Canadian Urological Association guideline on male urethral stricture

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Abstract

Urethral stricture is fundamentally a fibrosis of the urethral epithelial and associated corpus spongiosum, which in turn, causes obstruction of the urethral lumen. Patients with urethral stricture most commonly present with lower urinary tract symptoms, urinary retention or urinary tract infection but may also experience a broad spectrum of other signs and symptoms, including genitourinary pain, hematuria, abscess, ejaculatory dysfunction, or renal failure. When urethral stricture is initially suspected based on clinical assessment, cystoscopy is suggested as the modality that most accurately establishes the diagnosis. This recommendation is based on several factors, including the accuracy of cystoscopy, as well as its wide availability, lesser overall cost, and comfort of urologists with this technique. When recurrent urethral stricture is suspected, we suggest performing retrograde urethrography to further stage the length and location of the stricture or referring the patient to a physician with expertise in reconstructive urology. Ultimately, the treatment decision depends on several factors, including the type and acuity of patient symptoms, the presence of complications, prior interventions, and the overall impact of the urethral stricture on the patient's quality of life. Endoscopic treatment, either as dilation or internal urethrotomy, is suggested rather than urethroplasty for the initial treatment of urethral stricture. This recommendation applies to men with undifferentiated urethral stricture and does not apply to trauma-related urethral injuries, penile urethral strictures (hypospadias, lichen sclerosus), or suspected urethral malignancy. In the setting of recurrent urethral stricture, urethroplasty is suggested rather than repeat endoscopic management but this may vary depending on patient preference and impact of the symptoms on the patient.

The purpose of this guideline is to provide a practical summary outlining the diagnosis and treatment of urethral stricture in the Canadian setting.

Introduction, epidemiology, and etiology

Urethral stricture is likely the oldest urological disease, with documentation of its existence over 4000 years ago.[1] The prevalence has likely changed over the course of human history. In the 19th century, it was thought that up to 20% of adult men developed urethral stricture.[2] Currently, the prevalence of urethral stricture may vary widely throughout the globe but in industrialized nations is reported to be approximately 0.9% based on epidemiological data.[3] Fundamentally, urethral stricture is a fibrosis of the urethral epithelial tissue and corpus spongiosum, which in turn, causes narrowing of the urethral lumen.[4] By convention, when located in the anterior urethra, the term stricture is used, but when located in the posterior urethra, the term stenosis is most appropriate.[5] As the urethral lumen progressively narrows, varying degrees of obstruction occur.

Urethral strictures can occur as a result of one of two general mechanisms. Injury to the outside of the spongiosum, leading to spongiofibrosis, can occur as a result of blunt or penetrating trauma. Alternatively, instrumentation or inflammatory disease can cause internal disruption of the urethral epithelium also leading to spongiofibrosis. In general, the etiology of stricture is categorized into iatrogenic, idiopathic, traumatic, congenital, and inflammatory causes.[6] Etiologies within these categories are broad, and include instrumentation (e.g. cystoscopy), transurethral resection of the prostate (TURP), indwelling catheter, treatment for prostate cancer, straddle injury, lichen sclerosis, and post-infectious strictures.

While not explicitly a cause of stricture, other epidemiological factors are associated with an increased likelihood of developing a urethral stricture. The likelihood of being diagnosed with a urethral stricture increases with age. For example, men aged 55–64 are 1.5 times more likely to have urethral stricture compared to controls under 55 years of age, with a steady increase in incidence throughout each subsequent decade peaking with a 12-fold risk in men over the age of 85.[4] There also appears to be an increased likelihood of developing a urethral stricture with declining socioeconomic status.[4]

Globally, urethral stricture accounts for a substantial amount of inpatient, ambulatory, and emergency room visits.[4] Accordingly, urethral stricture incurs a yearly individual average cost of disease estimated at $6000, with a total estimated cost of over $200 million per year in the U.S., independent of reduced patient quality of life.[4,7]

GRADE methodology

This guideline was developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Adolopment approach.[8] We established a guideline panel with five members with expertise in urology, urological surgery, reconstructive urology, and guideline methodology. No panel member was identified to have conflicts of interest limiting their participation on this panel.

