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Review – Reconstructive Urology

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# European Association of Urology Guidelines on Urethral Stricture Disease (Part 2): Diagnosis, Perioperative Management, and Follow-up in Males

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#### Abstract

*Context:* Urethral stricture management guidelines are an important tool for guiding evidence-based clinical practice.

**Objective:** To present a summary of the 2021 European Association of Urology (EAU) guidelines on diagnosis, classification, perioperative management, and follow-up of male urethral stricture disease.

*Evidence acquisition:* The panel performed a literature review on the topics covering a time frame between 2008 and 2018, and using predefined inclusion and exclusion criteria for the literature. Key papers beyond this time period could be included if panel consensus was reached. A strength rating for each recommendation was added based on a review of the available literature after panel discussion.

*Evidence synthesis:* Routine diagnostic evaluation encompasses history, patientreported outcome measures, examination, uroflowmetry, postvoid residual measurement, endoscopy, and urethrography. Ancillary techniques that provide a three-dimensional assessment and may demonstrate associated abnormalities include sonourethrography and magnetic resonance urethrogram, although these are not utilised routinely. The classification of strictures should include stricture location and calibre. Urethral rest after urethral manipulations is advised prior to offering urethroplasty. An assessment for urinary extravasation after urethroplasty is beneficial before catheter removal. The optimal time of catheterisation after urethrotomy is <72 h, but is unclear following urethroplasty and depends on various factors. Patients undergoing urethroplasty should be followed up for at least 1 yr. Objective and subjective outcomes should be assessed after urethral surgeries, including patient satisfaction and sexual function.

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**Conclusions:** Accurate diagnosis and categorisation is important in determining management. Adequate perioperative care and follow-up is essential for achieving successful outcomes. The EAU guidelines provide relevant evidence-based recommendations to optimise patient work-up and follow-up.

**Patient summary:** Urethral strictures have to be assessed adequately before planning treatment. Before surgery, urethral rest and infection prevention are advised. After urethral surgery, x-ray dye tests are advised before removing catheters to ensure that healing has occurred. Routine follow-up is required, including patient-reported outcomes. These guidelines aim to guide doctors in the diagnosis, care, and follow-up of patients with urethral stricture.

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## 1. Diagnosis of male urethral strictures

#### 1.1. Patient history

This should assess symptomatology, identify possible aetiology, note prior treatments and complications, and identify associated factors that could influence surgical outcome (Fig. 1 and Table 1).

Male urethral stricture disease (MUSD) presents in a variety of ways. A retrospective series (n = 611) revealed that lower urinary tract symptoms (LUTS) were the main mode of presentation (54.3%). Other less common modes were urinary retention (22.3%), urinary tract infection (UTI; 6.1%), and difficulty in catheterisation (4.8%) [1]. In another retrospective analysis (n = 214), the most common symptoms were weak stream (49%), incomplete emptying (27%), and urinary frequency (20%) [2]. Postvoid dribble is present in 73% of cases [3].

Pain is also a common feature affecting 22.9–71% of patients [1,4]. Pain can be felt in the bladder and/or urethra and is associated with more significant LUTS. Pain is more likely to be a feature in younger men and usually resolves following reconstructive surgery [4]. Other presentations (9%) include visible haematuria (3.1–5%), urethral abscess/ necrotising fasciitis (2.3%), urgency (14%), and incontinence (1-4%) [1,2].

The date of the most recent intervention (ie, dilatation) is important, as this will impact the timing of urethrography or surgery (see section 3.1).

Sexual problems are common in MUSD [5], whilst sexual function may be impacted by reconstructive surgery [6]; therefore, it is important to document sexual function using validated tools.

Health status is important as it influences the choice between a palliative and a curative treatment. Any factor that may impair healing should be identified (ie, diabetes, immunosuppression, and smoking). Oral tobacco usage or chewing of betel leaves can impact the decision regarding whether or not oral mucosa graft can be harvested. It is also important to note previous substitution flap or graft sites/ material for future surgical planning.

#### 1.2. Physical examination

The abdomen should be palpated to assess for a full bladder, and the presence of a suprapubic catheter (SPC) should be noted as it may be useful for antegrade cystoscopy or intraoperative sound placement. Genital examination should assess the size of the phallus, presence of chordee, presence of foreskin, any urethrocutaneous fistula, the position and size of the meatus, and any scarring. A biopsy to confirm lichen sclerosus (LS) may be performed if this influences the management approach [7] and is critical if there is any suspicion of malignancy.

