al. Erectile dysfunction following direct vision internal urethrotomy. Scand J Urol
	Nephrol, 1991. 25: 175.
	https://pubmed.ncbi.nlm.nih.gov/1947846/
226.	Yu, S.C., et al. High-pressure balloon dilation for male anterior urethral stricture: single-center
	experience. J Zhejiang Univ Sci B, 2016. 17: 722.
	https://pubmed.ncbi.nlm.nih.gov/27604864/
227.	Horiguchi, A., et al. Do Transurethral Treatments Increase the Complexity of Urethral Strictures?
	J Urol, 2018. 199: 508.
	https://pubmed.ncbi.nlm.nih.gov/28866464/
228.	Hudak, S.J., et al. Repeat transurethral manipulation of bulbar urethral strictures is associated with
	increased stricture complexity and prolonged disease duration. J Urol, 2012. 187: 1691.
	https://pubmed.ncbi.nlm.nih.gov/22425115/
229.	Akkoc, A., et al. Use and outcomes of amplatz renal dilator for treatment of urethral strictures. Int
2201	Braz J Urol, 2016. 42: 356.
	https://pubmed.ncbi.nlm.nih.gov/27256192/
230.	Nomikos, M., et al. The use of Amplatz renal dilators in the minimally invasive management of
200.	complex urethral strictures. Cent Eur J Urol, 2017. 70: 301.
	https://pubmed.ncbi.nlm.nih.gov/29104795/
001	Chhabra, J.S., <i>et al.</i> Urethral Balloon Dilatation: Factors Affecting Outcomes. Urol Int, 2016. 96: 427.
231.	· · · · · · · · · · · · · · · · · · ·
000	https://pubmed.ncbi.nlm.nih.gov/26845345/
232.	Kallidonis, P., et al. The use of S-curved coaxial dilator for urethral dilatation: Experience of a tertiary
	department. Urol Ann, 2018. 10: 375.
	https://pubmed.ncbi.nlm.nih.gov/30386089/
233.	Jackson, M.J., et al. Intermittent self-dilatation for urethral stricture disease in males. The Cochrane
	database of systematic reviews, 2014: CD010258.
	https://pubmed.ncbi.nlm.nih.gov/25523166/
234.	Greenwell, T.J., et al. Clean intermittent self-catheterization does not appear to be effective in the
	prevention of urethral stricture recurrence. Scand J Urol, 2016. 50: 71.
	https://pubmed.ncbi.nlm.nih.gov/26428415/
235.	Bodker A., et al. Treatment of recurrent urethral stricture by internal urethrotomy and intermittent
	self-catheterisation: A controlled study of a new therapy. J Urol., 1992. 148: 308.
	https://pubmed.ncbi.nlm.nih.gov/1635124/
236.	Kjaeergard B., et al. Prevention of urethral strictur 1635124e recurrence using clean intermittent self
	cathterisation. Jr J Urol., 1994. 73: 692.
	https://pubmed.ncbi.nlm.nih.gov/8032838/
237.	Khan S,, et al. Role of clean intermittent self catheterisation (CISC) in the prevention of recurrent
	urethral srtictures after internal optical urethrotomy. J Ayub Med Coll, JAMC, 2011. 23: 22.
	https://pubmed.ncbi.nlm.nih.gov/24800335/
238.	Rijal, A., et al. Intermittent self dilatationstill a viable option for treatment of urethral stricture
_00.	disease. Nepal Med Coll J, NMCJ, 2008. 10: 155.
	https://pubmed.ncbi.nlm.nih.gov/19253858/

- Zhang, K., *et al.* Efficacy and safety of local steroids for urethra strictures: a systematic review and meta-analysis. J Endourol, 2014. 28: 962.
   https://pubmed.ncbi.nlm.nih.gov/24745607/
- 240. Ergun, O., *et al.* A prospective, randomized trial to evaluate the efficacy of clean intermittent catheterization versus triamcinolone ointment and contractubex ointment of catheter following internal urethrotomy: long-term results. Int Urol Nephrol, 2015. 47: 909. https://pubmed.ncbi.nlm.nih.gov/25913052/
- 241. Regmi, S., *et al.* Efficacy of Use of Triamcinolone Ointment for Clean Intermittent Self Catheterization following Internal Urethrotomy. JNMA, 2018. 56: 745. https://pubmed.ncbi.nlm.nih.gov/30387461/
- 242. Moradi, M., *et al.* Safety and efficacy of Intraurethral Mitomycin C Hydrogel for prevention of posttraumatic anterior urethral stricture recurrence after internal urethrotomy. J Inj Violence Res, 2016. 8: 75. <u>https://pubmed.ncbi.nlm.nih.gov/27093204/</u>
- 243. Ali, L., *et al.* Efficacy of mitomycin C in reducing recurrence of anterior urethral stricture after internal optical urethrotomy. Korean J Urol, 2015. 56: 650.

https://pubmed.ncbi.nlm.nih.gov/26366278/

244. Kumar, S., *et al.* Efficacy of Optical Internal Urethrotomy and Intralesional Injection of Vatsala-Santosh PGI Tri-Inject (Triamcinolone, Mitomycin C, and Hyaluronidase) in the Treatment of Anterior Urethral Stricture. Adv Urol, 2014. 2014: 192710.

<u>https://pubmed.ncbi.nlm.nih.gov/25349604/</u>
 Redshaw, J.D., *et al.* Intralesional injection of mitomycin C at transurethral incision of bladder neck

- contracture may offer limited benefit: TURNS Study Group. J Urol, 2015. 193: 587. https://pubmed.ncbi.nlm.nih.gov/25200807/
- 246. Rezaei, M., *et al.* The effect of platelet-rich plasma injection on post-internal urethrotomy stricture recurrence. World J Urol, 2019. 37: 1959.

https://pubmed.ncbi.nlm.nih.gov/30535714/

- 247. Abdallah, M.M., *et al.* Thermo-expandable metallic urethral stents for managing recurrent bulbar urethral strictures: To use or not? Arab J Urol, 2013. 11: 85. https://pubmed.ncbi.nlm.nih.gov/26579252/
- 248. Wong, E., *et al.* Durability of Memokath urethral stent for stabilisation of recurrent bulbar urethral strictures -- medium-term results. BJU Int, 2014. 113 Suppl 2: 35. https://pubmed.ncbi.nlm.nih.gov/24053476/
- 249. Atesci, Y.Z., *et al.* Long-term results of permanent memotherm urethral stent in the treatment of recurrent bulbar urethral strictures. Int Braz J Urol, 2014. 40: 80. https://pubmed.ncbi.nlm.nih.gov/24642153/
- 250. Temeltas, G., *et al.* The long-term results of temporary urethral stent placement for the treatment of recurrent bulbar urethral stricture disease? Int Braz J Urol, 2016. 42: 351. https://pubmed.ncbi.nlm.nih.gov/27256191/
- 251. Jordan, G.H., *et al.* Effect of a temporary thermo-expandable stent on urethral patency after dilation or internal urethrotomy for recurrent bulbar urethral stricture: results from a 1-year randomized trial. J Urol, 2013. 190: 130.

https://pubmed.ncbi.nlm.nih.gov/23313208/

- 252. Erickson, B.A., *et al.* Management for prostate cancer treatment related posterior urethral and bladder neck stenosis with stents. J Urol, 2011. 185: 198. <u>https://pubmed.ncbi.nlm.nih.gov/21074796/</u>
- 253. Sertcelik, M.N., *et al.* Long-term results of permanent urethral stent Memotherm implantation in the management of recurrent bulbar urethral stenosis. BJU Int, 2011. 108: 1839.
- https://pubmed.ncbi.nlm.nih.gov/21756278/

   254.
   Jung, H.S., et al. Early experience with a thermo-expandable stent (memokath) for the management of recurrent urethral stricture. Korean J Urol, 2013. 54: 851.
- <u>https://pubmed.ncbi.nlm.nih.gov/24363867/</u>
   255. Buckley, J.C., *et al.* Removal of endoprosthesis with urethral preservation and simultaneous urethral reconstruction. J Urol, 2012. 188: 856.

https://pubmed.ncbi.nlm.nih.gov/22819407/

256. Angulo, J.C., *et al.* Urethroplasty After Urethral Urolume Stent: An International Multicenter Experience. Urology, 2018. 118: 213.

https://pubmed.ncbi.nlm.nih.gov/29751026/

257. Chapple, C.R., *et al.* Management of the failure of a permanently implanted urethral stent-a therapeutic challenge. Eur Urol, 2008. 54: 665. <u>https://pubmed.ncbi.nlm.nih.gov/18054424/</u>

258.	Angulo, J.C., <i>et al.</i> Urethral reconstruction in patients previously treated with Memokath urethral endoprosthesis. Acta Urol Esp, 2019. 43: 26.
259.	https://pubmed.ncbi.nlm.nih.gov/30100140/ Ekerhult, T.O., <i>et al.</i> Limited experience, high body mass index and previous urethral surgery are risk factors for failure in open urethroplasty due to penile strictures. Scand J Urol, 2015. 49: 415.
260.	https://pubmed.ncbi.nlm.nih.gov/25854925/ Joshi, P.M., <i>et al</i> . A novel composite two-stage urethroplasty for complex penile strictures: A multicenter experience. Indian J Urol, 2017. 33: 155.
	https://pubmed.ncbi.nlm.nih.gov/28469305/
261.	Kozinn, S.I., <i>et al.</i> Management of complex anterior urethral strictures with multistage buccal mucosa graft reconstruction. Urology, 2013. 82: 718. https://pubmed.ncbi.nlm.nih.gov/23876581/
262.	Pfalzgraf, D., <i>et al.</i> Redo-urethroplasty: comparison of early functional results and quality of life in penile and bulbar strictures. World J Urol, 2014. 32: 1191.
263.	https://pubmed.ncbi.nlm.nih.gov/24154812/ Kulkarni, S., et al. Lichen sclerosus of the male genitalia and urethra: surgical options and results in a multicenter international experience with 215 patients. Eur Urol, 2009. 55: 945. https://pubmed.ncbi.nlm.nih.gov/18691809/
264.	Shukla, A.R., <i>et al.</i> The 2-stage hypospadias repair. Is it a misnomer? J Urol, 2004. 172: 1714. https://pubmed.ncbi.nlm.nih.gov/15371797/
265.	Mori, R.L., <i>et al.</i> Staged urethroplasty in the management of complex anterior urethral stricture disease. Transl Androl Urol, 2015. 4: 29. https://pubmed.ncbi.nlm.nih.gov/26816806/
266.	Horiguchi, A. Substitution urethroplasty using oral mucosa graft for male anterior urethral stricture disease: Current topics and reviews. Int J Urol, 2017. 24: 493. https://pubmed.ncbi.nlm.nih.gov/28600871/
267.	Mangera, A., <i>et al.</i> Management of anterior urethral stricture: an evidence-based approach. Curr Opin Urol, 2010. 20: 453. https://pubmed.ncbi.nlm.nih.gov/20827208/
268.	Mangera, A., et al. A systematic review of graft augmentation urethroplasty techniques for the treatment of anterior urethral strictures. Eur Urol, 2011. 59: 797.
269.	https://pubmed.ncbi.nlm.nih.gov/21353379/ Barbagli, G., <i>et al.</i> Current controversies in reconstructive surgery of the anterior urethra: a clinical overview. Int Braz J Urol, 2012. 38: 307.
270.	https://pubmed.ncbi.nlm.nih.gov/22765862/ Hudak, S.J. Use of overlapping buccal mucosa graft urethroplasty for complex anterior urethral strictures. Transl Androl Urol, 2015. 4: 16. https://pubmed.ncbi.nlm.nih.gov/26813234/
271.	Martins, F.E., <i>et al.</i> Management of Long-Segment and Panurethral Stricture Disease. Adv Urol, 2015. 2015: 853914. https://pubmed.ncbi.nlm.nih.gov/26779259/
272.	Aldaqadossi, H., <i>et al.</i> Dorsal onlay (Barbagli technique) versus dorsal inlay (Asopa technique) buccal mucosal graft urethroplasty for anterior urethral stricture: A prospective randomized study. Int J Urol, 2014. 21: 185. https://pubmed.ncbi.nlm.nih.gov/23931150/
273.	Barbagli, G., <i>et al.</i> Retrospective outcome analysis of one-stage penile urethroplasty using a flap or graft in a homogeneous series of patients. BJU Int, 2008. 102: 853. https://pubmed.ncbi.nlm.nih.gov/18485036/
274.	Barbagli, G., <i>et al.</i> Long-term followup and deterioration rate of anterior substitution urethroplasty. J Urol, 2014. 192: 808. https://pubmed.ncbi.nlm.nih.gov/24533999/
275.	Fu, Q., <i>et al.</i> Substitution urethroplasty for anterior urethral stricture repair: comparison between lingual mucosa graft and pedicled skin flap. Scand J Urol, 2017. 51: 479. https://pubmed.ncbi.nlm.nih.gov/28738760/
276.	Goel, A., <i>et al.</i> Buccal mucosal graft urethroplasty for penile stricture: only dorsal or combined dorsal and ventral graft placement? Urology, 2011. 77: 1482. https://pubmed.ncbi.nlm.nih.gov/21354596/
277.	Xu, Y.M., <i>et al.</i> Outcome of 1-stage urethroplasty using oral mucosal grafts for the treatment of urethral strictures associated with genital lichen sclerosus. Urology, 2014. 83: 232. https://pubmed.ncbi.nlm.nih.gov/24200196/