In August 2018, the panel prioritized three key questions to address in this guideline related to the identification of urethral stricture and its treatment. The panel also identified the critical outcomes upon which the recommendations were made: stricture recurrence, improvement in lower urinary tract symptoms (LUTS), quality of life, additional procedures, and stricture-related complications. The methodology team from Cochrane Canada conducted a comprehensive search of the literature for published systematic reviews and reviews published in clinical practice guidelines that addressed the key questions. We identified a guideline published by the American Urological Association (AUA) in which the evidence was reviewed up to January 2015.[9]

The search of the AUA review was updated from January 2014 to October 2018 in Medline, Embase, and Central and identified 1429 citations. Citations were subsequently screened by members of the guideline panel and the Cochrane Canada team for comparative studies and studies evaluating the effects of one intervention or test, or studies addressing factors such as patient values and preferences, resources, equity, acceptability, or feasibility. When possible, comparative data and a calculated risk ratio was pooled using RevMan 5.2. Data from studies evaluating one intervention were pooled using an unweighted average. For recommendation 1, evidence was synthesized from six studies for test accuracy of retrograde urethrogram (RUG) or sonourethrogram (SUG) previously identified in the AUA review; for recommendation 2, six studies from the AUA review and 22 new studies were synthesized; and, for recommendation 3, 11 from the AUA review and 21 new studies were synthesised (see Appendix for syntheses and references to included studies; available at *cuaj.ca*). The risk of bias of the studies and the certainty of the evidence were assessed using the GRADE approach.[10-16] The evidence was presented in evidence profiles and Evidence to Decision Tables using GRADEpro (See Appendix; available at *cuaj.ca*). The guideline panel developed the recommendations by consensus during two teleconference meetings. The panel considered the desirable and undesirable effects of the interventions, the value placed on the outcomes, the required resources, the acceptability of the interventions to all stakeholders, the impact on health equity, and the feasibility of the interventions. The strength of each recommendation was rated as either strong or conditional. Strong recommendations were made when all the desirable consequences of treatment outweighed the undesirable consequences, and are worded as "*recommends*." Conditional recommendations were made when the desirable consequences probably outweighed the undesirable consequences, and are worded as "*suggests*" (Table 1). The final recommendations were reviewed and approved by the guideline panel.

Table 1. Implications of strong and conditional recommendations

Implications	Strong recommendation	Conditional recommendation
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Most individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guidelines could be used as a quality criterion or performance indicator.	Clinicians should recognize that different choices will be appropriate for each individual and that clinicians must help each individual arrive at a management decision consistent with the individual's values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences.
For policy-makers	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

Presentation and assessment

Signs and symptoms

Regardless of the mechanism or injury, as the scar tissue contracts, there is generally a reduction in the caliber of the urethral lumen. Most of the symptoms related to urethral stricture are thought to be directly related to this decrease in urethral caliber. Typical symptoms are LUTS, such as weak urinary stream, straining to void, urinary hesitancy, nocturia, frequency, and the sensation of incomplete emptying.[17] Other signs and symptoms, such as genitourinary pain, urinary tract infection (UTI), ejaculatory dysfunction, urethral discharge, and hematuria, may also occur. A significant proportion of patients with urethral stricture will experience significant complications requiring emergent urological care, including acute urinary retention, UTI, difficult catheterization, renal failure, or peri-urethral abscess.[18] Additionally, some of these complications can be considered life-threatening. For example, urethral stricture is a known risk factor for Fournier's gangrene.

Assessment

Patients suspected of having a urethral stricture should be evaluated with history, physical examination, serum creatinine, and urinalysis. The initial evaluation may also include a combination of patient-reported measures, such as the International Prostate Symptom Score (IPSS), uroflowmetry, and ultrasound post-void residual (PVR) urine measurement. When a stricture is suspected, cystourethroscopy or retrograde urethrography have been historically used to confirm the diagnosis. Ancillary investigative tools used in special circumstances include urethral ultrasonography and magnetic resonance imaging (MRI).

Diagnosis: Should men with suspected urethral stricture undergo cystoscopy as the most accurate method to diagnose a clinically significant urethral stricture?

Recommendations: We suggest using cystoscopy rather than urethrography for the initial diagnosis of suspected urethral stricture *(conditional recommendation, low certainty in evidence of effects)*. We suggest performing retrograde urethrography to further stage urethral stricture or referring the patient to a physician with expertise in reconstructive urology when a recurrent stricture is suspected *(conditional recommendation, low certainty in evidence of effects)*. We suggest against using MRI for routine initial diagnosis of suspected stricture *(conditional recommendation, low certainty in evidence of effects)*.