The urethra is felt for signs of induration, which is typical with significant fibrosis. Digital rectal examination (DRE) palpating the prostate for signs of enlargement, whether benign or malignant, is essential as this may be the cause of

| Table 1 – | <ul> <li>EAU Urethral</li> </ul> | Stricture G | uidelines | Panel | recommendations | on | diagnosis | of mal | e urethral | strictures |
|-----------|----------------------------------|-------------|-----------|-------|-----------------|----|-----------|--------|------------|------------|
|           |                                  |             |           |       |                 |    |           |        |            |            |

| Recommendations  | Strength rating |
|--|-----------------|
| Use a validated patient-reported outcome measure (PROM) to assess symptom severity and impact upon quality of life in men undergoing surgery for urethral stricture disease. | Strong          |
| Use a validated tool to assess sexual function in men undergoing surgery for urethral stricture disease.   | Strong          |
| Perform uroflowmetry and estimation of postvoid residual in patients with suspected urethral stricture disease.  | Strong          |
| Perform retrograde urethrography to assess stricture location and length in men with urethral stricture disease being considered for reconstructive surgery.                 | Strong          |
| Combine retrograde urethrography with voiding cystourethrography to assess (nearly) obliterative strictures, stenoses, and pelvic fracture urethral injuries.                | Strong          |
| Use clamp devices in preference to the Foley catheter technique for urethrographic evaluation to reduce pain.  | Weak            |
| Perform cystourethroscopy as an adjunct to imaging if further information is required.   | Weak            |
| Combine retrograde urethroscopy and antegrade cystoscopy to evaluate pelvic fracture urethral injuries as an adjunct to imaging if further information is required.          | Weak            |
| Consider MRI urethrography as an ancillary test in posterior urethral stenoses.  | Strong          |
| EAU = European Association of Urology; MRI = magnetic resonance imaging.   |                 |

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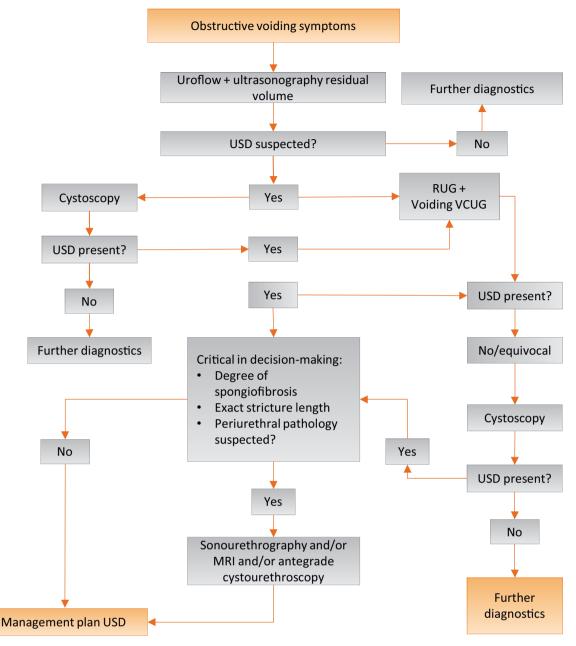


Fig. 1 – Diagnostic flowchart of patients with suspected urethral stricture disease. MRI = magnetic resonance imaging; RUG = retrograde urethrography; USD = urethral stricture disease; VCUG = voiding cystourethrogram.

patients' LUTS. In cases of posterior urethral stenosis, DRE can assess rectal adherence to the prostate and tissue mobility [8].

## 1.3. Further diagnostic evaluation

## 1.3.1. Patient-reported outcome measures

Jackson et al [9] validated the urethral stricture surgery (USS)specific patient-reported outcome measures (PROM), and this has been further validated in several other languages.

#### 1.3.2. Urinalysis and urine culture

Urinalysis is an essential component of the evaluation. If infection is identified, urine culture to isolate the causative

organism and sensitivity to antibiotics should be requested [10].