278. Jinga, V., et al. Ventral buccal mucosa graft urethroplasty for penile urethral strictures: a predictable failure? Chirurgia (Bucur), 2013. 108: 245. https://pubmed.ncbi.nlm.nih.gov/23618576/ 279. Mellon, M.J., et al. Ventral onlay buccal mucosa urethroplasty: a 10-year experience. Int J Urol, 2014. 21: 190. https://pubmed.ncbi.nlm.nih.gov/23980634/ 280. Lumen, N., et al. Urethroplasty for urethral strictures: quality assessment of an in-home algorithm. Int J Urol, 2010. 17: 167. https://pubmed.ncbi.nlm.nih.gov/20070412/ 281. Salako, A.A., et al. Pendulous urethral stricture: peculiarities and relevance of longitudinal penile fascio-cutaneous flap reconstruction in poor resource community. Urol J, 2014. 10: 1088. https://pubmed.ncbi.nlm.nih.gov/24469655/ Jiang, J., et al. Combined Dorsal Plus Ventral Double-Graft Urethroplasty in Anterior Urethral 282. Reconstruction. Indian J Surg, 2015. 77: 996. https://pubmed.ncbi.nlm.nih.gov/27011497/ 283. Dogra, P.N., et al. Erectile dysfunction after anterior urethroplasty: a prospective analysis of incidence and probability of recovery--single-center experience. Urology, 2011. 78: 78. https://pubmed.ncbi.nlm.nih.gov/21550645/ 284. lqbal, Z., et al. Comparison of onlay and circumferential tubular fasciocutaneous penile skin flap for penile urethral strictures. J. Med. Sci, 2015. 23: 134. https://www.researchgate.net/publication/321342370 285. Peterson, A.C., et al. Heroic measures may not always be justified in extensive urethral stricture due to lichen sclerosus (balanitis xerotica obliterans). Urology, 2004. 64: 565. https://pubmed.ncbi.nlm.nih.gov/15351594/ 286. Palminteri, E., et al. Urethral reconstruction in lichen sclerosus. Curr Opin Urol, 2012. 22: 478. https://pubmed.ncbi.nlm.nih.gov/22965317/ 287. Chapple, C., et al. SIU/ICUD Consultation on Urethral Strictures: The management of anterior urethral stricture disease using substitution urethroplasty. Urology, 2014. 83: S31. https://pubmed.ncbi.nlm.nih.gov/24411214/ 288. Shakir, N.A., et al. Excision and Primary Anastomosis Reconstruction for Traumatic Strictures of the Pendulous Urethra. Urology, 2019. 125: 234. https://pubmed.ncbi.nlm.nih.gov/30125648/ 289. Hampson, L.A., et al. Male urethral strictures and their management. Nat Rev Urol, 2014. 11: 43. https://pubmed.ncbi.nlm.nih.gov/24346008/ 290. Kulkarni, S.B., et al. Redo hypospadias surgery: current and novel techniques. Res Rep Urol, 2018. 10: 117. https://pubmed.ncbi.nlm.nih.gov/30320039/ 291. Craig, J.R., et al. Management of adults with prior failed hypospadias surgery. Transl Androl Urol, 2014. 3: 196. https://pubmed.ncbi.nlm.nih.gov/26816767/ 292. Rourke, K., et al. Transitioning patients with hypospadias and other penile abnormalities to adulthood: What to expect? Can Urol Assoc J, 2018. 12: S27. https://pubmed.ncbi.nlm.nih.gov/29681271/ 293. Lee, O.T., et al. Predictors of secondary surgery after hypospadias repair: a population based analysis of 5,000 patients. J Urol, 2013. 190: 251. https://pubmed.ncbi.nlm.nih.gov/23376710/ 294. Spilotros, M., et al. Penile urethral stricture disease. J Clin Urol, 2018. 12: 145. https://journals.sagepub.com/doi/10.1177/2051415818774227 295. Wu, M., et al. Management of failed hypospadias: choosing the right method and achieving optimal results. Int Urol Nephrol, 2018. 50: 1795. https://pubmed.ncbi.nlm.nih.gov/30121720/ 296. Kiss, A., et al. Long-term psychological and sexual outcomes of severe penile hypospadias repair. J Sex Med, 2011. 8: 1529. https://pubmed.ncbi.nlm.nih.gov/21091883/ 297. Morrison, C.D., et al. Surgical Approaches and Long-Term Outcomes in Adults with Complex Reoperative Hypospadias Repair. J Urol, 2018. 199: 1296. https://pubmed.ncbi.nlm.nih.gov/29198998/ 298. Myers, J.B., et al. Treatment of adults with complications from previous hypospadias surgery. J Urol, 2012. 188: 459. https://pubmed.ncbi.nlm.nih.gov/22698621/

- 299. Aldamanhori, R.B., et al. Contemporary outcomes of hypospadias retrieval surgery in adults. BJU Int, 2018. 122: 673. https://pubmed.ncbi.nlm.nih.gov/29671932/
- 300. Pandey, A., et al. The Staged Urethroplasty with Vascularised Scrotal Flap and Buccal Mucosa Graft after Failed Hypospadias Surgery: A Reliable Technique with a Novel Tool. Urol Int, 2017. 99: 36. <u>https://pubmed.ncbi.nlm.nih.gov/28285314/</u>
- 301. Li, H.B., *et al.* One-stage dorsal lingual mucosal graft urethroplasty for the treatment of failed hypospadias repair. Asian J Androl, 2016. 18: 467. https://pubmed.ncbi.nlm.nih.gov/26228042/
- Bastian, P.J., *et al.* Single-stage dorsal inlay for reconstruction of recurrent peno-glandular stenosis.
   World J Urol, 2012. 30: 715.
   <a href="https://pubmed.ncbi.nlm.nih.gov/21989815/">https://pubmed.ncbi.nlm.nih.gov/21989815/</a>
- 303. Xu, Y.M., *et al.* Intermediate-Term Outcomes and Complications of Long Segment Urethroplasty with Lingual Mucosa Grafts. J Urol, 2017. 198: 401.
   https://pubmed.ncbi.nlm.nih.gov/28286073/
- Xu, Y.M., *et al.* Treatment of urethral strictures using lingual mucosas urethroplasty: experience of 92 cases. Chin Med J (Engl), 2010. 123: 458.
   https://pubmed.ncbi.nlm.nih.gov/20193487/
- Barbagli, G., *et al.* Correlation Between Primary Hypospadias Repair and Subsequent Urethral Strictures in a Series of 408 Adult Patients. Eur Urol Focus, 2017. 3: 287. https://pubmed.ncbi.nlm.nih.gov/28753858/
- 306. Liu, Y., *et al.* One-stage dorsal inlay oral mucosa graft urethroplasty for anterior urethral stricture. BMC Urol, 2014. 14: 35.
  - https://pubmed.ncbi.nlm.nih.gov/24885070/
- 307. Warner, J.N., et al. A Multi-institutional Evaluation of the Management and Outcomes of Longsegment Urethral Strictures. Urology, 2015. 85: 1483. https://pubmed.ncbi.nlm.nih.gov/25868738/
- 308. Blaschko, S.D., *et al.* Repeat urethroplasty after failed urethral reconstruction: outcome analysis of 130 patients. J Urol, 2012. 188: 2260.
  - https://pubmed.ncbi.nlm.nih.gov/23083654/
- 309. Belsante, M.J., *et al.* The contemporary management of urethral strictures in men resulting from lichen sclerosus. Transl Androl Urol, 2015. 4: 22. <u>https://pubmed.ncbi.nlm.nih.gov/26816805/</u>
- 310. Treiyer, A., *et al.* [Treatment of urethral meatus stenosis due to Balanitis xerotic obliterans. Long term results using the meatoplasty of Malone]. Actas Urol Esp, 2011. 35: 494. https://pubmed.ncbi.nlm.nih.gov/21514696/
- Babu, P., *et al.* Evaluation of Jordan's meatoplasty for the treatment of fossa navicularis strictures. A retrospective study. Cent Eur J Urol, 2017. 70: 103.
   https://pubmed.ncbi.nlm.nih.gov/28461997/
- 312. Meeks, J.J., *et al.* Distal urethroplasty for isolated fossa navicularis and meatal strictures. BJU Int, 2012. 109: 616.
  - https://pubmed.ncbi.nlm.nih.gov/21615852/
- 313. Tijani, K.H., *et al.* Dorsal Island Penile Fasciocutaneous Flap for Fossa Navicularis and Meatal Strictures: Short and Intermediate Term Outcome in West African Men. Urol J, 2015. 12: 2267. https://pubmed.ncbi.nlm.nih.gov/26341770/
- 314. Onol, S.Y., *et al.* Reconstruction of distal urethral strictures confined to the glans with circular buccal mucosa graft. Urology, 2012. 79: 1158.
- https://pubmed.ncbi.nlm.nih.gov/2244949/

   315.
   Campos-Juanatey, F., et al. Single-stage tubular urethral reconstruction using oral grafts is an alternative to classical staged approach for selected penile urethral strictures. Asian J Androl, 2020. 22: 134.
  - https://pubmed.ncbi.nlm.nih.gov/31441450/
- 316. Morey, A.F., et al. Proximal bulbar urethroplasty via extended anastomotic approach--what are the limits? J Urol, 2006. 175: 2145. <u>https://pubmed.ncbi.nlm.nih.gov/16697823/</u>
- 317. Morey, A.F., *et al.* SIU/ICUD Consultation on Urethral Strictures: Anterior urethra--primary anastomosis. Urology, 2014. 83: S23. https://pubmed.ncbi.nlm.nih.gov/24373726/

- 318. Ekerhult, T.O., *et al.* Low risk of sexual dysfunction after transection and nontransection urethroplasty for bulbar urethral stricture. J Urol, 2013. 190: 635. https://pubmed.ncbi.nlm.nih.gov/23485502/
- Chen, M.L., *et al.* Substitution urethroplasty is as successful as anastomotic urethroplasty for short bulbar strictures. Can J Urol, 2014. 21: 7565.
   https://pubmed.ncbi.nlm.nih.gov/25483766/
- 320. Suh, J.G., *et al.* Surgical Outcome of Excision and End-to-End Anastomosis for Bulbar Urethral Stricture. Korean J Urol, 2013. 54: 442.
- <u>https://pubmed.ncbi.nlm.nih.gov/23878686/</u>
   Siegel, J.A., *et al.* Repeat Excision and Primary Anastomotic Urethroplasty for Salvage of Recurrent Bulbar Urethral Stricture. J Urol, 2015. 194: 1316.