This recommendation is based on several factors, including the accuracy of cystoscopy, as well as its wide availability, lesser cost, and comfort of urologists with this technique. In this setting, literature review identified six studies that assessed RUG and/or SUG compared to cystoscopy with confirmation by surgery as the reference standard.[19-24] Based on the literature, there is a lower certainty of evidence for the sensitivity and specificity of urethrography when using a prevalence of 60% urethral stricture in clinically suspected men. Ultimately, the use of urethrography at initial diagnosis likely leads to greater numbers of missed cases of urethral stricture (2–4 more per 100 men) and unnecessary treatment (0–6 more per 100 men) than when performing cystoscopy (Table 2). Moreover, cystoscopy is widely available in most clinical settings and requires fewer resources (such as costs, equipment, and training) than urethrography with less radiation exposure (specific to RUGs). However, RUG over cystoscopy accurately determines urethral stricture location and length, which is of paramount importance, especially when evaluating patients who are at risk for failure of endoscopic treatment, such as in the setting of recurrent

Table 2. Test accuracy data for RUG and SUG based on 40% and 60% prevalence of urethral stricture by clinical suspicion

	Urethrogram: RUG		Urethrogram: SUG	
	Sensitivity	0.94	Sensitivity	0.90
	Specificity	0.90	Specificity	1.00
Outcome	Effect per 100 patients tested			
	Pre-test probability of 60%		Pre-test probability of 40%	
	Urethrogram: RUG	**Urethrogram: SUG**	**Urethrogram: RUG**	**Urethrogram: SUG**
True positives	56 (0–0)	54 (0–0)	38 (0–0)	36 (0–0)
	2 more TP in urethrogram: RUG		2 more TP in urethrogram: RUG	
False negatives	4 (60–60)	6 (60–60)	2 (40–40)	4 (40–40)
	2 fewer FN in urethrogram: RUG		2 fewer FN in urethrogram: RUG	
True negatives	36 (0–0)	40 (0–0)	54 (0–0)	60 (0–0)
	4 fewer TN in urethrogram: RUG		6 fewer TN in urethrogram: RUG	
False positives	4 (40–40)	0 (40–40)	6 (60–60)	0 (60–60)
	4 more FP in urethrogram: RUG		6 more FP in urethrogram: RUG	

FN: false negative; FP: false positive; RUG: retrograde urethrogram; SUG: sonourethrogram; TP: true positive.

stricture, traumatic strictures, radiations stenoses, and stricture associated with hypospadias. Lastly, the benefits of using MRI were outweighed by the expense, lack of resources, and impracticality of MRI, and could be best reserved for select cases, including complex trauma (pelvic fracture urethral injury), suspected urethral malignancy, radiotherapy-induced urethral stenosis, or associated rectourethral fistula.

Treatment options

The decision to treat a urethral stricture depends on several factors, including symptoms and complications related to urethral stricture (urinary infection, pain, abscess, gross hematuria, renal dysfunction, urinary retention), prior interventions for urethral stricture disease, and the impact of the urethral stricture on the patient's quality of life. Once diagnosed, urologists can offer the patient urethral dilation, direct visual internal urethrotomy (DVIU), urethroplasty, or perineal urethrostomy for the treatment of urethral stricture.

One of the original (and still most frequent) treatments of urethral stricture disease is urethral dilation. It is an in-office treatment that can be performed either using urethral sounds or using a wire plus either a balloon dilator or sequentially sized disposable dilators placed using a Seldinger technique. A DVIU is usually done in the operating room and uses a urethrotome ("cold knife") or laser to incise through the scar. There is no evidence that DVIU is superior to dilation, or that any specific technique (for example laser vs. cold knife incision) is superior; in general, results are modest for well-selected strictures (<1 cm bulbar strictures with minimal spongiofibrosis and ≤2 prior dilations/incisions).[25] As initial treatment for patients with long (≥2 cm) bulbar urethral strictures, penile stricture, or recurrent urethral stricture, endoscopic treatments typically have a low rate of success in the long-term. Likewise, after two failed endoscopic treatments, the chance of cure is essentially zero, and the procedure becomes a recurring, temporary management strategy.

Urethroplasty involves either anastomotic (complete surgical excision of the stricture with urethral re-anastomosis) or augmentation (tissue transfer to increase urethral caliber) techniques. Anastomotic urethroplasty is most appropriate for anterior urethral strictures, where there is a relatively short stricture (<2 cm in length) in bulbar urethra. It has a very good success rate (>90%), a low complication rate, and potentially lower recurrence rate when compared to other urethroplasty techniques.[26] The other common approach to urethroplasty involves the augmentation of the urethral lumen. This can be carried out using a variety of potential grafts (most commonly oral mucosal grafts) or genital (penile) fasciocutaneous flaps. There are a variety of technical considerations that go into selecting an operative approach in these cases; in general, both grafts and flaps have equivalent success rates but flaps are associated with more morbidity.[27]

When tissue transfer is indicated, most urologists performing urethroplasty use an oral mucosal graft as the primary tissue source. Allograft, xenograft, or synthetic materials should not be used to perform urethroplasty outside of study protocols. In patients with recurrent stricture who are not candidates for urethroplasty, self-catheterization after DVIU may help maintain urethral patency for longer periods. Perineal urethrostomy is also a long-term treatment option for patients as an alternative to urethroplasty.[28]

