

Management of the Recurrent Male Urethral Stricture

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Abstract Urethral stricture disease negatively impacts quality of life and leads to significant urologic pathology including lower urinary tract symptoms, recurrent urinary tract infections, and potentially more severe sequelae such as detrusor dysfunction, renal failure, urethral carcinoma, and Fournier's gangrene. Open urethral reconstruction is considered a durable and definitive treatment for urethral stricture with lifetime success rates ranging from 75–100 %; however, strictures do recur up to 10 years after surgery. Recurrence rates vary by repair type. There also is no agreed-upon modality for recurrence surveillance, but there are many modalities with varying degrees of invasiveness. Recurrent strictures may be managed endoscopically or via open repair. We review stricture recurrence rates, surveillance modalities, risk factors, and management options.

Keywords Urethral stricture recurrence · Urethroplasty · Buccal tissue · Stricture · Lower urinary tract symptoms · Urethral obstruction

Introduction

Urethral stricture disease negatively impacts quality of life and may be a cause of large economic burden [1, 2]. It is more prevalent in historically vulnerable and underserved patients including older men, African American men, and the inner city populations [1], which may stem from higher rates of trauma, genitourinary infections, and increased instrumentation. In addition to lower urinary tract symptoms (LUTs) and recurrent urinary tract infections (UTIs), long-standing obstruction may lead to more severe sequelae such as detrusor dysfunction, renal failure, urethral carcinoma, as well as Fournier's gangrene [1, 3]. The annual expenditure for the treatment of urethral stricture disease in 2000 was estimated to be \$191 million, most of which was attributed to outpatient surgery visits [1].

Open urethral reconstruction is considered a durable and definitive treatment for urethral stricture with lifetime success rates ranging from 75–100 % [4]. In spite of relatively high success rates and durability of the operative repair, strictures do recur up to 10 years after surgery and therefore patients require close follow-up [5]. One might even go as far as saying that once one has undergone urethral reconstruction they become a reconstructive urology patient for life.

Urethral Stricture Recurrence Rates

Evaluation of urethral stricture recurrence is challenging. There are no current guidelines outlining the surveillance regimens and follow-up protocols for patients who have undergone urethral reconstruction or what constitutes recurrence [6]. Additionally, the reconstruction literature is quite heterogeneous with variable stricture location, length, and etiology, patient comorbidities including prior radiation, concomitant smoking, and vasculopathy, and variable reconstructive

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techniques with a host of graft materials utilized. Finally, most studies include a mix of patients whose strictures involve different segments of the anterior and posterior urethra and who have had prior endoscopic management or failed open repair [7, 8]. Given this variability, it is challenging to compare studies, techniques, and outcomes.

A review of current practice patterns of urethral stricture by newly certifying or recertifying American urologists showed that only 3.9 % performed urethroplasties (of which 90.7 % were end-primary anastomosis (EPA) and 0.9 % utilized a graft) and 96.2 % performed either dilation or direct vision internal urethrotomy (DVIU) [9•].

Overall, endoscopic management, via either urethral dilation or DVIU (which can be performed using a cold knife, Holmium laser, or Plasmakinetic knife) generally has poorer outcomes compared to open repair. Recurrences following endoscopic treatments range between 23 and 92 % [10–13, 14•, 15–17] (Table 1). Additionally, a review of 340 reconstruction cases by Hudak et al. focusing on endoscopically treated patients showed that patients with greater than two endoscopic treatments for urethral stricture developed more complex strictures and an increased need for graft urethroplasty compared to patients who had 0 to 1 endoscopic procedures. Although there was a higher percentage of failed urethroplasty in the multiple DVIU group, it was not statistically significant [18].

Anterior bulbar urethral strictures managed with EPA have a recurrence rate between 5 and 15 % [19–38] (Table 2). Anterior urethral strictures managed with grafting using either penile or preputial skin or buccal or lingual mucosa have slightly higher recurrence rates ranging anywhere from 3.1 to 58 % (Table 2). Generally, buccal mucosa has a better success rate than penile skin [23]. Oral mucosa is an ideal urethral substitute given ease of handling and harvest, lack of hair, robustness, compatibility with a wet environment, and ability to “take” early with high success rates [39]. Posterior urethral strictures, which are usually managed with anastomotic urethroplasty, have recurrence rates between 4 and 14 % [40–43] (Table 3).