#### 1.3.3. Uroflowmetry and postvoid residual estimation

Although the classic pattern is a prolonged plateau shape with reduced maximum urinary flow (Q<sub>max</sub>), the interpretation of flow patterns is subjective and an unreliable tool to detect MUSD [11]. To overcome this, Lambert and colleagues [11] developed a statistical model based on uroflow and found this to predict urethral stricture with sensitivity of 80–81% and specificity of 77–78%. Uroflowmetry is usually followed by ultrasound measurement of postvoid residual (PVR), which is helpful in identifying patients in chronic urinary retention.

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In most patients with MUSD, pressure flow studies are not necessary, except in patients with suspected bladder dysfunction. A common reason to undertake pressure flow studies is when detrusor hypo/acontractility is suspected, as these patients may need to perform intermittent selfcatheterisation (ISC) postoperatively. The only urodynamic parameter found to distinguish MUSD from benign prostatic obstruction (BPO) is urethral closure pressure, which is lower in the former due to the constrictive nature of the obstruction (22.07 vs 28.4 cmH<sub>2</sub>O, p = 0.0039, r = 0.61, BPO vs stricture) [12].

#### 1.3.4. Urethrography

Retrograde urethrogram (RUG) assesses stricture presence, location, length, and any associated abnormalities (ie, false passages and diverticula).

The sensitivity and specificity of RUG in diagnosing strictures are 91% and 72%, respectively [13]. The positive and negative predictive values were, respectively, 89% and 76% [13]. RUG underestimates stricture length compared with operative findings [14].

The main limitations of RUG are the challenges in assessing very distal strictures and the proximal limit of strictures, which do not allow passage of enough contrast. If RUG is combined with voiding cystourethrography (VCUG), then the urethra proximal to the stricture can be visualised and stricture length in (nearly) obliterative strictures can be assessed more accurately. This technique also allows assessment of the gap in pelvic fracture urethral injury (PFUI) [15]. Other limitations of RUG are that it can provide only a two-dimensional assessment of stricture, and the results may be affected by the amount of penile stretch [16], degree of pelvic rotation, and body habitus [17]. Risks of the procedure include infection, discomfort [12], and contrast reaction from intravasation of contrast, in addition to radiation exposure. Clamp devices (Brodny, Knutson) to facilitate injection of the contrast are available and have been found to be less painful than using a Foley catheter to occlude the urethra whilst performing RUG [18].

## 1.3.5. Cystourethroscopy

Cystourethroscopy allows for accurate visual detection of a suspected stricture or can rule out a stricture as a cause of obstructive voiding [13]. Narrowing of the urethral lumen can be visualised before the onset of changes in flow rate and symptoms [19]. The presence of LS or other pathology (ie, foreign body or hair) can also be evaluated, but not the stricture length as the calibres of most cystoscopes is greater than most symptomatic strictures [20]. To overcome this, some have used smaller-calibre ureteroscopes (6.5 and 4.5 Fr) [20]. The advantage of this is that it also allows an assessment of the bladder prior to surgery and may identify other pathology such as bladder stones. Cystourethroscopy is particularly important for diagnosing bulbomembranous stricture, which can be missed on RUG.

Combined retrograde urethroscopy and antegrade cystoscopy via an SPC tract is used by some to evaluate PFUI and plan the surgical approach. This allows an evaluation of the length of the defect, bladder neck competence, bladder neck scarring, presence of bony spicules, or other fistulae/ false passages or stones [21].

#### 1.3.6. Ultrasound

Sonourethrography (SUG; ultrasound of the urethra) is a noninvasive method of assessing MUSD including stricture location and length, and the degree of associated spongio-fibrosis, which provides three-dimensional information [22]. It can be performed in the outpatient setting and is of relatively low cost.

SUG was shown to diagnose stricture presence with greater accuracy [18,23] and is more accurate at estimating stricture length compared with RUG (respectively, 94% and 59% correlation with intraoperative findings; p < 0.001) [14]. Intraoperative SUG findings were reported to alter the planned reconstructive approach (based on preoperative RUG) in 19% of men undergoing anterior urethral reconstruction [17].

The main limitations of SUG are lower sensitivity for the detection of bulbar strictures, operator dependency, and the need for urethral distension requiring intraurethral anaesthesia. In addition, SUG needs specialised training, which is likely to be why it is currently not used widely.

#### 1.3.7. Magnetic resonance imaging

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

MRI urethrogram was found to be as accurate as RUG at detecting stricture site and assessing stricture length in anterior urethral strictures [24]. MRI is more accurate at diagnosing associated pathologies (ie, diverticula, tumours, fistulae, and stones) [25].