Clinically important outcomes

Treatment of a patient with urethral stricture involves consideration of several potentially important outcomes, including the degree, acuity, and type of symptoms, as well as associated complications, risks of treatment, and patient preference. Clinically important outcomes for this guideline were determined using a combination of expert opinion and existing literature on patient preference.[29,30] Given that the majority of patients with urethral stricture LUTS or urinary retention as a consequence of urethral stricture, improvement in LUTS or avoidance of urinary retention is undoubtedly an important outcome.[17] In addition to LUTS, patients may also experience sexual dysfunction and/or genitourinary pain related to urethral stricture or as a consequence of treatment. Given the broad spectrum of signs and symptoms, improvement in health-related quality of life is important to consider. While most patients experience symptoms, many may also experience complications due to stricture or treatment. Lastly, the need for repeated lifelong procedures requires some consideration in the decision-making process. The clinical outcomes determined to be most important based on the committee's opinion and reviewed literature are listed in Table 3 in order of decreasing importance.

Initial treatment: Should endoscopic management (dilation or DVIU) compared to urethroplasty be used for men with the initial diagnosis of urethral stricture?

Recommendation: We suggest endoscopic management as the initial treatment of the symptomatic undifferentiated stricture (*conditional recommendation, low certainty in evidence of effects*).

To generate this recommendation, the evidence from the AUA guideline was updated from 2014 to 2018.[9] There were

Table 3. Clinically important outcomes

Improvement in lower urinary tract symptoms
Health-related quality of life
Need for further procedures
Complications (stricture and treatment related)
Sexual dysfunction
Genitourinary pain

28 relevant, non-randomized studies, with five comparing endoscopic management to urethroplasty.[31-58] Table 4 outlines stricture recurrence rates and other outcomes among non-randomized, non-comparative studies stratified by procedure. After incorporation into our evidence-to-decision framework, it was determined that in men initially presenting with symptomatic urethral strictures, DVIU or urethral dilation, can be performed prior to offering urethroplasty. This recommendation does not apply to those patients with strictures that have a high rate of recurrence from endoscopic treatment. These complex cases include strictures from failed hypospadias repairs, penile urethral strictures, lichen sclerosis-related strictures, trauma-related urethral strictures, strictures longer than 2 cm, and those with a completely obliterated lumen. Primary urethral cancer is a rare malignancy often presenting with locally advanced disease. Patients with suspected urethral malignancy should be diagnosed with biopsy and managed appropriately.[59]

The justification for this PICO recommendation is based on low levels of certainty. Overall, recurrence rates are moderately in favor of urethroplasty over endoscopic treatments (15.5% vs. 38.5%, respectively) in this setting. For those complications with data available in both treatment groups, including other urinary, infection, bleeding, and other complications, the risk was at least 4% greater with urethroplasty than endoscopic management (Table 5). No direct cost-effectiveness studies were identified in this specific instance. However, with the lower recurrence rates, the initial cost of urethroplasty may be similar or outweigh the cost of repeated endoscopic treatments. Endoscopic management is in every urologist's armamentarium and, therefore, is widely available and accessible as compared to surgeons trained in urethral reconstruction. Lastly, patient preference may initially lean toward minimally invasive techniques prior to reconstruction.

Recurrent stricture: Should urethroplasty compared to endoscopic treatment (either dilation or DVIU) be used for men with recurrent urethral stricture?

Recommendation: In the setting of men with recurrent urethral stricture failing prior endoscopic treatment, we suggest performing urethroplasty rather than repeat endoscopic management (DVIU or dilation) (*conditional recommendation, very low certainty in evidence of effects*).

For this specific PICO question, no randomized controlled trials were identified comparing urethroplasty to endoscopic treatment (either dilation or DVIU) for men with recurrent urethral stricture. One comparative study[60] and 31 non-comparative studies[44,48,51,61-88] were identified, including 21 studies assessing urethroplasty[62,64-68,70-74,76,79-87] and 10 studies assessing endoscopic treatment.[44,48,51,61,63,69,75,77,78,88]

In this specific setting, the benefits of urethroplasty are moderately greater than endoscopic management, with an approximate 16% recurrence rate vs. a greater than 50% rate of stricture recurrence (~53%) (Table 6). Both comparative studies and case series demonstrated higher rates of stricture recurrence with endoscopic management when compared to urethroplasty. Additionally, in studies that report details of previous treatment, repeat endoscopic treatment may increase stricture complexity, increase urethroplasty complexity, and

Table 4. Benefits and harms of endoscopic management vs. urethroplasty of urethral stricture