https://pubmed.ncbi.nlm.nih.gov/26003205/

- 322. Granieri, M.A., *et al.* Critical Analysis of Patient-reported Complaints and Complications After Urethroplasty for Bulbar Urethral Stricture Disease. Urology, 2015. 85: 1489. https://pubmed.ncbi.nlm.nih.gov/25868735/
- 323. Chapman, D., *et al.* Independent Predictors of Stricture Recurrence Following Urethroplasty for Isolated Bulbar Urethral Strictures. J Urol, 2017. 198: 1107. https://pubmed.ncbi.nlm.nih.gov/28483575/
- 324. Levy, M., *et al.* The Impact of Age on Urethroplasty Success. Urology, 2017. 107: 232. https://pubmed.ncbi.nlm.nih.gov/28579068/
- 325. Akyuz, M., *et al.* Characteristics of the urethroplasty and our approach-Experience in patients with urethral stricture. Turk J Urol, 2019. 45: 307.
- <u>https://pubmed.ncbi.nlm.nih.gov/30468425/</u>
   Barbagli, G., *et al.* Treatments of 1242 bulbar urethral strictures: multivariable statistical analysis of results. World J Urol, 2019. 37: 1165.

https://pubmed.ncbi.nlm.nih.gov/30220045/

- 327. Ekerhult, T.O., *et al.* Sclerosis as a predictive factor for failure after bulbar urethroplasty: a prospective single-centre study. Scand J Urol, 2018. 52: 302. https://pubmed.ncbi.nlm.nih.gov/30382795/
- 328. Kahokehr, A.A., *et al.* A Critical Analysis of Bulbar Urethroplasty Stricture Recurrence: Characteristics and Management. J Urol, 2018. 200: 1302.

https://pubmed.ncbi.nlm.nih.gov/30012364/

- 329. Sawant, A.S., *et al.* An Audit of Urethroplasty Techniques used for Managing Anterior Urethral Strictures at a Tertiary Care Teaching Institute-What We Learned. J Clin Diagn Res, 2018. 12: PC17. <u>https://www.researchgate.net/publication/323677279</u>
- 330. Waterloos, M., et al. Excision and Primary Anastomosis for Short Bulbar Strictures: Is It Safe to Change from the Transecting towards the Nontransecting Technique? Biomed Res Int, 2018. 2018: 3050537.

https://pubmed.ncbi.nlm.nih.gov/30515389/

- 331. Chapman, D.W., *et al.* Non-Transecting Techniques Reduce Sexual Dysfunction After Anastomotic Bulbar Urethroplasty: Results of a Multi-Institutional Comparative Analysis. J Urol, 2018. https://pubmed.ncbi.nlm.nih.gov/30266331/
- 332. Ivaz, S., *et al.* The Nontransecting Approach to Bulbar Urethroplasty. Urol Clin North Am, 2017. 44: 57.

https://pubmed.ncbi.nlm.nih.gov/27908372/

333. Horiguchi, A., *et al.* Surgical and patient-reported outcomes of urethroplasty for bulbar stricture due to a straddle injury. World J Urol, 2020. 38: 1805.

https://pubmed.ncbi.nlm.nih.gov/31559477/

- 334. Beysens, M., et al. Anastomotic Repair versus Free Graft Urethroplasty for Bulbar Strictures: A Focus on the Impact on Sexual Function. Adv Urol, 2015. 2015: 912438. <u>https://pubmed.ncbi.nlm.nih.gov/26494997/</u>
- 335. Barbagli, G., et al. Long-term followup of bulbar end-to-end anastomosis: a retrospective analysis of 153 patients in a single center experience. J Urol, 2007. 178: 2470. https://pubmed.ncbi.nlm.nih.gov/17937939/
- 336. Jordan, G.H., *et al.* The technique of vessel sparing excision and primary anastomosis for proximal bulbous urethral reconstruction. J Urol, 2007. 177: 1799. https://pubmed.ncbi.nlm.nih.gov/17437823/
- 337. Andrich, D.E., *et al.* Non-transecting anastomotic bulbar urethroplasty: a preliminary report. BJU Int, 2012. 109: 1090.

https://pubmed.ncbi.nlm.nih.gov/21933325/

338.	Virasoro, R., <i>et al.</i> International multi-institutional experience with the vessel-sparing technique to reconstruct the proximal bulbar urethra: mid-term results. World J Urol, 2015. 33: 2153.
339.	https://pubmed.ncbi.nlm.nih.gov/25690318/ Elkady, E., <i>et al.</i> Bulbospongiosus Muscle Sparing Urethroplasty Versus Standard Urethroplasty: A Comparative Study. Urology, 2019. 126: 217.
	https://pubmed.ncbi.nlm.nih.gov/30605695/
340.	Yuri, P., <i>et al.</i> Comparison Between End-to-end Anastomosis and Buccal Mucosa Graft in Short Segment Bulbar Urethral Stricture: a Meta-analysis Study. Acta Med Indones, 2016. 48: 17. <u>https://pubmed.ncbi.nlm.nih.gov/27241540/</u>
341.	Choudhary, A.K., et al. Is anastomotic urethroplasty is really superior than BMG augmented dorsal
0111	onlay urethroplasty in terms of outcomes and patient satisfaction: Our 4-year experience. Can Urol Assoc J, 2015. 9: E22.
	https://pubmed.ncbi.nlm.nih.gov/25624962/
342.	Haines, T., <i>et al.</i> The effect of urethral transection on erectile function after anterior urethroplasty. World J Urol, 2017. 35: 839.
	https://pubmed.ncbi.nlm.nih.gov/27562579/
343.	Erickson, B.A., <i>et al.</i> Prospective analysis of ejaculatory function after anterior urethral reconstruction. J Urol, 2010. 184: 238.
	https://pubmed.ncbi.nlm.nih.gov/20483147/
344.	Vasudeva, P., et al. Dorsal versus ventral onlay buccal mucosal graft urethroplasty for long-segment
	bulbar urethral stricture: A prospective randomized study. Int J Urol, 2015. 22: 967.
345.	https://pubmed.ncbi.nlm.nih.gov/26138109/ Barbagli, G., <i>et al.</i> Muscle- and nerve-sparing bulbar urethroplasty: a new technique. Eur Urol, 2008. 54: 335.
	https://pubmed.ncbi.nlm.nih.gov/18384930/
346.	Fredrick, A., et al. Functional Effects of Bulbospongiosus Muscle Sparing on Ejaculatory Function
	and Post-Void Dribbling after Bulbar Urethroplasty. J Urol, 2017. 197: 738.
	https://pubmed.ncbi.nlm.nih.gov/27686691/
347.	Abouassaly, R., et al. Augmented anastomotic urethroplasty. J Urol, 2007. 177: 2211.
	https://pubmed.ncbi.nlm.nih.gov/17509322/
348.	Bugeja, S., et al. Non-transecting bulbar urethroplasty. Transl Androl Urol, 2015. 4: 41.
	https://pubmed.ncbi.nlm.nih.gov/26816808/
349.	Barbagli, G., et al. Clinical outcome and quality of life assessment in patients treated with perineal
	urethrostomy for anterior urethral stricture disease. J Urol, 2009. 182: 548.
250	https://pubmed.ncbi.nlm.nih.gov/19524945/
350.	Secrest, C.L. Staged urethroplasty: indications and techniques. Urol Clin North Am, 2002. 29: 467. https://pubmed.ncbi.nlm.nih.gov/12371236/
351.	Pfalzgraf, D., et al. Two-staged urethroplasty: buccal mucosa and mesh graft techniques. Aktuelle
001.	Urol, 2010. 41 Suppl 1: S5.
	https://pubmed.ncbi.nlm.nih.gov/20094954/
352.	Levine, M.A., et al. Revision urethroplasty success is comparable to primary urethroplasty: a
	comparative analysis. Urology, 2014. 84: 928.
	https://pubmed.ncbi.nlm.nih.gov/25129537/
353.	Pfalzgraf, D., et al. Staged urethroplasty: comparison of early functional results and quality of life in
	mesh graft and buccal mucosa technique. Can J Urol, 2015. 22: 7720.
	https://pubmed.ncbi.nlm.nih.gov/25891336/
354.	Viers, B.R., et al. Urethral Reconstruction in Aging Male Patients. Urology, 2018. 113: 209.
	https://pubmed.ncbi.nlm.nih.gov/29031840/
355.	Ahyai, S.A., et al. Outcomes of Ventral Onlay Buccal Mucosa Graft Urethroplasty in Patients after
	Radiotherapy. J Urol, 2015. 194: 441.
050	https://pubmed.ncbi.nlm.nih.gov/25846417/
356.	Breyer, B.N., <i>et al.</i> Multivariate analysis of risk factors for long-term urethroplasty outcome. J Urol,
	2010. 183: 613. https://www.mad.nabi.nlm.nih.gov/20018218/
357.	https://pubmed.ncbi.nlm.nih.gov/20018318/
557.	Kinnaird, A.S., <i>et al.</i> Stricture length and etiology as preoperative independent predictors of recurrence after urethroplasty: A multivariate analysis of 604 urethroplasties. Can Urol Assoc J, 2014. 8: E296.
	https://pubmed.ncbi.nlm.nih.gov/24940453/

- 358. Verla, W., et al. Independent risk factors for failure after anterior urethroplasty: a multivariate analysis on prospective data. World J Urol, 2020. https://pubmed.ncbi.nlm.nih.gov/32076822/
- 359. Rosenbaum, C.M., *et al.* Redo buccal mucosa graft urethroplasty: success rate, oral morbidity and functional outcomes. BJU Int, 2016. 118: 797. https://pubmed.ncbi.nlm.nih.gov/27170089/
- 360. Javali, T.D., *et al.* Management of recurrent anterior urethral strictures following buccal mucosal graft-urethroplasty: A single center experience. Urol Ann, 2016. 8: 31. https://pubmed.ncbi.nlm.nih.gov/26834398/
- 361. Vetterlein, M.W., et al. The Impact of Surgical Sequence on Stricture Recurrence after Anterior 1-Stage Buccal Mucosal Graft Urethroplasty: Comparative Effectiveness of Initial, Repeat and Secondary Procedures. J Urol, 2018. 200: 1308.
  - https://pubmed.ncbi.nlm.nih.gov/30126826/
- 362. Hussein, M.M., *et al.* The use of penile skin graft versus penile skin flap in the repair of long bulbopenile urethral stricture: a prospective randomized study. Urology, 2011. 77: 1232. https://pubmed.ncbi.nlm.nih.gov/21208648/
- 363. Kulkarni, S.B., *et al.* Management of Panurethral Stricture Disease in India. J Urol, 2012. 188: 824. <u>https://pubmed.ncbi.nlm.nih.gov/27908373/</u>
- 364. Hussein, M.M., *et al.* Urethroplasty for treatment of long anterior urethral stricture: buccal mucosa graft versus penile skin graft-does the stricture length matter? Int Urol Nephrol, 2016. 48: 1831. https://pubmed.ncbi.nlm.nih.gov/27401984/
- 365. El Dahshoury, Z.M. Modified annular penile skin flap for repair of pan-anterior urethral stricture. Int Urol Nephrol, 2009. 41: 889.

https://pubmed.ncbi.nlm.nih.gov/19189226/

- 366. Mathur, R.K., *et al*. Tunica albuginea urethroplasty for panurethral strictures. Urol J, 2010. 7: 120. <u>https://pubmed.ncbi.nlm.nih.gov/20535700/</u>
- 367. Meeks, J.J., *et al.* Urethroplasty with abdominal skin grafts for long segment urethral strictures. J Urol, 2010. 183: 1880.