Risk Factors for Stricture Recurrence

Risk factors for urethral stricture recurrence include smoking, stricture length, obesity, and diabetes mellitus. A review by Breyer et al. of 443 patients with anterior and posterior urethral strictures examined risk factors for recurrence [44]. Smoking (HR 1.8), prior DVIU (HR 1.7), and prior urethroplasty (HR 1.8) predicted increased risk of stricture recurrence. Diabetes mellitus was associated with an increased risk of stricture recurrence (HR 2.0), though it was not statistically significant. Additionally, stricture length greater than 4 cm was a risk factor for recurrence [44]. Yalcinkaya et al. looked at risk factors for recurrence in 40 patients with anterior strictures and did not find a correlation with age or stricture etiology. Outcomes were worse for strictures longer than 7 cm (88 % stricture-free rate in strictures less than 7 cm vs 40 % stricture-free rate for strictures greater than 7 cm at 43.4 months follow-up) and panurethral strictures [27]. Similarly, a retrospective review by Barbagli et al. of 375 patients who underwent one-stage bulbar urethroplasties either via EPA, augmented anastomotic repair, or penile or oral grafts showed no difference in success by age or etiology. Additionally, penile skin grafts were associated with higher recurrence rates than buccal mucosal graft (40.4 vs 17.2 %) [23]. Another review by Breyer et al. of 381 patients undergoing anterior and posterior urethroplasty found that BMI of 25–35 (HR 1.7), diabetes (HR 1.9), and previous DVIU (HR 1.7) were also risk factors for recurrence [45]. Similarly a retrospective review by Privratsky et al. in men undergoing onlay bulbar urethroplasty found patients with BMI >35 had higher recurrence rates [46]. A retrospective review from Glass et al. examining outcome in 29 patients who developed anterior or posterior strictures following radiation therapy found no decrease in success rate at 40 months follow-up [47]. Similarly, Rourke et al. looked at 35 men with radiation-induced stricture disease and found no increase in stricture recurrence following urethroplasty at 50.5 months follow-up [48].

Table 1 Stricture recurrence after initial endoscopic management

Reference	Year	# Pts	Stx type	Stx length	Treatment	F/u (months)	Recurrence
[10]	2015	60	NR	NR	Plasmakinetic knife or DVIU	12	37 % after DVIU, 23 % Plasmakinetic knife
[11]	2014	136	Anterior + posterior	1.3 cm	DVIU with cold knife vs Plasmakinetic knife	NR	37 % after plasmakinetic, 33 % after cold knife
[12]	2011	51	Anterior + posterior	1.1–1.2 cm	DVIU with cold knife vs laser	12	47 % after cold knife, 19 % after laser
[13]	2012	50	Anterior + posterior	1.86 cm	DVIU with cold knife vs laser	12	56 % after laser, 40 % after cold knife
[14•]	2010	74	Anterior	1.5 cm	DVIU	14	92 %
[15]	2004	126	Anterior + posterior	1.1 cm	DVIU	25	46–56 %
[16]	1998	163	NR	NR	DVIU + dilation	24	61 % after DVIU, 88 % after dilation
[17]	1996	224	Anterior	1.6 cm	DVIU	98	68 %