Outcomes Number of participants (studies)	Certainty of the evidence (GRADE)	Study event rates		Relative effect (95% CI)	Anticipated absolute effects	
		With urethroplasty	With endoscopic management (dilation or DVIU)		Risk with urethroplasty	Risk difference with endoscopic management (dilation or DVIU)
Stricture recurrence – Comparative 1655 (5 observational studies)[1-5]	⊕OOO VERY LOW	231/1103 (20.9%)	189/552 (34.2%)	**RR 2.19** (1.46–3.27)	209 per 1000	**249 more per 1000** (96 more to 475 more)
Complications – Initial & recurrent stricture – Comparative 193 (1 observational study)[2]	⊕OOO VERY LOW	8/95 (8.4%)	12/98 (12.2%)	**RR 1.45** (0.62–3.40)	84 per 1000	**38 more per 1000** (32 fewer to 202 more)
Stricture recurrence – Non-comparative 2616 (22 observational studies)[6-27]	⊕OOO VERY LOW	87/563 (15.5%)	790/2053 (38.5%)	Not pooled	Not pooled	Not pooled
Quality of Life (postop scores) – Non-comparative 60 (1 observational study)[8]	⊕OOO VERY LOW	–	–	–	Not pooled	Not pooled
Complications – Non-comparative 1976 (9 observational studies)[6,7,9,11,12,17,18,19,28]	⊕OOO VERY LOW	87/622 (14.0%)	32/1354 (2.4%)	Not pooled	Not pooled	Not pooled

CI: confidence interval; DIVU: direct visual internal urethrotomy; RR: relative risk.

Table 5. Harms of endoscopic management vs. urethroplasty for initial urethral stricture

Complication	No of participants (studies)	Study event rates (%)	
		With urethroplasty	With endoscopic management (dilation or DVIU)
Erectile dysfunction	130 (2 studies)	26/130 (20.0%)	–
Urinary incontinence	90 (1 study)	9/90 (10.0%)	–
Other urinary	348 (5 studies)	25/127 (19.7%)	1/221 (0.5%)
Infection	331 (4 studies)	4/37 (10.8%)	2/294 (0.7%)
Bleeding	405 (6 studies)	5/37 (13.5%)	15/368 (4.1%)
Fluid extravasation	152 (2 studies)	–	9 /152 (5.9%)
Swelling	37 (1 study)	12/37 (32.4%)	–
Fistula complications	37 (1 study)	1/37 (2.7%)	–
Overall/any	132 (1 study)	–	5/132 (3.8%)
Other	314 (4 studies)	5/127 (3.9%)	0/187 (0.0%)

DVIU: direct visual internal urethrotomy.

increase the rate of stricture recurrence with treatment (Table 7). The symptomatic recurrence rate after endoscopic treatment may vary and depends on stricture etiology, location, length, and the number of failed prior endoscopic treatments. While there may be similar initial rates of complications (26–27%) over the long-term course of the disease, urethroplasty may offer a lower risk of complications than endoscopic management due to the cumulative rate of complications related to the need for repeat endoscopic treatments (Table 8). Moreover, this does not take into account complications directly related to stricture, only treatment-related complications. Other factors, such as cost, equity, and patient preference, play a role in determining the best course of treatment in this setting. The initial cost of urethroplasty may be moderately greater than endoscopic treatment but over the long-term, with the subsequent risk of stricture recurrence, urethroplasty is typically more cost-effective. While urethroplasty is less widely available than endoscopic treatment and requires additional training, it remains the preferred options when all outcomes are considered, despite this difference in equity. When considering patient preference, most men who have multiple recurrences may prefer urethroplasty but a shared decision-making model will help to understand patients' values and preferences. Most men who have poor quality of life due to recurrent stricture will likely choose urethroplasty. Men who are frail with multiple comorbidities and who want to avoid an in-hospital operative procedure, scheduling, timing, or hospital stay, may choose DVIU or dilation for a recurrent stricture.

Special circumstances

While these guideline recommendations apply to most patients presenting with urethral stricture, several etiologies and circumstances warrant specific mention.

Trauma stenoses (pelvic fracture urethral injury, straddle trauma)

The scope of this guideline is not intended to review the management of patients with acute anterior or pelvic fracture urethral injuries (PFUI). A Canadian review of the subject has been recently published.[89] In general, the initial management of PFUI remains controversial. Options include suprapubic tube insertion or primary endoscopic realignment (retrograde or antegrade). Regardless of initial treatment, most patients after pelvic fracture will develop urethral stenosis. It is recommended that this resultant PFUI-related urethral stenosis be treated with delayed urethral reconstruction. Endoscopic maneuvers, including "cut to the light," should be avoided

Table 6. Benefits and harms of urethroplasty vs. endoscopic management for recurrent strictures