https://pubmed.ncbi.nlm.nih.gov/20303098/

368. Tavakkoli Tabassi, K., *et al.* Dorsally Placed Buccal Mucosal Graft Urethroplasty in Treatment of Long Urethral Strictures Using One-Stage Transperineal Approach. International scholarly research notices, 2014. 2014: 792982.

https://pubmed.ncbi.nlm.nih.gov/27437449/

- 369. Alsagheer, G.A., *et al.* Management of long segment anterior urethral stricture (≥ 8cm) using buccal mucosal (BM) graft and penile skin (PS) flap: outcome and predictors of failure. Int Braz J Urol, 2018. 44: 163.
  - https://pubmed.ncbi.nlm.nih.gov/29211404/
- 370. DeLong, J., *et al.* Augmented perineal urethrostomy using a dorsal buccal mucosal graft, bi-institutional study. World J Urol, 2017. 35: 1285. <u>https://pubmed.ncbi.nlm.nih.gov/28108798/</u>
- 371. Lumen, N., *et al.* Perineal Urethrostomy: Surgical and Functional Evaluation of Two Techniques.
   BioMed Res Int, 2015. 2015: 365715.

https://pubmed.ncbi.nlm.nih.gov/25789316/

- 372. Myers, J.B., *et al*. The outcomes of perineal urethrostomy with preservation of the dorsal urethral plate and urethral blood supply. Urology, 2011. 77: 1223. https://pubmed.ncbi.nlm.nih.gov/21215434/
- 373. French, D., *et al.* The "7-flap" perineal urethrostomy. Urology, 2011. 77: 1487. https://pubmed.ncbi.nlm.nih.gov/21256550/
- 374. McKibben, M.J., *et al.* Versatile algorithmic midline approach to perineal urethrostomy for complex urethral strictures. World J Urol, 2019. 37: 1403.

https://pubmed.ncbi.nlm.nih.gov/30334075/

- 375. Bascom, A., *et al.* Assessment of Wound Complications After Bulbar Urethroplasty: The Impact of a Lambda Perineal Incision. Urology, 2016. 90: 184.
- https://pubmed.ncbi.nlm.nih.gov/26777749/
- 376. Lin, Y., *et al.* Perineal midline vertical incision verses inverted-U incision in the urethroplasty: which is better? World J Urol, 2018. 36: 1267.
- <u>https://pubmed.ncbi.nlm.nih.gov/29541891/</u>
   Starke, N.R., *et al.* '7-flap' perineal urethrostomy: an effective optio
- 377. Starke, N.R., et al. '7-flap' perineal urethrostomy: an effective option for obese men with devastated urethras. Can J Urol, 2015. 22: 7902. <u>https://pubmed.ncbi.nlm.nih.gov/26267029/</u>

- 378. Granieri, M.A., et al. The evolution of urethroplasty for bulbar urethral stricture disease: lessons learned from a single center experience. J Urol, 2014. 192: 1468. https://pubmed.ncbi.nlm.nih.gov/24859444/
- 379. Fuchs, J.S., et al. Changing Trends in Reconstruction of Complex Anterior Urethral Strictures: From Skin Flap to Perineal Urethrostomy. Urology, 2018. 122: 169. https://pubmed.ncbi.nlm.nih.gov/30138682/
- 380. Lopez, J.C., et al. Perineostomy: the last oportunity. Int Braz J Urol, 2015. 41: 91. https://pubmed.ncbi.nlm.nih.gov/25928514/
- 381. Murphy, G.P., et al. Urinary and Sexual Function after Perineal Urethrostomy for Urethral Stricture Disease: An Analysis from the TURNS. J Urol, 2019. 201: 956. https://pubmed.ncbi.nlm.nih.gov/30676476/
- 382. Ramchandani, P., et al. Vesicourethral anastomotic strictures after radical prostatectomy: efficacy of transurethral balloon dilation. Radiology, 1994. 193: 345.
  - https://pubmed.ncbi.nlm.nih.gov/7972741/
- 383. Ishii, G., et al. High pressure balloon dilation for vesicourethral anastomotic strictures after radical prostatectomy. BMC Urol, 2015. 15: 62.
  - https://pubmed.ncbi.nlm.nih.gov/26134267/
- 384. Kumar, P., et al. Management of post-radical prostatectomy anastomotic stricture by endoscopic transurethral balloon dilatation. Scand J Urol Nephrol, 2007. 41: 314. https://pubmed.ncbi.nlm.nih.gov/17763223/
- 385. LaBossiere, J.R., et al. Endoscopic Treatment of Vesicourethral Stenosis after Radical Prostatectomy: Outcomes and Predictors of Success. J Urol, 2016. 195: 1495. https://pubmed.ncbi.nlm.nih.gov/26719028/
- 386. Kravchick, S., et al. Transrectal ultrasonography-guided injection of long-acting steroids in the treatment of recurrent/resistant anastomotic stenosis after radical prostatectomy. J Endourol, 2013. 27:875.
  - https://pubmed.ncbi.nlm.nih.gov/23461798/
- 387. Hayashi, T., et al. Successful treatment of recurrent vesicourethral stricture after radical prostatectomy with holmium laser: report of three cases. Int J Urol, 2005. 12: 414. https://pubmed.ncbi.nlm.nih.gov/15948734/
- 388. Merrick, G.S., et al. Risk factors for the development of prostate brachytherapy related urethral strictures. J Urol, 2006. 175: 1376.
  - https://pubmed.ncbi.nlm.nih.gov/16516001/
- 389. Bang, S.L., et al. Post Prostatectomy Vesicourethral Stenosis or Bladder Neck Contracture with Concomitant Urinary Incontinence: Our Experience and Recommendations. Curr Urol, 2017. 10: 32. https://pubmed.ncbi.nlm.nih.gov/28559775/
- 390. Matsushita, K., et al. Pubovesical fistula: a rare complication after treatment of prostate cancer. Urology, 2012. 80: 446.
  - https://pubmed.ncbi.nlm.nih.gov/22698471/
- 391. Gupta, S., et al. Pubic symphysis osteomyelitis in the prostate cancer survivor: clinical presentation, evaluation, and management. Urology, 2015. 85: 684. https://pubmed.ncbi.nlm.nih.gov/25733290/
- 392. Shapiro, D.D., et al. Urosymphyseal Fistulas Resulting From Endoscopic Treatment of Radiationinduced Posterior Urethral Strictures. Urology, 2018. 114: 207. https://pubmed.ncbi.nlm.nih.gov/29305945/
- 393. Sukumar, S., et al. The Devastated Bladder Outlet in Cancer Survivors After Local Therapy for Prostate Cancer. Curr Bladder Dysf Rep, 2016. 11: 79.
- https://www.researchgate.net/publication/299530474 394. Ramirez, D., et al. Deep lateral transurethral incisions for recurrent bladder neck contracture: promising 5-year experience using a standardized approach. Urology, 2013. 82: 1430. https://pubmed.ncbi.nlm.nih.gov/24054130/
- 395. Yurkanin, J.P., et al. Evaluation of cold knife urethrotomy for the treatment of anastomotic stricture after radical retropubic prostatectomy. J Urol, 2001. 165: 1545. https://pubmed.ncbi.nlm.nih.gov/11342914/
- 396. Giannarini, G., et al. Cold-knife incision of anastomotic strictures after radical retropubic prostatectomy with bladder neck preservation: efficacy and impact on urinary continence status. Eur Urol, 2008. 54: 647.

https://pubmed.ncbi.nlm.nih.gov/18155824/

- 397. Brede, C., *et al.* Continence outcomes after treatment of recalcitrant postprostatectomy bladder neck contracture and review of the literature. Urology, 2014. 83: 648. https://pubmed.ncbi.nlm.nih.gov/24365088/
- 398. Popken, G., et al. Anastomotic stricture after radical prostatectomy. Incidence, findings and treatment. Eur Urol, 1998. 33: 382. https://pubmed.ncbi.nlm.nih.gov/9612681/

399. Gousse, A.E., *et al.* Two-stage management of severe postprostatectomy bladder neck contracture associated with stress incontinence. Urology, 2005. 65: 316.
 <u>https://pubmed.ncbi.nlm.nih.gov/15708045/</u>

400. Lagerveld, B.W., *et al.* Holmium:YAG laser for treatment of strictures of vesicourethral anastomosis after radical prostatectomy. J Endourol, 2005. 19: 497. https://pubmed.ncbi.nlm.nih.gov/15910265/

401. Brodak, M., *et al.* Bipolar transurethral resection of anastomotic strictures after radical prostatectomy. J Endourol, 2010. 24: 1477.

https://pubmed.ncbi.nlm.nih.gov/20653423/

- 402. Eltahawy, E., *et al.* Management of recurrent anastomotic stenosis following radical prostatectomy using holmium laser and steroid injection. BJU Int, 2008. 102: 796. https://pubmed.ncbi.nlm.nih.gov/18671784/
- 403. Sourial, M.W., *et al.* Mitomycin-C and urethral dilatation: A safe, effective, and minimally invasive procedure for recurrent vesicourethral anastomotic stenoses. Urol Oncol, 2017. 35: 672 e15. https://pubmed.ncbi.nlm.nih.gov/28844555/
- 404. Kranz, J., *et al.* Differences in Recurrence Rate and De Novo Incontinence after Endoscopic Treatment of Vesicourethral Stenosis and Bladder Neck Stenosis. Front Surg, 2017. 4: 44. https://pubmed.ncbi.nlm.nih.gov/28848735/
- 405. Ozturk, H. Treatment of recurrent vesicourethral anastomotic stricture after radical prostatectomy using plasma-button vaporization. Scand J Urol, 2015. 49: 371. https://pubmed.ncbi.nlm.nih.gov/25697282/
- 406. Vanni, A.J., *et al.* Radial urethrotomy and intralesional mitomycin C for the management of recurrent bladder neck contractures. J Urol, 2011. 186: 156.

https://pubmed.ncbi.nlm.nih.gov/21575962/

- 407. Nagpal, K., *et al.* Durable Results of Mitomycin C Injection with Internal Urethrotomy for Refractory Bladder Neck Contractures: Multi-institutional Experience. Urol Pract, 2015. 2: 250. https://www.auajournals.org/doi/abs/10.1016/j.urpr.2014.12.007
- 408. Farrell, M.R., *et al.* Visual Internal Urethrotomy With Intralesional Mitomycin C and Short-term Clean Intermittent Catheterization for the Management of Recurrent Urethral Strictures and Bladder Neck Contractures. Urology, 2015. 85: 1494.
  - https://pubmed.ncbi.nlm.nih.gov/26099892/
- 409. Lyon, T.D., *et al.* Bipolar Transurethral Incision of Bladder Neck Stenoses with Mitomycin C Injection. Adv Urol, 2015. 2015: 758536.

https://pubmed.ncbi.nlm.nih.gov/26635876/

- 410. Kahokehr, A.A., *et al.* Posterior urethral stenosis after prostate cancer treatment: contemporary options for definitive management. Transl Androl Urol, 2018. 7: 580. https://pubmed.ncbi.nlm.nih.gov/30211048/
- 411. Nikolavsky, D., *et al.* Open reconstruction of recurrent vesicourethral anastomotic stricture after radical prostatectomy. Int Urol Nephrol, 2014. 46: 2147. https://pubmed.ncbi.nlm.nih.gov/25134944/
- 412. Kirshenbaum, E.J., *et al.* Patency and Incontinence Rates After Robotic Bladder Neck Reconstruction for Vesicourethral Anastomotic Stenosis and Recalcitrant Bladder Neck Contractures: The Trauma and Urologic Reconstructive Network of Surgeons Experience. Urology, 2018. 118: 227.