Table 2 Stricture recurrence following anterior urethroplasty

Reference	Year	# Pts	Stx type	Stx length	Technique	F/u (months)	Recurrence
[19]	2015	268	Bulbar	2.1 cm	EPA	41.5	6.00 %
[20]	2014	45	Anterior	<2 cm	EPA	28.4	13.3
[21]	2014	213	Bulbar	NR	EPA	12	10
[22]	2013	33	Bulbar	1.5 cm	EPA	42.6	12.1
[23]	2008	165	Bulbar	NR	EPA	53	9.1
[24]	2003	166	Anterior + posterior	NR	EPA	180	14 %
[25]	2002	168	Anterior	1.7 cm	EPA	70	5 %
[26]	1997	98	Anterior	<2 cm	EPA	54.5	15.30 %
[27]	2015	40	Anterior	NR	Dorsla onlay buccal	43.4	12 % if <7 cm, 60 % >7 cm
[28]	2015	38	Bulbar/bulbomembraneous	3 cm	Ventral onlay buccal	26.5	28.9
[29]	2014	114	Anterior + posterior	3.1	Ventral onlay bucca	28.9	21 %
[20]	2014	45	Anterior	5.9 cm	Buccal augmented dorsal onlay	32.8	15.6
[30]	2014	17	Anterior	NR	Penile fasciocutaneous flaps	60	17.6
[31]	2014	87	Anterior	2.3-5.2	Dorsal buccal one stage inlay	25.8	10.3
[21]	2014	213	Bulbar	NR	Buccal	12	13
[32]	2014	359	Anterior	NR	Penile skin or buccal	118	26.2
[33]	2014	72	Bulbar/bulbomembraneous	2.4 cm	EPA + substitution	10.2	30.3
[34]	2014	58	Anterior + posterior	4.8 cm	Preputial skin flap	42	29 %
[35]	2014	47	Anterior	4.7 cm	Dorsal onlay vs dorsal inlay	23	12.8
[36]	2013	163	Bulbar	4.5 cm	Dorsal onlay augmented	31	3.1
[37]	2012						
[23]	2008	170	Bulbar	NR	Oral grafting	53	18.2
[24]	2003	166	Anterior + posterior	NR	Substitution urethroplasty	180	58 %
[38]	2002	53	Bulbar	3.64	Ventral onlay bucca	25	5.70 %

Surveillance for Stricture Recurrence

There are many surveillance modalities with a wide range of cost, availability, invasiveness, and potential complications. These non-standardized follow-up regimens include history and physical examination and validated questionnaires such as the American Urological Association International Prostate Symptom Score (AUA-IPSS) or the UREThRAL stricture score, which incorporates stricture etiology, number of strictures, retention (obliterative versus non-obliterative), anatomic location, and stricture length [49]. Additional modalities include urinalysis and urine culture (UCx), post-void residual (PVR), uroflowmetry (UF), urethral ultrasound (US), retrograde urethrogram (RUG), voiding cystourethrogram (VCUG), urethral calibration, and flexible cystoscopy [4, 8].

These methods are often used in varying combinations in a multi-tier process [4]. The sensitivity of UF compared to RUG/VCUG varies with the maximum flow rate and specificity increases as flow rate decreases. Sensitivity for the non-invasive UF is 92 % with flow rates less than 20 ml/s and specificity increases to 93 % with flow rates less than 10 ml/s. The positive predictive value is 73 % with flow rates less than 10 ml/s, and negative predictive value is 96 % with flow rates less than 20 ml/s [4, 50, 51]. Choudhary et al. compared US versus RUG to intraoperative confirmation of stricture. With RUG and US, sensitivity increased as stricture length increased and specificity was generally high for all stricture lengths [52]. Although the studies in that series were performed primarily for stricture diagnosis, they may have utility in stricture recurrence surveillance. Widely available in almost every urology office,

Table 3 Stricture recurrence following posterior urethroplasty

Reference	Year	# Pts	Stx type	Stx Length	Technique	F/u (months)	Recurrence
[40]	2005	155	Posterior	NR	Anastamotic	244	10 %
[41]	1997	82	Posterior	NR	Anastamotic	12	11 %
[42]	1991	74	Posterior	NR	Anastamotic		4 %
[43]	2007	134	Posterior	NR	Anastamotic	32.9	14 %

cystoscopy has traditionally been used for determination of urethral stricture and is presumed to provide 100 % sensitivity and specificity [4]. Per recent SIU/ICUD guidelines, cystoscopy is recommended as the most specific for the diagnosis of urethral stricture and may be considered an adjunctive procedure for staging urethral strictures, particularly if other imaging studies are equivocal. Additionally, cystoscopy is particularly helpful in assessing the bladder neck and posterior urethra in the setting of a posterior urethral disruption due to pelvic fracture [6]. Following urethral stricture repair, flexible cystoscopy may be used to calibrate the urethral lumen and may be considered the optimal modality to assess for stricture recurrence [6]. PVR measurement has not been independently validated in urethral stricture disease [4].