In addition, in a study of patients with posterior urethral stenosis, MRI measurement of stenosis length was more accurate than that measured by RUG [26]. In patients with PFUI, MRI measurement of pubourethral stump angle predicted the need for an elaborated approach [27].

MRI provides the greatest anatomical detail of all modalities, but is expensive and more complex to interpret. The technique is not commonly used for routine situations.

## 2. Classification of male urethral strictures

#### 2.1. According to stricture location

Classification according to stricture location is important as this will affect further management (Table 2) [28].

Strictures extending towards the membranous urethra are termed bulbomembranous strictures.

Penobulbar strictures should be differentiated from multifocal strictures, defined by two or more narrowed segments—either in the same urethral segment or in different segments—but preserving healthy urethral areas between them.

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## Table 2 – Male urethra stricture locations and anatomic landmarks for classification

| Urethral segment         |                                     | Location—anatomic landmarks  |
|--------------------------|-------------------------------------|--|
| Anterior urethra         | Meatal strictures                   | External urethral meatus; may extend into the fossa navicularis of the glans   |
|                          | Penile strictures                   | Between fossa navicularis and bulbar urethra   |
|                          | Bulbar strictures                   | Starting at the penoscrotal junction and ending at the level of the urogenital diaphragm   |
|                          | Penobulbar strictures               | From penile urethra into the bulbar segment (compromising long segments of urethra)  |
| Posterior urethra        | Membranous urethral stenosis        | Segment traversing the urogenital diaphragm, from proximal bulbar to distal verumontanum   |
|                          | Prostatic urethral stenosis         | Segment through the prostatic gland, starting at the proximal membranous<br>urethra and extending to the bladder neck                            |
|                          | Bladder neck stenosis               | Junction between the prostatic urethra and the bladder, requiring that the prostatic gland is in situ (ie, after TURP or simple prostatectomies) |
|                          | Vesicourethral anastomosis stenosis | Narrowing or obliteration at anastomotic site after radical prostatectomy  |
| TURP = transurethral res | section of the prostate.            |  |

#### Table 3 – EAU Urethral Stricture Guidelines Panel classification of male urethral stricture

| Category                               | Description                               | Urethral lumen (Fr)                 | Degree |  |
|--|---|-------------------------------------|--------|--|
| 0                                      | Normal urethra in imaging techniques      |                                     |        |  |
| 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)            |        |  |
| EAU = European Association of Urology. |   |                                     |        |  |

#### Table 4 - EAU Urethral Stricture Guidelines Panel recommendations on perioperative management of male urethral strictures

| Recommendations   | Strength rating |
|---|-----------------|
| Do not perform urethroplasty within 3 mo of any form of urethral manipulation.  | Weak            |
| Administer an intraoperative prophylactic regimen with antibiotics at the time of urethral surgery.   | Strong          |
| Remove the catheter within 72 h after uncomplicated direct vision internal urethrotomy or urethral dilatation.  | Weak            |
| Perform a form of validated urethrography after urethroplasty to assess for urinary extravasation prior to catheter removal.  | Strong          |
| Perform first urethrography 7–10 d after uncomplicated urethroplasty to assess whether catheter removal is possible, especially in patients with bother from their urethral catheter. | Strong          |
| EAU = European Association of Urology.  |                 |

#### 2.2. According to stricture tightness

It has been demonstrated that men usually do not experience subjective obstructive symptoms until the urethral lumen has a diameter below 10 Fr [29].

The European Association of Urology (EAU) stricture panel proposes the following classification upon degree of male urethral narrowing (Table 3).

#### Perioperative management of male urethral 3. strictures

#### 3.1. Urethral rest

After any form of urethral manipulation (urethral catheter, ISC, dilation, and DVIU), a period of urethral rest is necessary in order to allow tissue recovery and stricture "maturation" before considering urethroplasty (Table 4). 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, an SPC should be inserted. Terlecki et al [30] proposed a diagnostic evaluation after 2 mo and urethroplasty after 3 mo of urethral rest. 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, with longer periods of rest in those contexts.

#### 3.2. Antibiotics

For MUSD, antibiotic practices should be in accordance with the strong recommendations of the EAU guidelines on urological infections: (1) screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa, and (2) treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions.