Outcomes Number of participants (studies)	Certainty of the evidence (GRADE)	Study event rates		Relative effect (95% CI)	Anticipated absolute effects	
		With endoscopic management (dilation or DVIU)	With urethroplasty		Risk with endoscopic management (dilation or DVIU)	Risk difference with urethroplasty
Stricture - Comparative 179 (1 observational study)[60]	⊕OOO VERY LOW	92/124 (74.2%)	30/55 (54.5%)	**RR 0.74** (0.57–0.96)	**74 per 100**	**19 fewer per 100** (from 32 fewer to 3 fewer)
Stricture – Non-comparative 4408 (31 observational studies)[44,48,51,61-88]	⊕OOO VERY LOW	306/623 (49.1%)	603/3785 (15.9%)	Not pooled	Not pooled	Not pooled
Complications (counts) 681 (11 observational studies)[60,63,65-67,69,76,78,79,82,86]	⊕OOO VERY LOW	47/174 (27.0%)	133/507 (26.0%)	Not pooled	Not pooled	Not pooled

CI: confidence interval; DVIU: direct visual internal urethrotomy.

Table 7. Benefits of urethroplasty vs. endoscopic management for recurrent strictures by prior baseline characteristics

Study or subgroup	No of participants (studies)	Study event rates (%)	
		With endoscopic management (dilation or DVIU)*	With urethroplasty*
Prior endoscopy (DVIU and/or dilation)	1671 (14 studies)	192/386 (50%)	137/1285 (11%)
Prior urethroplasty	625 (12 studies)	149/241 (62%)	75/384 (20%)

*Patients may have had multiple previous procedures (multiple previous endoscopies with or without prior urethroplasty). DVIU: direct visual internal urethrotomy.

Table 8. Harms of urethroplasty vs. endoscopic management for recurrent strictures by specific complications

Complication	No of participants (studies)	Study event rates (%)	
		With endoscopic management (dilation or DVIU)	With urethroplasty
Erectile dysfunction	206 (3 studies)	-	34/206 (17%)
UTI	241 (4 studies)	18/130 (14%)	10/111 (9.0%)
Urinary incontinence	245 (4 studies)	6/43 (14%)	17/202 (8.4%)
Bleeding	168 (2 studies)	6/87 (6.9%)	0/81 (0%)
Extravasation	87 (1 study)	10/87 (11%)	–
Fistula complications	227 (3 studies)	–	19/227 (8.4%)
Diverticulum	210 (2 studies)	–	5/210 (2.4%)

DVIU: direct visual internal urethrotomy; UTI: urinary tract infection.

since they usually do not result in a durable response, delay the treatment course, and may increase the complexity of the future repair.[90] Reconstruction usually occurs at 3–6 months' post-trauma. The vast majority of these stenoses can be repaired trans-perineally in a single-stage operation with a high degree of success (>90%). Maneuvers to bridge the gap include urethral mobilization, development of the intra-crural space, infra-pubectomy, and rerouting the urethra around the corporal body.

Patients who suffer a "straddle" urethral injury to the bulbar can be initially managed with catheter realignment or insertion of a suprapubic catheter. Catheter realignment, however, may increase the rate of stricture development.[88,91] The mechanism of injury to the bulbar urethra is a compression type of force of the urethra against the pubis. This results in a transmural injury to the corpus spongiosum.[92] Patients with a resultant symptomatic urethral stricture after a straddle injury likely are best treated with urethroplasty since urethral pathology reveals extensive fibrosis of the corpus spongiosum. Commonly, this can be done with an excision and primary anastomosis. Because of this fibrosis, repeated endoscopic dilations or DVIUs are usually unsuccessful and may increase the complexity of the repair, including the need for tissue transfer techniques.[88,91]

Hypospadias-associated urethral strictures (HAUS)

Urethral stricture is one the most common problems encountered in patients with hypospadias presenting as adults.[93-96] Hypospadias is the most common cause of iatrogenic stricture in men under the age of 45 and may occur in up to 10% of patients with hypospadias.[93,97] Development of stricture may be related to the use of preputial flaps, tubularized tissue, or proximal hypospadias.[98] Patients often present insidiously with a long-standing history of LUTS, episodic UTI, and/or acute urinary retention. There are several unique considerations when treating patients with HAUS. These patients often present with multiple associated problems, including LUTS (even in the absence of stricture) (50–82%), urethrocutaneous fistula (16–30%), persisting hypospadias (14–43%), penile curvature (14–24%), UTI (15–25%), lichen sclerosus (8–43%), or genitourinary pain (10%).[93,99-103] Patients frequently have a history multiple previous surgeries.[93,99-103] Accordingly, physical examination is abnormal, with attenuation of the glans, glans cleft, and ventral Dartos with visible scarring and fibrosis. Assessment with flexible cystoscopy or urethrography can be challenging owing to an abnormally situated or stenotic meatus. Use of a pediatric cystoscope or ureteroscope in this setting can be useful in evaluating the urethra with minimal manipulation. Urethral stricture in adult patients with hypospadias can also be difficult to classify but generally falls into one of four categories based on length, location, and previous surgeries. The first and most common is a long "pan-penile" stricture involving the majority of the penile urethra in the setting of previous (and often multiple) hypospadias surgery. The second group comprises a "junctional stricture," which is a stricture of variable length at the junction of previous hypospadias repair and native urethra. Patients may also develop an isolated bulbar urethral stricture after hypospadias repair. The last group is that of urethral stricture developing in the setting of previously untreated hypospadias.[104]