In addition to different levels of invasiveness, these studies also are associated with variable costs. A review by Zaid et al. showed variable urethral stricture surveillance practice patterns led to first postoperative year surveillance costs that ranged from \$205 to \$1784 per patient for anterior strictures and \$404 to \$961 for posterior strictures [53].

Currently, there is no universally agreed-upon surveillance regimen. Some have argued for a symptom-based and risk-stratified tiered approach to surveillance [4, 54]. Patients with lower risk of recurrences, such as those undergoing an EPA or with no risk factors predisposing to recurrence may be followed with symptom score vs higher risk patients who may need more invasive evaluation [54]. At our facility, we follow all patients who have undergone urethroplasty with annual physical examination, AUA symptom scores, noninvasive flow test, and post-void residuals. These tools are augmented with cystoscopy or retrograde urethrography when there is a suspicion for recurrence. Similarly, per the SIU/ICUD panel, although there is no ideal agreed-upon method, surveillance should consist of a combination of multiple modalities, starting with less invasive ones, such as validated questionnaires, combined with objective noninvasive measurements with targeted interventions based on these findings [6].

Management of the Recurrent Urethral Stricture

Stricture recurrence following primary endoscopic treatment (DVIU or dilation) is generally managed with open surgery. It is well established that recurrence rates after endoscopic treatment are quite high ranging from 37–92 % in newly diagnosed strictures (Table 1). Although commonly performed, multiple repeat endoscopic treatments for recurrent strictures have very low success rates and should be discouraged. A review by Heyns et al. evaluating repeat DVIU or urethral dilation for strictures shows that endoscopic management for strictures recurring within 3 months is of limited value at 24 months follow-up and of no value in at 48 months. Following one, two, or three repeated endoscopic treatments, stricture-free

rates were approximately 60, 30, and 0 % at 24 months and about 60, 0, and 0 % at 48 months, respectively. Notable is the 0 % stricture-free rate at 24 months following three endoscopic procedures [16]. A review by Santucci et al. showed an even lower stricture-free rate (12 % at 43 months) after a single DVIU and 0 % after multiple procedures [14•]. An adjunct to endoscopic management may be the use of intralesional mitomycin C injection, although further follow-up is warranted [55, 56]. Thus, it is generally recommended that after failed initial DVIU or dilation, one should proceed with open urethral reconstruction for recurrent stricture. In addition to patient outcome, one must consider the cost of repeat endoscopic interventions vs definitive open repair. Although an individual endoscopic intervention may be less costly, the high failure rate requiring repeat intervention will eventually render this option more costly. Wright et al. performed a decision tree analysis for 1–2-cm bulbar urethral strictures comparing DVIU to urethroplasty. With a presumed success rate of 50 % for the first DVIU and 20 % for the second, they found that proceeding with one DVIU prior to open urethroplasty was the most cost-effective approach [57]. However, an analysis by Rourke et al. found primary urethroplasty more cost-effective vs initial DVIU. This was based on a lower success rate of 27 % for DVIU [58].

Recurrent bulbar stricture following operative urethroplasty may be initially managed either endoscopically or via open approach, but we feel that penile strictures should not be managed with DVIU. Barbagli et al. reviewed stricture recurrences following bulbar onlay urethroplasty and found 45 % of recurrences occurred at the anastomotic sites (equally proximal and distal). These were typically associated with a fibrous annular ring at the site of recurrence [59]. Consequently, endoscopic management of these is feasible. Rosenbaum et al. performed DVIU for short recurrences following buccal grafting with an overall success of 60.5 % at a mean of 15-month follow-up [60]. Thus, short recurrences of the bulbar urethra following urethroplasty may be managed endoscopically.