An intraoperative prophylactic regimen with antibiotics (according to local antibiotic resistance profiles) is effective in reducing the rate of postoperative surgical site and UTI,

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## (A) Surgeries with low-risk of recurrence

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

|   | 3 mo | 12 mo            | 24 mo ª       |
|---|------|------------------|---------------|
| Uroflow   | +    | +                | +             |
| PROM (incl. sexual function)                            | +    | +                | +             |
| Anatomic evaluation<br>(urethrocystoscopy/RUG-<br>VCUG) | + b  | On<br>indication | On indication |

## (B) Surgeries with standard risk of recurrence

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

|   | 3 mo | 12 mo | 24 mo | 5 yr °           |
|---|------|-------|-------|------------------|
| Uroflow   | +    | +     | +     | +                |
| PROM (incl. sexual function)                            | +    | +     | +     | +                |
| Anatomic evaluation<br>(urethrocystoscopy/RUG-<br>VCUG) | +    | +     | +     | On<br>indication |

Fig. 2 – EAU Urethral Stricture Guidelines Panel follow-up protocol proposal after male urethroplasty: (A) surgeries with a low risk of recurrence and (B) surgeries with standard risk of recurrence.

EAU = European Association of Urology; BXO = balanitis xerotica obliterans; LS = lichen sclerosus; PROM = patient-reported outcome measures; RUG = retrograde urethrogram; VCUG = voiding cystourethrography.

<sup>a</sup>Follow-up could be discontinued after 2 yr, advising the patient to seek for urological evaluation if symptoms worsened. Academic centres could increase the length of follow-up for research purposes.

<sup>b</sup>The panel suggests performing an anatomic assessment at 3 mo.

<sup>c</sup>Follow-up could be discontinued after 5 yr, advising the patient to seek for urological evaluation if symptoms worsened. 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.

both of which are contributors to failure of the repair [31]. Although most urologists continue with postoperative antibiotics upon and even beyond catheter removal, there is no evidence that such prolonged administration reduces the infective complication rate [31].

## 3.3. Catheter management

After uncomplicated endoluminal treatment, the catheter should be removed within 72 h [32].

After perineostomy or the first stage of staged urethroplasty, the catheter can be removed without need for urethrography after 3–5 d [33].

After one-stage urethroplasty and closure of the urethral plate after staged urethroplasty, urinary extravasation at the site of reconstruction must be avoided [34]. For this

purpose, urinary diversion by either a transurethral catheter or an SPC with an urethral stent can be used. With respect to the type of catheter material, a prospective randomised (but underpowered) trial comparing silicone versus hydrogelcoated latex transurethral catheters showed no significant difference in the time to stricture recurrence or in the overall recurrence rate [34]. The size of the urethral catheter utilised usually varies between 14 and 20 Fr [35,36].

After urethroplasty, an indwelling catheter is commonly left in situ for 2–3 wk [36,37]. After 3 wk, an extravasation rate of 2.2–11.5% at urethrography has been reported after different types of urethroplasty [33,37,38]. However, success with early catheter removal has also been reported. After excision and primary anastomosis for noncomplicated anterior strictures, no significant difference was demonstrated in extravasation (6.8% vs 4.5%) and recurrence rates

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#### Table 5 – EAU Urethral Stricture Guidelines Panel recommendations on follow-up after male urethroplasty

| Recommendations  | Strength rating |
|--|-----------------|
| Offer follow-up to all patients after urethroplasty surgery.                                       | Strong          |
| Offer a routine follow-up of at least 1 yr after urethroplasty.                                    | Strong          |
| Adopt a risk-adjusted follow-up protocol.  | Weak            |
| Use cystoscopy or retrograde urethrography to assess anatomic success after urethroplasty surgery. | Weak            |
| Use PROM questionnaires to assess subjective outcomes and patient satisfaction.                    | Strong          |
| Use validated questionnaires to evaluate sexual function after urethral stricture surgeries.       | Strong          |
| EAU = European Association of Urology; PROM = patient-reported outcome measure.                    |                 |

(4.9% vs 5.2%) between catheter removal at 1 or 2 wk, respectively [39]. Poelaert et al [35] reported an extravasation rate of 3.5% versus 8.3% when the catheter was removed  $\leq$ 10 versus >10 d after all types of urethroplasty, but patients with catheterisation of >10 d had longer and more complex strictures.