https://pubmed.ncbi.nlm.nih.gov/29777787/

413. Mundy, A.R., *et al.* Posterior urethral complications of the treatment of prostate cancer. BJU Int, 2012. 110: 304.

https://pubmed.ncbi.nlm.nih.gov/22340079/

- 414. Dinerman, B.F., *et al.* Robotic-Assisted Abdomino-perineal Vesicourethral Anastomotic Reconstruction for 4.5 Centimeter Post-prostatectomy Stricture. Urol Case Rep, 2017. 14: 1. https://pubmed.ncbi.nlm.nih.gov/28607874/
- 415. Schuettfort, V.M., *et al.* Transperineal reanastomosis for treatment of highly recurrent anastomotic strictures after radical retropubic prostatectomy: extended follow-up. World J Urol, 2017. 35: 1885. https://pubmed.ncbi.nlm.nih.gov/28674908/

416.	Pfalzgraf, D., et al. Open retropubic reanastomosis for highly recurrent and complex bladder neck
	stenosis. J Urol, 2011. 186: 1944.
447	https://pubmed.ncbi.nlm.nih.gov/21944115/
417.	Giudice, C.R., et al. Surgical approach to vesicourethral anastomotic stricture following radical
	prostatectomy. Actas Urol Esp, 2016. 40: 124.
418.	https://pubmed.ncbi.nlm.nih.gov/26515118/ Faris, S.F., et al. Urinary diversions after radiation for prostate cancer: indications and treatment.
410.	Urology, 2014. 84: 702.
	https://pubmed.ncbi.nlm.nih.gov/25168555/
419.	Rosenbaum, C.M., et al. The T-plasty as therapy for recurrent bladder neck stenosis: success rate,
110.	functional outcome, and patient satisfaction. World J Urol, 2017. 35: 1907.
	https://pubmed.ncbi.nlm.nih.gov/28929299/
420.	Shu, H.Q., et al. Laparoscopic T-Plasty for the Treatment of Refractory Bladder Neck Stenosis. Am
	J Mens Health, 2019. 13: 1557988319873517.
	https://pubmed.ncbi.nlm.nih.gov/31470756/
421.	Musch, M., et al. Robot-assisted laparoscopic Y-V plasty in 12 patients with refractory bladder neck
	contracture. J Robot Surg, 2018. 12: 139.
	https://pubmed.ncbi.nlm.nih.gov/28451939/
422.	Avallone, M.A., et al. Robotic-assisted Laparoscopic Subtrigonal Inlay of Buccal Mucosal Graft for
	Treatment of Refractory Bladder Neck Contracture. Urology, 2019. 130: 209.
	https://pubmed.ncbi.nlm.nih.gov/31063762/
423.	Blakely, S., et al. Dorsal Onlay Urethroplasty for Membranous Urethral Strictures: Urinary and
	Erectile Functional Outcomes. J Urol, 2016. 195: 1501.
· · · ·	https://pubmed.ncbi.nlm.nih.gov/26602890/
424.	Chi, A.C., <i>et al.</i> Urethral strictures and the cancer survivor. Curr Opin Urol, 2014. 24: 415.
105	https://pubmed.ncbi.nlm.nih.gov/24809412/
425.	Fuchs, J.S., et al. Improving Outcomes of Bulbomembranous Urethroplasty for Radiation-induced
	Urethral Strictures in Post-Urolume Era. Urology, 2017. 99: 240.
106	https://pubmed.ncbi.nlm.nih.gov/27496299/
426.	Glass, A.S., <i>et al.</i> Urethroplasty after radiation therapy for prostate cancer. Urology, 2012. 79: 1402.
427.	https://pubmed.ncbi.nlm.nih.gov/22521189/ Chung, P.H., et al. Incidence of Stress Urinary Incontinence After Posterior Urethroplasty for
427.	Radiation-induced Urethral Strictures. Urology, 2018. 114: 188.
	https://pubmed.ncbi.nlm.nih.gov/29191643/
428.	Rourke, K., et al. Observations and outcomes of urethroplasty for bulbomembranous stenosis after
	radiation therapy for prostate cancer. World J Urol, 2016. 34: 377.
	https://pubmed.ncbi.nlm.nih.gov/26047655/
429.	Meeks Joshua, J., et al. Urethroplasty for Radiotherapy Induced Bulbomembranous Strictures: A
	Multi-Institutional Experience. J Urol, 2011. 185: 1761.
	https://pubmed.ncbi.nlm.nih.gov/21420123/
430.	Palmer, D.A., et al. Urethroplasty for high risk, long segment urethral strictures with ventral buccal
	mucosa graft and gracilis muscle flap. J Urol, 2015. 193: 902.
	https://pubmed.ncbi.nlm.nih.gov/25261802/
431.	Patil, M.B., et al. Total bladder and posterior urethral reconstruction: salvage technique for
	defunctionalized bladder with recalcitrant posterior urethral stenosis. J Urol, 2015. 193: 1649.
	https://pubmed.ncbi.nlm.nih.gov/25534328/
432.	Pisters, L.L., et al. Salvage prostatectomy with continent catheterizable urinary reconstruction: a
	novel approach to recurrent prostate cancer after radiation therapy. J Urol, 2000. 163: 1771.
400	https://pubmed.ncbi.nlm.nih.gov/10799179/
433.	Ullrich, N.F., et al. A technique of bladder neck closure combining prostatectomy and intestinal
	interposition for unsalvageable urethral disease. J Urol, 2002. 167: 634.
434.	https://pubmed.ncbi.nlm.nih.gov/11792934/ De, E., <i>et al</i> . Salvage prostatectomy with bladder neck closure, continent catheterizable stoma and
404.	bladder augmentation: feasibility and patient reported continence outcomes at 32 months. J Urol,
	2007. 177: 2200.
	https://pubmed.ncbi.nlm.nih.gov/17509319/
435.	Spahn, M., et al. Last resort in devastated bladder outlet: bladder neck closure and continent
	vesicostomylong-term results and comparison of different techniques. Urology, 2010. 75: 1185.
	https://pubmed.ncbi.nlm.nih.gov/20206979/

436. Sack, B.S., et al. Cystectomy and Urinary Diversion for the Management of a Devastated Lower Urinary Tract Following Prostatic Cryotherapy and/or Radiotherapy. WMJ, 2016. 115: 70. https://pubmed.ncbi.nlm.nih.gov/27197339/ 437. Lumen, N., et al. Perineal anastomotic urethroplasty for posttraumatic urethral stricture with or without previous urethral manipulations: a review of 61 cases with long-term followup. J Urol, 2009. 181: 1196. https://pubmed.ncbi.nlm.nih.gov/19152939/ 438. Brandes, S. Initial management of anterior and posterior urethral injuries. Urol Clin North Am, 2006. 33:87. https://pubmed.ncbi.nlm.nih.gov/16488283/ 439. Koraitim, M.M. Complex pelvic fracture urethral distraction defects revisited. Scand J Urol, 2014. 48:84. https://pubmed.ncbi.nlm.nih.gov/23883274/ 440. Kulkarni, S.B., et al. Posterior urethral stricture after pelvic fracture urethral distraction defects in developing and developed countries, and choice of surgical technique. J Urol, 2010. 183: 1049. https://pubmed.ncbi.nlm.nih.gov/20092843/ 441. Barbagli, G., et al. The spectrum of pelvic fracture urethral injuries and posterior urethroplasty in an Italian high-volume centre, from 1980 to 2013. Arab J Urol, 2015. 13: 32. https://pubmed.ncbi.nlm.nih.gov/26019976/ 442. Cai, W., et al. Bipolar plasma vaporization using plasma-cutting and plasma-loop electrodes versus cold-knife transurethral incision for the treatment of posterior urethral stricture: a prospective, randomized study. Clinics (Sao Paulo), 2016. 71: 1. https://pubmed.ncbi.nlm.nih.gov/26872076/ 443. Tausch, T.J., et al. Unintended negative consequences of primary endoscopic realignment for men with pelvic fracture urethral injuries. J Urol, 2014. 192: 1720. https://pubmed.ncbi.nlm.nih.gov/24972309/ 444. Horiguchi, A., et al. Primary Realignment for Pelvic Fracture Urethral Injury Is Associated With Prolonged Time to Urethroplasty and Increased Stenosis Complexity. Urology, 2017. 108: 184. https://pubmed.ncbi.nlm.nih.gov/28606774/ 445. Hong, Y.K., et al. Predictors for success of internal urethrotomy in patients with urethral contracture following perineal repair of pelvic fracture urethral injuries. Injury, 2017. 48: 1035. https://pubmed.ncbi.nlm.nih.gov/28259378/ 446. Koraitim, M.M. Unsuccessful outcomes after posterior urethroplasty: definition, diagnosis, and treatment. Urology, 2012. 79: 1168. https://pubmed.ncbi.nlm.nih.gov/22449452/ 447. Ali, S., et al. Delayed Single Stage Perineal Posterior Urethroplasty. J Coll Phys Surg-Pakistan, JCPSP, 2015. 25: 438. https://pubmed.ncbi.nlm.nih.gov/26100998/ 448. Helmy, T.E., et al. Internal urethrotomy for recurrence after perineal anastomotic urethroplasty for posttraumatic pediatric posterior urethral stricture: could it be sufficient? J Endourol, 2013. 27: 693. https://pubmed.ncbi.nlm.nih.gov/23441683/ 449. Hussain, A., et al. Outcome of end-to-end urethroplasty in post-traumatic stricture of posterior urethra. J Coll Phys Surg-Pakistan, JCPSP, 2013. 23: 272. https://pubmed.ncbi.nlm.nih.gov/23552538/ 450. Fu, Q., et al. Use of anastomotic urethroplasty with partial pubectomy for posterior urethral obliteration injuries: 10 years experience. World J Urol, 2009. 27: 695. https://pubmed.ncbi.nlm.nih.gov/19238398/ 451. Kulkarni, S.B., et al. Management of complex and redo cases of pelvic fracture urethral injuries. Asian J Urol, 2018. 5: 107. https://pubmed.ncbi.nlm.nih.gov/29736373/ 452. Mundy, A.R., et al. Urethral trauma. Part II: Types of injury and their management. BJU Int, 2011. 108: 630. https://pubmed.ncbi.nlm.nih.gov/21854524/ 453. Singh, B.P., et al. Impact of prior urethral manipulation on outcome of anastomotic urethroplasty for post-traumatic urethral stricture. Urology, 2010. 75: 179. https://pubmed.ncbi.nlm.nih.gov/19854488/ 454. Gomez, R.G., et al. SIU/ICUD Consultation on Urethral Strictures: Pelvic fracture urethral injuries. Urology, 2014. 83: S48.