In most instances, endoscopic treatments (dilation or urethrotomy) offers little chance of cure, given that urethral dilation and urethrotomy are least successful in penile strictures and strictures greater than 2 cm in length, which is typical of HAUS.[52] Treatment with urethroplasty can be successfully performed and is likely preferred, especially in young adults, but may vary depending on patient preference and expectations.

In general, adult hypospadias surgery is frequently successful, with reported "success" rates of 75–88%.[94,99-106] However, on average, two or more operations are required to treat HAUS and associated problems.[94,102,105] Additionally, these surgeries incur a 26–68% risk of complications, likely because the ventral penile skin and Dartos fascia is deficient and poorly vascularized.[94,99-106] Because of the potential complexity of urethroplasty in this population, perineal urethrostomy can also be a highly successful option for these patients who are either too unwell or unwilling to undergo urethroplasty.

Bladder neck contracture (BNC)

"Bladder neck contracture" (BNC) refers to the narrowing of the bladder neck following surgical treatment of bladder outlet obstruction (e.g., benign prostatic enlargement). BNC may occur following monopolar or bipolar TURP or other energy sources of tissue ablation, including photoselective vaporization of the prostate (PVP), holmium laser enucleation (HoLEP), or ablation of the prostate (HoLAP), and thulium vaporenucleation laser (Thu-VEP). The mechanism of and etiology of BNC is not clearly understood but may be influenced by excessive resection and fulguration of the bladder neck and the hypertrophic scarring that results. The estimated incidence of BNC rages from 0–9.6%.[107] The presentation of BNC often occurs within the first six months after prostate surgery and may include both voiding and storage symptoms, as with other urethral strictures. Risk factors for BNC include low adenoma weight, unmanaged preoperative infections, long resection time, extensive resection of the bladder neck, diabetes, smoking, and cardiovascular disease.[107] Once diagnosed, urethral dilation is often the first-line treatment in patients with a short BNC, although up to 90% may recur within the first two years. Other treatment options include bladder neck incision (BNI) using either a hot-knife, cold-knife, or laser technique, although one method is not known to be superior over another. Self-calibration using in/out catheters may be a tool to stabilize the bladder neck following BNI. Techniques combining bladder neck ablation with transurethral injection of cytotoxic agents (e.g., mitomycin C) yield variable results but can be associated with significant complications, including extravasation or bladder neck necrosis. Permanent suprapubic catheters or open reconstruction using Y-V plasty techniques can be considered for recalcitrant BNC when repeated endoscopic attempts fail.

Vesicourethral anastomotic stenosis (VUAS)

VUAS, or sometimes imprecisely also referred to as "bladder neck contracture") occurs in approximately 5–10% of men after radical prostatectomy.[108,109] The etiology is multifactorial and is likely the result of both technical challenges at the time of prostatectomy and adverse postoperative healing (such as postoperative hematoma or urine leak, or subsequent radiation therapy). In the setting of an asymptomatic VUAS, observation is appropriate, as in some patients, the treatment of a VUAS results in de novo or worsening of urinary incontinence.[110] Paradoxically, in some patients, treatment of the VUAS can actually improve post-prostatectomy incontinence by passively improving the coaptation of the external urethral sphincter.[110] Patients who are symptomatic or those who have a VUAS <14 French and are contemplating post-prostatectomy incontinence surgery should be treated initially with a urethral dilation or minimally invasive endoscopic procedures; often, multiple procedures are necessary, but in most cases, this is eventually successful.[111] Usually, a stepwise approach of a minimally traumatic urethral dilation, followed by a cold knife/electrocautery or laser incision of the stricture, and finally a deep incision or resection to the fat can be attempted, with success rates increasing with move invasive treatment methods.[110,112] Endoscopic injection of steroid solution into the VUAS may improve patency, however, the use of mitomycin appears to have a risk of serious adverse events.[110,113] In cases where endoscopic interventions have failed, a tapering schedule of intermittent catheterization has been used to improve long-term patency rates.[110] In rare cases, open reconstruction may be contemplated, however, this is a technically challenging procedure that will result in urinary incontinence that will almost certainly require the placement of an artificial urinary sphincter. While undertaking the treatment of VUAS, the physician should be aware of the rare but serious complication of fistulation to the pubic symphysis.[114] This almost uniformly occurs in patients with a history of radiation therapy and, in many cases, develops after endoscopic procedures to treat VUAS. A patient will have severe pelvic pain; an MRI of the pelvis should be done to confirm the diagnosis. Treatment of this complication usually requires a urinary diversion.