Prior to catheter removal after urethroplasty, it is important to assess for urinary extravasation to avoid ensuing complications including periurethral inflammation, abscess formation, and fistulation [33,37]. Some authors have identified urinary extravasation as a predictive factor for stricture recurrence, especially with high-grade leaks (defined as length  $\geq$ 1.03 cm and width  $\geq$ 0.32 cm) [33,35]. In cases of persistent and significant urinary extravasation, the catheter should be maintained or reinserted and the examination repeated after 1 wk [37]. However, low-grade ("wisp like") extravasation does not appear to affect longterm restricture rate, and the catheter can be removed in these cases [33,40]. In case of any doubt about the significance of extravasation, it is safest to keep the catheter in for an additional week and redo the assessment.

Although there is no evidence that one imaging (pericatheter RUG and VCUG) modality is superior to the other, pericatheter RUG 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 examination [33,40]. External clinical signs of impaired wound healing (eg, abscess formation and wound dehiscence) are also associated with a high risk (71.4%) of leakage [35].

#### 4. Follow-up of male urethral strictures

#### 4.1. Rationale for follow-up after urethral surgery

The rationale is to detect and manage any complication or recurrence (Table 5). Up to 54% of patients after anterior urethroplasty [41] would present with complications with short to medium follow-up. Though urethroplasty provides the highest chances for patency, some patients will experience recurrence [42].

#### 4.2. Definition of success after urethroplasty surgery

The "traditional academic" definition of success after urethroplasty has been considered as the lack of any postoperative intervention for restricture [43]. This definition is problematic as it ignores asymptomatic or even symptomatic recurrences with patients not willing to undergo further surgeries [43].

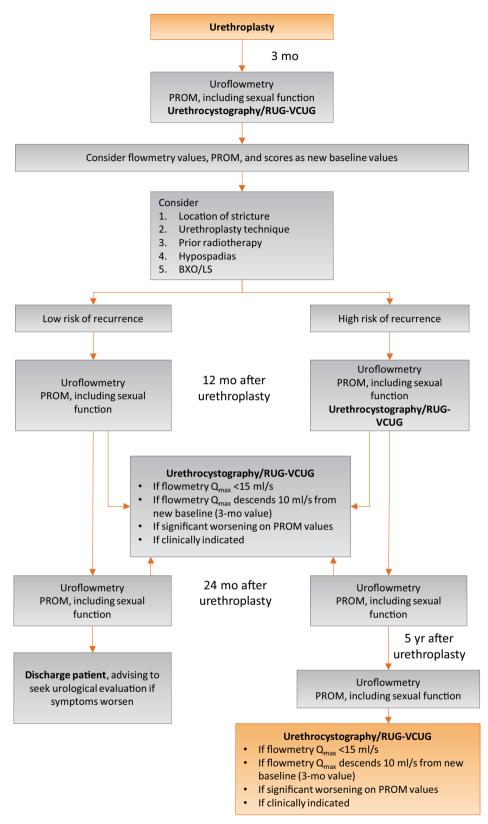
A more objective definition is the "anatomic success", considered as normal urethral lumen during RUG or cystoscopy, regardless of patient symptoms. Stricture recurrence or anatomical failure is considered by some groups as urethral narrowing found to be endoscopically impassable—without force—using a 16F flexible endoscope [19]. This definition is stricter, as up to 35% of cystoscopic recurrences after bulbar urethroplasty remain asymptomatic and thus would have been considered successful if a "traditional" definition was used [19]. Not all anatomic recurrent strictures would need further treatment, and intervention is suggested when associated with recurrence of symptoms, stricture-related high PVRs, or a stricture calibre of <14F—even if the two latter ones are asymptomatic [43].

In contemporary practice, 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 whilst maintaining quality of life or to minimise symptoms, reduce disability, and improve health-related quality of life by restoring normal urinary function [44]. Even if the surgeon has reconstructed a wide and patent urethra, if patients experience complications or perceive their urinary function as not improved, they will not rate their outcome as successful [43]. Table 6 summarises known predictors for dissatisfaction after urethral surgery. Kessler et al [45] reported that only 78.3% of patients with clinical success described themselves as (very) satisfied, whilst 80% of clinical failures considered themselves as (very) satisfied with their outcomes. Owing to this evident discrepancy between surgeon's and patient's assessments, PROMs have been developed for the follow-up after urethroplasty [9,44].