455.	Koraitim, M.M. Transpubic urethroplasty revisited: total, superior, or inferior pubectomy? Urology, 2010. 75: 691.
	https://pubmed.ncbi.nlm.nih.gov/19962726/
456.	Xu, Y.M., et al. Surgical treatment of 31 complex traumatic posterior urethral strictures associated
	with urethrorectal fistulas. Eur Urol, 2010. 57: 514.
	https://pubmed.ncbi.nlm.nih.gov/19282100/
457.	Koraitim, M.M., et al. Perineal repair of pelvic fracture urethral injury: in pursuit of a successful
	outcome. BJU Int, 2015. 116: 265.
	https://pubmed.ncbi.nlm.nih.gov/24552421/
458.	Hosseini, J., et al. Dorsal versus ventral anterior urethral spatulation in posterior urethroplasty. Urol
	J, 2010. 7: 258.
	https://pubmed.ncbi.nlm.nih.gov/21170856/
459.	Zhang, L., et al. The application of valgus urethral mucosa anastomosis in the operation of posterior
	urethral stricture. Int Urol Nephrol, 2015. 47: 491.
	https://pubmed.ncbi.nlm.nih.gov/25613432/
460.	Gomez, R.G., et al. Reconstruction of Pelvic Fracture Urethral Injuries With Sparing of the Bulbar
	Arteries. Urology, 2016. 88: 207.
	https://pubmed.ncbi.nlm.nih.gov/26616094/
461.	Verla, W., et al. Vessel-sparing Excision and Primary Anastomosis. J Visual Exp, JoVE, 2019.
	https://pubmed.ncbi.nlm.nih.gov/30663665/
462.	Xie, H., et al. Preliminary Experience of Nontransecting Urethroplasty for Pelvic Fracture-related
	Urethral Injury. Urology, 2017. 109: 178.
	https://pubmed.ncbi.nlm.nih.gov/28735015/
463.	Wang, P., et al. Modified urethral pull-through operation for posterior urethral stricture and long-term
	outcome. J Urol, 2008. 180: 2479.
	https://pubmed.ncbi.nlm.nih.gov/18930502/
464.	Yin, L., et al. Urethral pull-through operation for the management of pelvic fracture urethral
	distraction defects. Urology, 2011. 78: 946.
	https://pubmed.ncbi.nlm.nih.gov/21777964/
465.	Unterberg, S.H., et al. Robotic-assisted Proximal Perineal Urethroplasty: Improving Visualization and
	Ergonomics. Urology, 2019. 125: 230.
	https://pubmed.ncbi.nlm.nih.gov/30452962/
466.	Singh, S.K., et al. Transperineal bulboprostatic anastomotic repair of pelvic fracture urethral
	distraction defect and role of ancillary maneuver: A retrospective study in 172 patients. Urol Ann,
	2010. 2: 53.
	https://pubmed.ncbi.nlm.nih.gov/20882154/
467.	Ranjan, P., et al. Post-traumatic urethral strictures in children: what have we learned over the years?
	J Pediatr Urol, 2012. 8: 234.
	https://pubmed.ncbi.nlm.nih.gov/21764640/
468.	Podesta, M., et al. Delayed surgical repair of posttraumatic posterior urethral distraction defects in
	children and adolescents: long-term results. J Pediatr Urol, 2015. 11: 67 e1.
	https://pubmed.ncbi.nlm.nih.gov/25869826/
469.	Waterloos, M., et al. Urethroplasty for urethral injuries and trauma-related strictures in children and
	adolescents: a single-institution experience. J Pediatr Urol, 2019. 15: 176 e1.
470	https://pubmed.ncbi.nlm.nih.gov/30581060/
470.	Singla, M., et al. Posttraumatic posterior urethral strictures in childrenmanagement and
	intermediate-term follow-up in tertiary care center. Urology, 2008. 72: 540.
	https://pubmed.ncbi.nlm.nih.gov/18619659/
471.	Voelzke, B.B., et al. Blunt pediatric anterior and posterior urethral trauma: 32-year experience and
	outcomes. J Pediatr Urol, 2012. 8: 258.
470	https://pubmed.ncbi.nlm.nih.gov/21664873/
472.	Hosseini, J., et al. Effects of Anastomotic Posterior Urethroplasty (Simple or Complex) on Erectile
	Function: a Prospective Study. Urol J, 2018. 15: 33.
470	https://pubmed.ncbi.nlm.nih.gov/29299889/
473.	Tang, C.Y., <i>et al.</i> Erectile dysfunction in patients with traumatic urethral strictures treated with anastomotic urethroplasty: a single-factor analysis. Can J Urol, 2012. 19: 6548.
	https://pubmed.ncbi.nlm.nih.gov/23228290/
474.	Feng, C., et al. The relationship between erectile dysfunction and open urethroplasty: a systematic
	review and meta-analysis. J Sex Med, 2013. 10: 2060.
	https://pubmed.ncbi.nlm.nih.gov/23656595/

- 475. El-Assmy, A., *et al.* Erectile dysfunction post-perineal anastomotic urethroplasty for traumatic urethral injuries: analysis of incidence and possibility of recovery. Int Urol Nephrol, 2015. 47: 797. https://pubmed.ncbi.nlm.nih.gov/25778817/
- 476. Koraitim, M.M. Predictors of erectile dysfunction post pelvic fracture urethral injuries: a multivariate analysis. Urology, 2013. 81: 1081.

https://pubmed.ncbi.nlm.nih.gov/23465164/

- 477. Anger, J.T., *et al.* Ejaculatory profiles and fertility in men after posterior urethroplasty for pelvic fracture-urethral distraction defect injuries. BJU Int, 2008. 102: 351. https://pubmed.ncbi.nlm.nih.gov/18702781/
- 478. El-Assmy, A., *et al.* Ejaculatory function after anastomotic urethroplasty for pelvic fracture urethral injuries. Int Urol Nephrol, 2015. 47: 497. https://pubmed.ncbi.nlm.nih.gov/25655257/
- 479. Bagga, H.S., *et al*. The mechanism of continence after posterior urethroplasty. Arab J Urol, 2015. 13: 60. https://pubmed.ncbi.nlm.nih.gov/26019981/
- 480. Fu, Q., *et al.* Recurrence and complications after transperineal bulboprostatic anastomosis for posterior urethral strictures resulting from pelvic fracture: a retrospective study from a urethral referral centre. BJU Int, 2013. 112: E358. https://pubmed.ncbi.nlm.nih.gov/23773274/
- 481. Garg, G., *et al.* Outcome of patients with failed pelvic fracture-associated urethral repair: a single center 10-year experience. Turkish J Urol, 2019. 45: 139. https://pubmed.ncbi.nlm.nih.gov/30475700/
- 482. Ibrahim, A.G., *et al.* Results of delayed repair of posterior urethral disruption injuries in Maiduguri. Surg Pract, 2013. 17: 92.

https://www.researchgate.net/publication/263719232

- 483. Kulkarni, S.B., *et al.* Laparoscopic omentoplasty to support anastomotic urethroplasty in complex and redo pelvic fracture urethral defects. Urology, 2015. 85: 1200. https://pubmed.ncbi.nlm.nih.gov/25818909/
- 484. Mehmood, S., *et al.* Outcome of anastomotic posterior urethroplasty with various ancillary maneuvers for post-traumatic urethral injury. Does prior urethral manipulation affect the outcome of urethroplasty? Urol Ann, 2018. 10: 175.

https://pubmed.ncbi.nlm.nih.gov/29719330/

- 485. Hwang, J.H., *et al.* Clinical factors that predict successful posterior urethral anastomosis with a gracilis muscle flap. Korean J Urol, 2013. 54: 710. https://pubmed.ncbi.nlm.nih.gov/24175047/
- 486. Bhagat, S.K., *et al.* Redo-urethroplasty in pelvic fracture urethral distraction defect: an audit. World J Urol, 2011. 29: 97.

https://pubmed.ncbi.nlm.nih.gov/20204376/

- 487. Gupta, N.P., *et al.* Does a previous end-to-end urethroplasty alter the results of redo end-to-end urethroplasty in patients with traumatic posterior urethral strictures? Int J Urol, 2008. 15: 885. https://pubmed.ncbi.nlm.nih.gov/18721207/
- 488. Mundy, A.R., *et al*. Entero-urethroplasty for the salvage of bulbo-membranous stricture disease or trauma. BJU Int, 2010. 105: 1716.

https://pubmed.ncbi.nlm.nih.gov/19930173/

489. Schwender, C.E., *et al.* Technique and results of urethroplasty for female stricture disease. J Urol, 2006. 175: 976.

https://pubmed.ncbi.nlm.nih.gov/16469596/

490. Gormley, E.A. Vaginal flap urethroplasty for female urethral stricture disease. Neurourol Urodyn, 2010. 29 Suppl 1: S42.

https://pubmed.ncbi.nlm.nih.gov/20419801/

- 491. Romman, A.N., *et al.* Distal intramural urethral pathology in women. J Urol, 2012. 188: 1218. <u>https://pubmed.ncbi.nlm.nih.gov/22902013/</u>
- 492. Popat, S., *et al.* Long-term management of luminal urethral stricture in women. Int Urogynecol J, 2016. 27: 1735.

https://pubmed.ncbi.nlm.nih.gov/27026141/

- 493. Migliari, R., et al. Dorsal buccal mucosa graft urethroplasty for female urethral strictures. J Urol, 2006. 176: 1473.
- https://pubmed.ncbi.nlm.nih.gov/16952664/
- 494. Gozzi, C., *et al.* Volar onlay urethroplasty for reconstruction of female urethra in recurrent stricture disease. BJU Int, 2011. 107: 1964. <u>https://pubmed.ncbi.nlm.nih.gov/21083639/</u>

495.	Petrou, S.P., <i>et al.</i> Dorsal vaginal graft urethroplasty for female urethral stricture disease. BJU Int, 2012. 110: E1090.
	https://pubmed.ncbi.nlm.nih.gov/22594612/
496.	Patil, S., et al. Anastomotic urethroplasty in female urethral stricture guided by cystoscopy - a point
	of technique. J Surg Tech nd Case Rep, 2013. 5: 113.
	https://pubmed.ncbi.nlm.nih.gov/24741435/
497.	Akman, R.Y., et al. Geriatrik ya grubu kadinlarda üretra darliklari tani ve tedavi. Turkish J Geriatr,
	2013. 16.
	http://geriatri.dergisi.org/abstract.php?lang=tr&id=735
498.	Heidari, F., et al. On demand urethral dilatation versus intermittent urethral dilatation: results and
	complications in women with urethral stricture. Nephro-Urol Monthly, 2014. 6: e15212.
	https://pubmed.ncbi.nlm.nih.gov/24783171/
499.	Goel, A., et al. Dorsal onlay buccal mucosal graft urethroplasty in female urethral stricture disease: a
	single-center experience. Int Urogynecol J, 2014. 25: 525.
	https://pubmed.ncbi.nlm.nih.gov/24154743/
500.	Kaushal, D., et al. Dorsal onlay vaginal mucosal graft urethroplasty for refractory female urethral
	stricture. Int J Med Health Res, 2018. 4: 51.
	http://www.medicalsciencejournal.com/archives/2018/vol4/issue5/4-5-23
501.	Blander, D.S., et al. Endoluminal magnetic resonance imaging in the evaluation of urethral diverticula
	in women. Urology, 2001. 57: 660.
	https://pubmed.ncbi.nlm.nih.gov/11306374/
502.	Ying, T., et al. Value of transrectal ultrasonography in female traumatic urethral injuries. Urology,
	2010. 76: 319.
	https://pubmed.ncbi.nlm.nih.gov/20156650/
503.	Massey, J.A., <i>et al.</i> Obstructed Voiding in the Female. Brit J Urol, 1988. 61: 36.
504	https://pubmed.ncbi.nlm.nih.gov/3342298/
504.	Averous, M., et al. [Urethral stenosis in the young girl, myth or reality? Comparison of clinical,
	radiological, instrumental and urodynamic data (author's transl)]. J Urol (Paris), 1981. 87: 67.
505	https://pubmed.ncbi.nlm.nih.gov/7276599/
505.	Heising, J., <i>et al.</i> [Meatus stenosis of girlsclinical demonstration and therapy (author's transl)]. Urologe A, 1978. 17: 292.
	https://pubmed.ncbi.nlm.nih.gov/706007/
506.	Dalela, D., et al. W-V flap: a new technique for reconstruction of female distal urethral stricture using
500.	vestibular mucosa. BMJ Case Rep, 2016. 2016.
	https://pubmed.ncbi.nlm.nih.gov/27170612/
507.	Tsivian, A., et al. Dorsal graft urethroplasty for female urethral stricture. J Urol, 2006. 176: 611.
	https://pubmed.ncbi.nlm.nih.gov/16813901/
508.	Tanello, M., et al. Use of Pedicle Flap from the Labia minora for the Repair of Female Urethral
	Strictures. Urol Int, 2002. 69: 95.
	https://pubmed.ncbi.nlm.nih.gov/12187036/
509.	Castillo, O.A., et al. [Urethroplasty with dorsal oral mucosa graft in female urethral stenosis]. Actas
	Urol Esp, 2011. 35: 246.
	https://pubmed.ncbi.nlm.nih.gov/21397358/
510.	Berglund, R.K., et al. Buccal mucosa graft urethroplasty for recurrent stricture of female urethra.
	Urology, 2006. 67: 1069.
	https://pubmed.ncbi.nlm.nih.gov/16635524/
511.	Hoag, N., et al. Vaginal-sparing ventral buccal mucosal graft urethroplasty for female urethral
	stricture: A novel modification of surgical technique. Investig Clin Urol, 2016. 57: 298.
	https://pubmed.ncbi.nlm.nih.gov/27437540/
512.	Nikolavsky, D., et al. Urologic Complications After Phalloplasty or Metoidioplasty. Clin Plastic Surg,
	2018. 45: 425.
	https://pubmed.ncbi.nlm.nih.gov/29908632/
513.	Lumen, N., et al. Endoscopic incision of short (<3 cm) urethral strictures after phallic reconstruction.
	J Endourol, 2009. 23: 1329.
	https://pubmed.ncbi.nlm.nih.gov/19566413/
514.	Pariser, J.J., et al. Buccal mucosal graft urethroplasty for the treatment of urethral stricture in the
	neophallus. Urology, 2015. 85: 927.