Radiation-induced urethral stenoses

Urethral stenosis is likely an under-recognized and underreported complication of pelvic radiotherapy.[108] Over time, patients undergoing radiotherapy for prostate cancer have an almost five-fold risk of developing urethral complications.[108] After brachytherapy, the incidence of urethral stenosis is 1–8% and likely occurs more frequently in high-dose protocols.[115-120] After contemporary external beam radiation therapy (EBRT), the incidence of posterior urethral stenosis is likely 2–4%.[108,121] Although urethral stenosis may occur within the first year after treatment, most patients typically present 5–7 years later.[122-124] Rates of stenosis following combination modality EBRT/brachytherapy (BT) occur more frequently and are usually more complex.[125] Treatment of radiotherapy-induced urethral stenosis has not been well-defined.[108,119,121]

Urethral stenosis after single-modality radiation treatment typically occurs at the proximal bulbar urethra and extends to the membranous urethra, with variable involvement of the prostatic apex. Radiation-associated stenoses are usually refractory to endoscopic techniques.[119] Urethroplasty, at least in properly selected patients with focal stenoses, appears to be a reasonable option for patients failing endoscopic treatments, with success rates of 69.7–89.6%.[122-124] The majority bulbomembranous stenoses after radiotherapy are amenable to anastomotic urethroplasty with tissue transfer reserved for strictures >3 cm in length. However, even in well-selected patients, urethroplasty in a radiated field has risks related to compromised vascular supply, tissue necrosis, obliterated tissue planes, and fibroblast dysfunction, potentially resulting in prolonged recovery and increased risk of complications.[126,127]

Bulbomembranous stenosis after radiation treatment is not typically an isolated problem and patients often have significant functional concerns both before and after treatment of urethral stenosis. Because of the field effect of radiation concurrent impairment in continence, erectile function and detrusor dysfunction is common.[121-124] In these cases, return to "normal" urological function is not a common occurrence. Additionally, because of the multifocality of the problem and advanced patient age, some patients to prefer intermittent endoscopic treatment over more invasive treatments. Generally, patients with extensive prostate necrosis, cavitation, prostatosymphyseal fistula, osteomyelitis, or a small functional bladder capacity are best served by urinary diversion in lieu of urethral reconstruction.[119,121] However, in well-selected and properly counselled patients with focal stenosis, urethral reconstruction is a viable option for establishing long-term urethral patency and improvement in lower urinary tract function.

Lichen sclerosus (LS)

LS is a chronic, lymphocyte-mediated skin disease; it was previously known as balanitis xerotica obliterans, but this is no longer the accepted term. It has an estimated prevalence of one in 300 men, with a peak incidence in men aged 30–50 years.[128] There is no proven etiology of LS but there have been theories tied to autoimmune conditions, hypogonadism, trauma, and genetics. There are documented associations with obesity, cardiovascular disease, and cigarette use.[128-130] LS is typically an insidious and progressive process that presents most commonly with phimosis, meatal stenosis (4–37%), or urethral stricture (20–30%).[131] Ongoing surveillance is recommended due to potential association with the development of squamous cell carcinoma, which can occur in 2–8% of men with LS.[129]

Treatment is predicated on the extent of the disease. Topical therapy is often employed in the form of topical corticosteroids, such as clobetasol (0.05%) or betamethasone (0.05%) twice a day for 8–12 weeks. This results in an improvement in the cutaneous manifestations of LS in 40–90% of patients. LS involving the prepuce often requires surgical intervention for phimosis — either dorsal slit or circumcision. When urethral stricture arises, the location, length, and progression of LS-associated stricture disease will guide treatment. Strictures related to LS tend to be progressive and it is important to counsel patients regarding the recalcitrant nature of LS-related strictures. Stricture may present simply as isolated meatal stenosis and may respond to dilation with or without the use of intra-urethral steroid administration.[132] Longer LS-related strictures often require urethroplasty with tissue transfer for durable treatment success. Genital skin flaps and grafts should be avoided due to risk of LS-related skin involvement.[133] Oral mucosa tissue grafts are the gold standard treatment for LS-related strictures.[134,135] Single and multistage reconstructive approaches are well-described and offer the best chance of success. Managing patient expectations is important with LS, given that it is typically a recurrent and progressive condition.

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