However, recurrence following open urethroplasty after a trial of endoscopic treatment or in those with a long stricture should be managed with repeat open reconstruction. A review of outcomes of treatment for recurrent stricture managed initially with either EPA or another type of reconstruction showed a 95 % stricture-free rate at mean follow-up 41.5 months [19]. This was compared to 94 % for EPA performed as a primary approach, suggesting that reoperative cases are not associated with decreased success [19]. Another review of recurrent strictures managed with either EPA, onlay graft, fasciocutaneous flap, or tubularized flap following various initial open urethroplasty approaches showed an overall 78 % stricture-free rate at 55-month follow-up [5•]. In this series, failures were associated with penile/bulbar location, hypospadias-related stricture, lichen sclerosis, and greater than two previously failed open repairs [5•].

Table 4 Stricture recurrence following repeat urethroplasty after initial open surgical failure

Reference	Year	# Pts	Stx type	Stx length	Technique	F/u (months)	Recurrence
[19]	2015	37	Bulbar	2.1–2.3 cm	EPA	41.5	5–6 %
[61]	2014	49	Anterior and posterior	4.9 cm	Mixed	50	12 %
[62]	2014	33	Anterior	2–6 cm	Mixed	NR	21.20 %
[63]	2011	43	Posterior	3.7 cm	EPA	29	16.3
[5•]	2012	130	Anterior and posterior	4.4 cm	Mixed	55	22 %
[64]	2002	69	Anterior	NR	Mixed	48	0 %
[65]	1997	31	Anterior and posterior	5.4 cm	Mixed	12	0
[66]	1996	20	Anterior	4.5 cm	Mixed	60	0

Table 4 lists additional studies showing overall recurrence rates between 0 and 22 % with repeat open procedures following recurrence after initial open repair [5•, 19, 61–66]. Therefore, the management of the patient with recurrent stricture after a definitive open surgical repair will depend heavily upon surgeon preference, stricture location, and stricture length. Those recurrences with a short diaphanous stricture

in the bulbar urethra may be appropriately managed with endoscopic intervention while recurrent longer strictures of the pendulous urethra may need a secondary open reconstruction.

One must always understand that in the devastated urethra, a perineal urethrostomy (PU) is a very appropriate option for permanent diversion. Peterson et al. evaluated patient satisfaction with perineal urethrostomy. In their study population of 63