https://pubmed.ncbi.nlm.nih.gov/25681247/

- 515. Wilson, S.C., *et al.* Fasciocutaneous flap reinforcement of ventral onlay buccal mucosa grafts enables neophallus revision urethroplasty. Ther Adv Urol, 2016. 8: 331. https://pubmed.ncbi.nlm.nih.gov/27904649/
- 516. Raigosa, M., *et al.* Male-to-Female Genital Reassignment Surgery: A Retrospective Review of Surgical Technique and Complications in 60 Patients. J Sex Med, 2015. 12: 1837. https://pubmed.ncbi.nlm.nih.gov/26139337/
- 517. Rossi Neto, R., *et al.* Gender reassignment surgery--a 13 year review of surgical outcomes. Int Braz J Urol, 2012. 38: 97.

https://pubmed.ncbi.nlm.nih.gov/22397771/

518. Waterloos, M., *et al.* Neo-vaginal advancement flaps in the treatment of urethral strictures in transwomen. Urology, 2019.

https://pubmed.ncbi.nlm.nih.gov/30779891/

- 519. Dubey, D., *et al.* Dorsal onlay buccal mucosa versus penile skin flap urethroplasty for anterior urethral strictures: results from a randomized prospective trial. J Urol, 2007. 178: 2466. https://pubmed.ncbi.nlm.nih.gov/17937943/
- 520. Sa, Y.L., *et al.* A comparative study of buccal mucosa graft and penile pedical flap for reconstruction of anterior urethral strictures. Chinese Med J, 2010. 123: 365. https://pubmed.ncbi.nlm.nih.gov/20193261/
- 521. Castagnetti, M., *et al.* Aptness and complications of labial mucosa grafts for the repair of anterior urethral defects in children and adults: single centre experience with 115 cases. World J Urol, 2009. 27: 799.

https://pubmed.ncbi.nlm.nih.gov/19301012/

- 522. Patterson, J.M., *et al.* Surgical techniques in substitution urethroplasty using buccal mucosa for the treatment of anterior urethral strictures. Eur Urol, 2008. 53: 1162. https://pubmed.ncbi.nlm.nih.gov/18609764/
- 523. Levy, A.C., *et al.* Refractory Urethral Stricture Management: Indications for Alternative Grafts and Flaps. Curr Urol Rep , 2018. 19: 20.

https://pubmed.ncbi.nlm.nih.gov/29479650/

- 524. Olajide, A.O., *et al.* Complications of transverse distal penile island flap: urethroplasty of complex anterior urethral stricture. Urol J, 2010. 7: 178. <u>https://pubmed.ncbi.nlm.nih.gov/20845294/</u>
- 525. Langston, J.P., *et al.* Synchronous urethral stricture reconstruction via 1-stage ascending approach: rationale and results. J Urol, 2009. 181: 2161. <u>https://pubmed.ncbi.nlm.nih.gov/19296985/</u>
- 526. Marchal, C., *et al.* Barbagli's dorsal urethroplasty. Analysis of results and factors for success. Arch Esp Urol, 2010. 63: 537.

https://pubmed.ncbi.nlm.nih.gov/20876950/

- 527. Schwentner, C., *et al.* Anterior urethral reconstruction using the circular fasciocutaneous flap technique: long-term follow-up. World J Urol, 2011. 29: 115. https://pubmed.ncbi.nlm.nih.gov/20379722/
- 528. Onol, S.Y., *et al.* Reconstruction of strictures of the fossa navicularis and meatus with transverse island fasciocutaneous penile flap. J Urol, 2008. 179: 1437. https://pubmed.ncbi.nlm.nih.gov/18295281/
- 529. Whitson, J.M., *et al.* Long-term efficacy of distal penile circular fasciocutaneous flaps for single stage reconstruction of complex anterior urethral stricture disease. J Urol, 2008. 179: 2259. https://pubmed.ncbi.nlm.nih.gov/18423682/
- 530. Mostafa, D., *et al.* Twin penile skin flap, is it the answer for repair of long anterior urethral strictures? Arab J Urol, 2018. 16: 224.

https://pubmed.ncbi.nlm.nih.gov/29892487/

- 531. Rogers, H.S., *et al.* Long-term results of one-stage scrotal patch urethroplasty. Br J Urol, 1992. 69: 621. <u>https://pubmed.ncbi.nlm.nih.gov/1638346/</u>
- 532. Gil-Vernet, A., *et al.* Scrotal flap epilation in urethroplasty: concepts and technique. J Urol, 1995. 154: 1723.

https://pubmed.ncbi.nlm.nih.gov/7563332/

- 533. Gil-Vernet, J., *et al.* A new biaxial epilated scrotal flap for reconstructive urethral surgery. J Urol, 1997. 158: 412.
- https://pubmed.ncbi.nlm.nih.gov/9224314/
- 534. Ahmad, H., *et al.* Bulbar uretheral stricture repair with buccal mucosa graft urethroplasty. J Pakistan Med Ass, JPMA, 2011. 61: 440. https://pubmed.ncbi.nlm.nih.gov/22204174/

535.	Barbagli, G., <i>et al.</i> Prediction of early and late complications after oral mucosal graft harvesting: multivariable analysis from a cohort of 553 consecutive patients. J Urol, 2014. 191: 688.
536.	https://pubmed.ncbi.nlm.nih.gov/24035880/ Hosseini, J., et al. Dorsal versus ventral oral mucosal graft urethroplasty. Urol J, 2011. 8: 48. https://pubmed.ncbi.nlm.nih.gov/21404203/
537.	Kulkarni, S., <i>et al.</i> One-sided anterior urethroplasty: a new dorsal onlay graft technique. BJU Int, 2009. 104: 1150.
	https://pubmed.ncbi.nlm.nih.gov/19388990/
538.	Moran, E., <i>et al.</i> Oral quality of life after buccal mucosal graft harvest for substitution urethroplasty. More than a bite? World J Urol, 2019. 37: 385.
520	https://pubmed.ncbi.nlm.nih.gov/29931527/ O'Riordan, A., et al. Outcome of dorsal buccal graft urethroplasty for recurrent bulbar urethral
539.	strictures. BJU Int, 2008. 102: 1148.
	https://pubmed.ncbi.nlm.nih.gov/18510658/
540.	Spilotros, M., et al. Buccal mucosal graft urethroplasty in men-risk factors for recurrence and
	complications: a third referral centre experience in anterior urethroplasty using buccal mucosal graft.
	Transl Androl Urol, 2017. 6: 510.
	https://pubmed.ncbi.nlm.nih.gov/28725593/
541.	Trivedi, S., et al. Urethral reconstruction in balanitis xerotica obliterans. Urol Int, 2008. 81: 285.
	https://pubmed.ncbi.nlm.nih.gov/18931544/
542.	Wang, K., et al. Dorsal onlay versus ventral onlay urethroplasty for anterior urethral stricture: a meta-
	analysis. Urol Int, 2009. 83: 342.
F 40	https://pubmed.ncbi.nlm.nih.gov/19829038/
543.	Lumen, N., <i>et al.</i> Urethral reconstruction using buccal mucosa or penile skin grafts: systematic review and meta-analysis. Urol Int, 2012. 89: 387.
	https://pubmed.ncbi.nlm.nih.gov/22889835/
544.	Sharma, A.K., et al. Lingual versus buccal mucosa graft urethroplasty for anterior urethral stricture: a
••••	prospective comparative analysis. Int J Urol, 2013. 20: 1199.
	https://pubmed.ncbi.nlm.nih.gov/23601029/
545.	Lumen, N., et al. Buccal Versus Lingual Mucosa Graft in Anterior Urethroplasty: A Prospective
	Comparison of Surgical Outcome and Donor Site Morbidity. J Urol, 2016. 195: 112.
	https://pubmed.ncbi.nlm.nih.gov/26241906/
546.	Abrate, A., et al. Lingual mucosal graft urethroplasty 12 years later: Systematic review and meta-
	analysis. Asian J Urol, 2019. 6: 230.
547.	https://pubmed.ncbi.nlm.nih.gov/31297314/ Chauhan, S., et al. Outcome of buccal mucosa and lingual mucosa graft urethroplasty in the
547.	management of urethral strictures: A comparative study. Urol Ann, 2016. 8: 36.
	https://pubmed.ncbi.nlm.nih.gov/26834399/
548.	Pal, D.K., et al. A comparative study of lingual mucosal graft urethroplasty with buccal mucosal graft
	urethroplasty in urethral stricture disease: An institutional experience. Urol Ann, 2016. 8: 157.
	https://pubmed.ncbi.nlm.nih.gov/27141184/
549.	Song, L.J., et al. Lingual mucosal grafts for anterior urethroplasty: a review. BJU Int, 2009. 104: 1052.
	https://pubmed.ncbi.nlm.nih.gov/19583725/
550.	Manoj, B., et al. Postauricular skin as an alternative to oral mucosa for anterior onlay graft
	urethroplasty: a preliminary experience in patients with oral mucosa changes. Urology, 2009. 74: 345.
551.	https://pubmed.ncbi.nlm.nih.gov/19428075/ Xu, Y.M., <i>et al</i> . Urethral reconstruction using colonic mucosa graft for complex strictures. J Urol,
551.	2009. 182: 1040.
552.	https://pubmed.ncbi.nlm.nih.gov/19616803/ Mangera, A., et al. Tissue engineering in urethral reconstructionan update. Asian J Androl, 2013.
552.	15: 89.
	https://pubmed.ncbi.nlm.nih.gov/23042444/
553.	el-Kassaby, A., et al. Randomized comparative study between buccal mucosal and acellular bladder
	matrix grafts in complex anterior urethral strictures. J Urol, 2008. 179: 1432.
554	https://pubmed.ncbi.nlm.nih.gov/18295282/
554.	Palminteri, E., <i>et al.</i> Long-term results of small intestinal submucosa graft in bulbar urethral reconstruction. Urology, 2012. 79: 695.
	https://pubmed.ncbi.nlm.nih.gov/22245298/