A logical and practical approach for urethral surgery outcomes would combine both anatomic (endoscopic) and patient-reported success [43]. As a panel, we suggest using a functional definition of success for its use in clinical practice, namely, a lack of symptoms and/or no need for further interventions. Collection also of objective anatomic outcomes would be for academic purposes, in order to allow a comparison of surgical outcomes among reconstructive urological surgeons and centres. Objective and subjective outcome measures should be assessed and reported simultaneously, but separately, when evaluating urethroplasty results [43].

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#### Fig. 3 – Follow-up after urethroplasty.

BXO = balanitis xerotica obliterans; LS = lichen sclerosus; PROM = patient-reported outcome measure; Q<sub>max</sub> = maximum flow rate; RUG = retrograde urethrography; VCUG = voiding cystourethrography.

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#### Table 6 – Predictors of patient dissatisfaction after urethral surgery

| Predictor/symptoms                  | Measure of effect    |
|-------------------------------------|----------------------|
| Weak/very weak urinary stream [45]  | NR                   |
| Penile curvature [45]               | NR                   |
| Penile shortening [45]              | NR                   |
| Worsening of erectile function [45] | NR                   |
| Impairment of sexual life [45]      | NR                   |
| Sexual activity alteration [61]     | OR4.36(1.54-12.37) * |
| Erection confidence (SHIM) [61]     | OR1.53(1.12-2.07) *  |
| Inability to ejaculate (MSHQ) [61]  | OR1.52(1.15-2.01) *  |
| Urethral pain [61]                  | OR1.71(1.05-2.77) *  |
| Bladder pain [61]                   | OR2.74(1.12-6.69) *  |
| Urinary strain (CLSS) [61]          | OR3.23(1.74-6.01) *  |
| Hesitancy (IPSS) [61]               | OR2.01(1.29-3.13) *  |
| Voiding quality of life (IPSS) [61] | OR1.96(1.42-2.72) *  |
| Penile shortening [55]              | OR2.26(1.39-3.69) ** |
| Chordee [55]                        | 2.26(1.44-4.19) **   |

CLSS = Core Lower Urinary Tract Symptom Score: IPSS = International Prostate Symptoms Score; MSHQ = Male Sexual Health Questionnaire; NR = not reported, but statistically significant; SHIM = Sexual Health Inventory for Men. , p < 0.05.

*p* < 0.001.

#### 5. Follow-up tools

#### 5.1. **Diagnostic tools**

#### 511 Calibration

The difference between calibration and urethral dilation is usually subjective as soft strictures may be dilated during calibration [46]. Therefore, urethral calibration should be used with caution for follow-up after urethroplasty.

#### 5.1.2. Urethrocystoscopy

Flexible urethrocystoscopy has been considered the most useful tool to confirm the presence or absence of a recurrent stricture [47,48]. In addition, it could be a measure to calibrate the lumen, bearing in mind the most commonly used endoscopes: 15.7F (5 mm diameter) or 17.3F (5.5 mm diameter) [48]. Urethrocystoscopy allows differentiation of recurrences as diaphragm/cross-bridging, which responds to single simple interventions or significant urethral restricture that requires repeated interventions or redo reconstructive surgery [49]. Endoscopic assessment at 3 mo after anterior urethroplasty can predict the risk for further reintervention at 1 yr [47]. The main problem with using urethrocystoscopy for routine follow-up is the low compliance of patients-only 54% underwent endoscopy at 1 yr after urethroplasty [19].

#### 5.1.3. RUG and VCUG

RUG combined with VCUG are commonly used to confirm suspected recurrence [50] or as part of a routine protocol to assess postoperative urethral patency [51].

## 5.1.4. Urethral ultrasound—SUG

The use of SUG as a follow-up tool is not very common. It would be a reliable tool for diagnostic recurrent strictures [50].

#### 5.2. Screening tools

These tools are used to assess whether there is suspicion of stricture recurrence and need for subsequent diagnostic evaluation (see section 1).