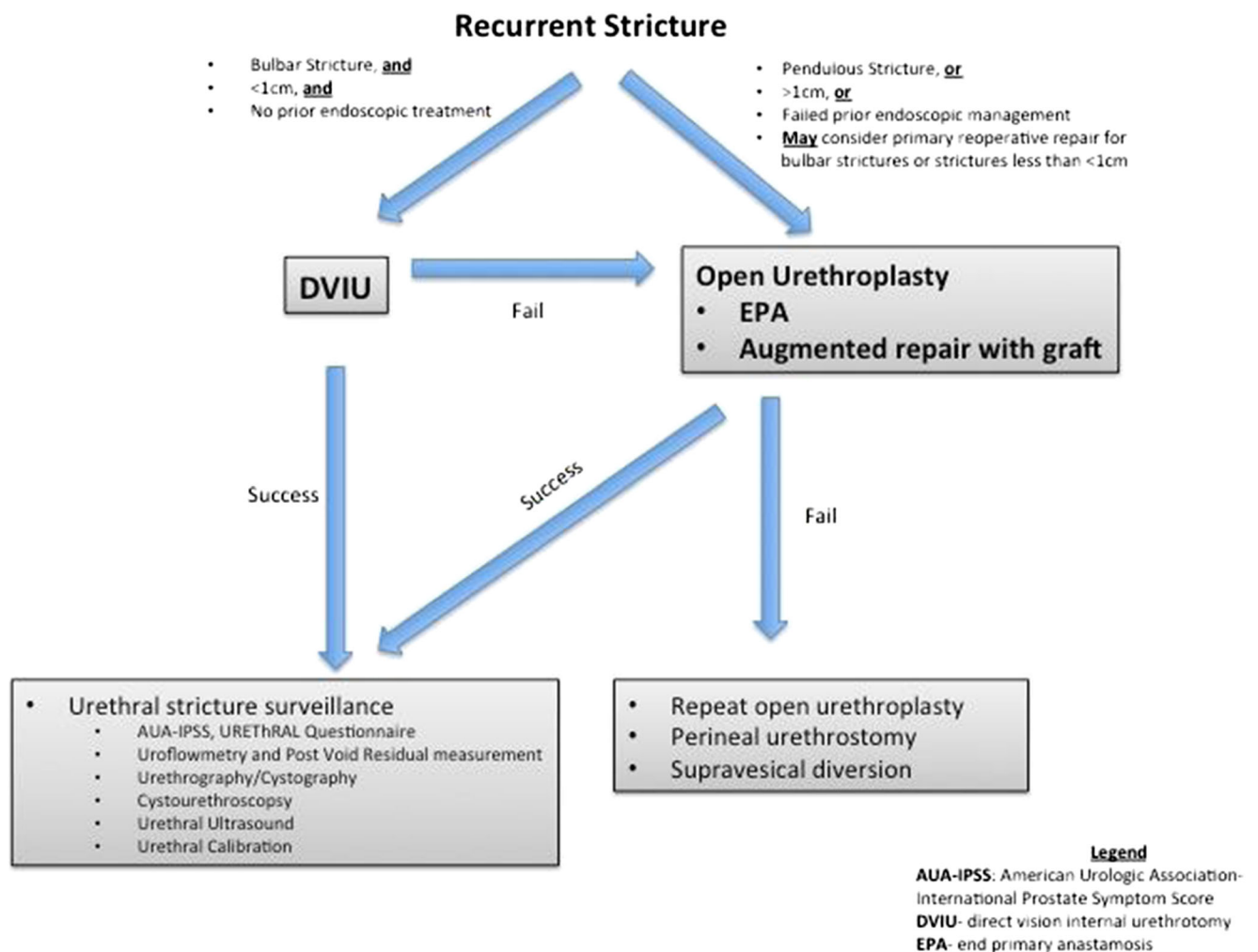


Fig. 1 Potential algorithm for management of the recurrent stricture following initial operative management

patients, 19 had undergone a first-stage procedure with functional creation of a PU and plans for an eventual second stage completion. However, nine of these patients opted to stay at the first stage. An additional 44 underwent formal PU. These patients were content with seated voiding with minimal complications. On follow-up interviews, these patients were all satisfied with their decision. Additionally, PU reconstruction can be performed as an outpatient procedure with earlier return to activity [67]. A retrospective review of 173 patients undergoing a perineal urethrostomy as a first stage in a complex repair found that at mean follow-up 62 months, 70 % were successful, and 78 % of patients were satisfied with the results obtained with the first stage PU surgery. In this series, 73.4 % decline to proceed with the second stage of urethroplasty [68]. Rarely, one may need to consider suprapubic urinary diversion in drastic cases of recalcitrant urethral stricture disease.

Figure 1 presents a potential algorithm for management of the recurrent stricture following initial operative management (either endoscopic or open urethroplasty). Recurrent strictures located in the bulbar urethra that are less than 1 cm and have not undergone prior endoscopic treatment may be managed endoscopically. However, these can also be treated via repeat open approach. All pendulous recurrences, strictures greater than 1 cm, and those that have failed endoscopic approach should be managed with repeat open surgery. The specific technique will depend on surgeon preference, stricture location, stricture length, and patient comorbidities. If there is recurrence following these, surgeons may consider a PU or suprapubic diversion.

Conclusions

Urethral stricture disease is a challenging disease entity. There are excellent durable surgical options; however, one must always remain vigilant for stricture recurrences which can occur many years after repair. These may be managed endoscopically or with open surgical repair, which may require more than one repair, and have a reasonable outcome. There is no agreed-upon surveillance modality, frequency, or duration of follow-up. Additionally, there is no standard definition for stricture recurrence.

Compliance with Ethical Standards

Conflict of Interest Uwais B. Zaid and Garjae Lavien each declare no potential conflicts of interest.

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