- 555. Xu, Y.M., *et al.* Outcome of small intestinal submucosa graft for repair of anterior urethral strictures. Int J Urol, 2013. 20: 622. <u>https://pubmed.ncbi.nlm.nih.gov/23131085/</u>
  556. Ram-Liebig, G., *et al.* Results of Use of Tissue-Engineered Autologous Oral Mucosa Graft for Urethral Reconstruction: A Multicenter, Prospective, Observational Trial. EBioMed, 2017. 23: 185. <u>https://pubmed.ncbi.nlm.nih.gov/28827035/</u>
- 557. Soave, A., *et al.* Substitution Urethroplasty with Closure Versus Nonclosure of the Buccal Mucosa Graft Harvest Site: A Randomized Controlled Trial with a Detailed Analysis of Oral Pain and Morbidity. Eur Urol, 2018. 73: 910. https://pubmed.ncbi.nlm.nih.gov/29198583/
- 558. Wong, E., *et al.* Does closure of the buccal mucosal graft bed matter? Results from a randomized controlled trial. Urology, 2014. 84: 1223.

https://pubmed.ncbi.nlm.nih.gov/25194996/

559. Rourke, K., *et al.* Effect of wound closure on buccal mucosal graft harvest site morbidity: results of a randomized prospective trial. Urology, 2012. 79: 443.

https://pubmed.ncbi.nlm.nih.gov/22119261/

- 560. Muruganandam, K., *et al.* Closure versus nonclosure of buccal mucosal graft harvest site: A prospective randomized study on post operative morbidity. Indian J Urol, 2009. 25: 72. https://pubmed.ncbi.nlm.nih.gov/19468433/
- 561. Terlecki, R.P., *et al.* Urethral rest: role and rationale in preparation for anterior urethroplasty. Urology, 2011. 77: 1477.

https://pubmed.ncbi.nlm.nih.gov/21513968/

- 562. McDonald, M.L., *et al.* Antimicrobial Practice Patterns for Urethroplasty: Opportunity for Improved Stewardship. Urology, 2016. 94: 237.
  - https://pubmed.ncbi.nlm.nih.gov/27138266/
- 563. Beckley, I., *et al.* Post-operative care following primary optical urethrotomy: Towards an evidence based approach. Brit J Med Surg Urol, 2012.

https://journals.sagepub.com/doi/abs/10.1016/j.bjmsu.2012.04.006

- 564. Erickson, B.A., *et al.* A prospective, randomized trial evaluating the use of hydrogel coated latex versus all silicone urethral catheters after urethral reconstructive surgery. J Urol, 2008. 179: 203. https://pubmed.ncbi.nlm.nih.gov/18001794/
- 565. Poelaert, F., *et al.* Duration of urethral catheterization after urethroplasty: how long is enough? Minerva Urol Nefrol, 2017. 69: 372.

https://pubmed.ncbi.nlm.nih.gov/27097155/

566. Yeung, L.L., *et al.* Urethroplasty practice and surveillance patterns: a survey of reconstructive urologists. Urology, 2013. 82: 471.

https://pubmed.ncbi.nlm.nih.gov/23896103/

- 567. Peng, X.F., *et al.* Effectiveness of Solifenacin for Managing of Bladder Spasms in Patients With Urethroplasty. Am J Mens Health, 2017. 11: 1580. https://pubmed.ncbi.nlm.nih.gov/28669278/
- 568. Granieri, M.A., *et al*. A Critical Evaluation of the Utility of Imaging After Urethroplasty for Bulbar Urethral Stricture Disease. Urology, 2016. 91: 203. https://pubmed.ncbi.nlm.nih.gov/26923442/
- 569. Solanki, S., *et al.* Evaluation of healing at urethral anastomotic site by pericatheter retrograde urethrogram in patients with urethral stricture. Urol Ann, 2014. 6: 325. https://pubmed.ncbi.nlm.nih.gov/25371610/
- 570. Sussman, R.D., *et al.* Novel pericatheter retrograde urethrogram technique is a viable method for postoperative urethroplasty imaging. Int Urol Nephrol, 2017. 49: 2157. https://pubmed.ncbi.nlm.nih.gov/28913706/
- 571. Vetterlein, M.W., *et al.* Characterization of a Standardized Postoperative Radiographic and Functional Voiding Trial after 1-Stage Bulbar Ventral Onlay Buccal Mucosal Graft Urethroplasty and the Impact on Stricture Recurrence-Free Survival. J Urol, 2019. 201: 563. https://pubmed.ncbi.nlm.nih.gov/30240692/
- 572. Bansal, A., *et al.* Early removal of urinary catheter after excision and primary anastomosis in anterior urethral stricture. Turkish J Urol, 2016. 42: 80. https://pubmed.ncbi.nlm.nih.gov/27274892/
- 573. Grossgold, E.T., *et al.* Routine Urethrography After Buccal Graft Bulbar Urethroplasty: The Impact of Initial Urethral Leak on Surgical Success. Urology, 2017. 104: 215. https://pubmed.ncbi.nlm.nih.gov/28214570/

574.	Al-Qudah, H.S., et al. Extended complications of urethroplasty. Int Braz J Urol, 2005. 31: 315.
	https://pubmed.ncbi.nlm.nih.gov/16137399/

- 575. Erickson, B.A., *et al.* Definition of Successful Treatment and Optimal Follow-up after Urethral Reconstruction for Urethral Stricture Disease. Urol Clin North Am, 2017. 44: 1. https://pubmed.ncbi.nlm.nih.gov/27908363/
- 576. Belsante, M.J., *et al.* Cost-effectiveness of risk stratified followup after urethral reconstruction: a decision analysis. J Urol, 2013. 190: 1292. https://pubmed.ncbi.nlm.nih.gov/23583856/
- 577. Voelzke, B.B. Critical review of existing patient reported outcome measures after male anterior urethroplasty. J Urol, 2013. 189: 182. https://pubmed.ncbi.nlm.nih.gov/23174257/
- 578. Jackson, M.J., *et al.* A prospective patient-centred evaluation of urethroplasty for anterior urethral stricture using a validated patient-reported outcome measure. Eur Urol, 2013. 64: 777. https://pubmed.ncbi.nlm.nih.gov/23664422/
- 579. Bertrand, L.A., *et al.* Measuring and Predicting Patient Dissatisfaction after Anterior Urethroplasty Using Patient Reported Outcomes Measures. J Urol, 2016. https://pubmed.ncbi.nlm.nih.gov/26907509/
- 580. Kessler, T.M., *et al.* Patient satisfaction with the outcome of surgery for urethral stricture. J Urol, 2002. 167: 2507.
  - https://pubmed.ncbi.nlm.nih.gov/11992068/
- 581. Maciejewski, C.C., *et al.* Chordee and Penile Shortening Rather Than Voiding Function Are Associated With Patient Dissatisfaction After Urethroplasty. Urology, 2017. 103: 234. https://pubmed.ncbi.nlm.nih.gov/28065809/
- 582. Meeks, J.J., *et al.* Stricture recurrence after urethroplasty: a systematic review. J Urol, 2009. 182: 1266. https://pubmed.ncbi.nlm.nih.gov/19683309/
- 583. Angermeier, K.W., *et al.* SIU/ICUD Consultation on Urethral Strictures: Evaluation and follow-up. Urology, 2014. 83: S8.
- <u>https://pubmed.ncbi.nlm.nih.gov/24275285/</u>
   584. Goonesinghe, S.K., *et al.* Flexible cystourethroscopy in the follow-up of posturethroplasty patients and characterisation of recurrences. Eur Urol, 2015. 68: 523.
- https://pubmed.ncbi.nlm.nih.gov/25913391/
   Seibold, J., *et al.* Urethral ultrasound as a screening tool for stricture recurrence after oral mucosa graft urethroplasty. Urology, 2011. 78: 696.
   https://pubmed.ncbi.nlm.nih.gov/21741691/
- 586. Lozano, J.L., *et al.* [Substitution urethroplasty. Long term follow up results in a group of 50 patients]. Arch Esp Urol, 2015. 68: 424.
  - https://pubmed.ncbi.nlm.nih.gov/26033762/
- 587. Abdelhameed, H., *et al.* The long-term results of lingual mucosal grafts for repairing long anterior urethral strictures. Arab J Urol, 2015. 13: 128. https://pubmed.ncbi.nlm.nih.gov/26413334/
- 588. Erickson, B.A., *et al.* Changes in uroflowmetry maximum flow rates after urethral reconstructive surgery as a means to predict for stricture recurrence. J Urol, 2011. 186: 1934. https://pubmed.ncbi.nlm.nih.gov/21944128/
- 589. DeLong, J., *et al.* Patient-reported outcomes combined with objective data to evaluate outcomes after urethral reconstruction. Urology, 2013. 81: 432. https://pubmed.ncbi.nlm.nih.gov/23374824/
- 590. Erickson, B.A., *et al.* The use of uroflowmetry to diagnose recurrent stricture after urethral reconstructive surgery. J Urol, 2010. 184: 1386.
  - https://pubmed.ncbi.nlm.nih.gov/20727546/
- 591. Warren, G.J., *et al.* The role of noninvasive testing and questionnaires in urethroplasty follow-up. Transl Androl Urol, 2014. 3: 221.
  - https://pubmed.ncbi.nlm.nih.gov/26816769/
- 592. Morey, A.F., *et al.* American Urological Association symptom index in the assessment of urethroplasty outcomes. J Urol, 1998. 159: 1192. https://pubmed.ncbi.nlm.nih.gov/9507830/
- 593. Heyns, C.F., *et al.* Prospective evaluation of the American Urological Association symptom index and peak urinary flow rate for the followup of men with known urethral stricture disease. J Urol, 2002. 168: 2051. https://pubmed.ncbi.nlm.nih.gov/12394706/

594.	Wessels, S.G., <i>et al.</i> Prospective evaluation of a new visual prostate symptom score, the international prostate symptom score, and uroflowmetry in men with urethral stricture disease. Urology, 2014. 83: 220.
	https://pubmed.ncbi.nlm.nih.gov/24231222/
595.	Schober, J.P., et al. Effect of Urethroplasty on Anxiety and Depression. J Urol, 2018. 199: 1552.
	https://pubmed.ncbi.nlm.nih.gov/29408454/
596.	Liu, J.S., et al. Practice Patterns in the Treatment of Urethral Stricture Among American Urologists:
	A Paradigm Change? Urology, 2015. 86: 830.
	https://pubmed.ncbi.nlm.nih.gov/26216643/
597.	Chung, P.H., et al. Evaluation of Generic Versus Condition-Specific Quality of Life Indicators for
	Successful Urethral Stricture Surgery. Urology, 2019. 126: 222.
	https://pubmed.ncbi.nlm.nih.gov/30580004/
598.	Evans, P., et al. A Prospective Study of Patient-reported Pain After Bulbar Urethroplasty. Urology,
	2018. 117: 156.
	https://pubmed.ncbi.nlm.nih.gov/29656064/
599.	Palminteri, E., et al. The impact of ventral oral graft bulbar urethroplasty on sexual life. Urology,
	2013. 81: 891.
	https://pubmed.ncbi.nlm.nih.gov/23434096/
600.	Patel, D.P., et al. Patient-Reported Sexual Function After Staged Penile Urethroplasty. Urology,
	2015. 86: 395.
	https://pubmed.ncbi.nlm.nih.gov/26199158/
601.	Liu, J.S., et al. Risk Factors and Timing of Early Stricture Recurrence After Urethroplasty. Urology,
	2016. 95: 202.
	https://pubmed.ncbi.nlm.nih.gov/27155311/
602.	Zaid, U.B., et al. The cost of surveillance after urethroplasty. Urology, 2015. 85: 1195.
	https://pubmed.ncbi.nlm.nih.gov/25819624/
603.	Han, J.S., et al. Risk of urethral stricture recurrence increases over time after urethroplasty. Int
	J Urol, 2015. 22: 695.
	https://pubmed.ncbi.nlm.nih.gov/25903524

### 13. CONFLICT OF INTEREST

All members of the Urethral Strictures Guidelines Panel have provided disclosure statements of all relationships that they have that might be perceived as a potential source of a conflict of interest. This information is publicly accessible through the European Association of Urology website: <u>http://www.uroweb.org/guidelines/</u>. This guidelines document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.

### **14. CITATION INFORMATION**

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