#### 5.2.1. Flow-rate analysis

Evaluating the Q<sub>max</sub> is the commonest follow-up tool. Different cut-off points from Q<sub>max</sub> 15 or 12 ml/s were suggested to consider the intervention as failure or to trigger confirmatory test for recurrence. There is no clear threshold, and 19% of patients with  $Q_{max}$  <14 ml/s would still have a patent urethra, allowing passage of a 15F cystoscope [52]. A comparison of both pre- and postoperative Q<sub>max</sub> levels was suggested, and a difference in Q<sub>max</sub> of  $\leq$ 10 ml/s is found to be a reliable screen tool for recurrence-sensitivity 92% and specificity 78% [51]. Unfortunately, this improvement after urethroplasty is significantly different between age groups [53]. Another parameter to consider is the shape of the voiding curve, recording it as flat (obstructed) or bell shaped [54]. An obstructive voiding curve demonstrated 93% sensitivity to predict recurrent strictures, whilst a combination of urinary symptoms and obstructive voiding curve achieved 99% sensitivity and 99% negative predictive value [54].

#### 5.2.2. PVR ultrasound measure

PVR ultrasound measure is significantly increased in patients with recurrent strictures compared with those without recurrences [50], but currently there is no literature support for its solo use to assess urethral stricture recurrence.

#### 5.2.3. Symptoms questionnaires

The International Prostate Symptoms Score (IPSS) showed significant improvement after successful urethroplasty and inverse significant correlation with  $Q_{max}$  [55]. The mean improvement of IPSS is around -11 points (range -19 to -5) [53]. A combination of IPSS and  $Q_{max}$  analysis was suggested to diagnose recurrences. The use of an IPSS cutoff of 10 points associated with  $Q_{max}\ > 15\ ml/s$  would prevent further invasive studies in 34% of patients, whilst only 4.3% of strictures <14 F would have been missed. The use of an IPSS cut-off of 15 points associated with Qmax >15 ml/s would prevent further invasive studies in 37% of cases, whilst 6% of strictures <14 F would have been missed [56].

#### 5.2.4. Quality of life assessment using disease-specific questionnaires

The USS-PROM [9,44] has been found to be useful for assessing outcomes in anterior urethroplasty patients [44]. PROM questionnaires should be implemented in each visit, as they are likely to improve, to check for functional success. Sexual function including erectile and ejaculatory functions should be evaluated by validated tools if not assessed in a condition-specific PROM.

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#### 6. Ideal interval and length of follow-up

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 [43].

After anterior urethroplasty, 21% of recurrences are clinically evident, and cystoscopically confirmed, after 3 mo [57] and 96% after 1 yr [49]. Of bulbar stricture recurrences, 23% would be detected during the 2nd year of follow-up and the percentage of recurrences would decrease thereafter [42].

Early recurrences are more frequent in patients with LS/balanitis xerotica obliterans (BXO) and older age, in longer strictures and when skin grafts were used [57]. Late recurrences (>5 yr after urethroplasty) could be observed in up to 15% of cases [42,52]. These appear mainly after substitution urethroplasties, especially the ones using skin as graft. Certainly, patients should be instructed to seek urological evaluation if they experience late recurrence symptoms [58]. Long-term follow-up could be offered in academic institutions, to provide detailed information of outcomes in particular contexts (Fig. 2-3).

#### 7. Risk-stratified proposals

As the risk of recurrence and side effects are related to the type of stricture and urethroplasty, a different follow-up schedule was proposed based upon risk stratification. This was shown to be cost effective, potentially saving up to 85% of costs at 5 yr [59]. If evidence of good anatomical outcome is obtained using cystourethroscopy or RUG/VCUG at 3-6 mo postoperatively, flowmetry and questionnaires should be considered as the new baseline. Thereafter, follow-up could be performed safely with noninvasive tests. Any significant decline (25-30%) in Qmax or Qmax - Qave should be investigated further with cystourethroscopy, even in patients who are symptom free [43,60]. Routine cystourethroscopy at 12-15 mo should be performed at the surgeon's discretion, based on the presence of any the following three factors: higher-risk patients, evidence of partial narrowing at 3-mo assessment, and low-volume surgeons [43].

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*Study concept and design:* Campos-Juanatey, Osman, Greenwell, Martins, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos, Lumen.

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Analysis and interpretation of data: Lumen, Campos-Juanatey, Greenwell, Martins, Osman, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos. *Drafting of the manuscript*: Campos-Juanatey, Osman, Greenwell, Martins, Riechardt, Waterloos, Barratt, Chan, Esperto, Ploumidis, Verla, Dimitropoulos, Lumen.

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