

Buccal mucosal grafts perform less favorably in a radiated setting after bulbar urethroplastyKennedy Dirk¹, Seth Thomas², Keith F. Rourke^{2,3}¹Department of Urology, Queen's University, Kingston, ON, Canada; ²Department of Urology, University of California, Irvine, CA, United States; ³Division of Urology, University of Alberta, Edmonton, AB, Canada

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ABSTRACT

Introduction: Buccal mucosal grafts (BMG) are the preferred tissue for substitution bulbar urethroplasty; however, it is unclear if BMG performs equally well across all stricture etiologies. The objective of this study was to examine etiology-specific outcomes of bulbar urethroplasty using BMG.

Methods: From September 2003 to May 2023, patients undergoing bulbar urethroplasty at a single center were evaluated. The primary outcome was stricture-free survival, with recurrence defined as stricture <16 Fr on followup cystoscopy. Secondary outcomes included 90-day complications (Clavien ≥2), patient-reported erectile dysfunction (ED), and satisfaction. Multivariable Cox regression analysis was used to evaluate variables

associated with stricture recurrence, and Chi-squared test to assess secondary outcomes.

Results: Of 914 patients undergoing bulbar urethroplasty using BMG with a median followup of 103 months (interquartile range [IQR] 57–163), 62 recurrences were observed. The one-, five-,

KEY MESSAGES

- In this large, single-center study of 914 patients with long-term followup, we specifically evaluate the impact of stricture etiology on outcomes following bulbar buccal mucosal graft urethroplasty.
- Our findings demonstrate that while overall durability remains excellent, radiation-associated strictures are independently associated with significantly inferior stricture-free survival and lower patient satisfaction, despite comparable perioperative complication and ED risk.
- This work provides clinically meaningful data that refine expectations for both surgeons and patients, highlighting radiation as a uniquely hostile biological environment for graft-based reconstruction.

and 10-year estimated stricture-free survival rates were 94.9%, 92.2%, and 91.0%, respectively. On multivariable assessment, stricture etiology, in particular radiation (hazard ratio [HR] 6.3, 95% confidence interval [CI] 3.0–13.0, $p < 0.0001$) was associated with stricture recurrence, as well as stricture length (HR 1.2, 95% CI 1.1–1.3, $p = 0.0001$), diabetes (HR 2.0, 95% C.I. 1.1–3.7, $p = 0.02$), and prior urethroplasty (HR 2.4, 95% CI 1.3–4.5, $p = 0.007$). For radiation strictures, the estimated stricture-free survival rates were 71.8%, 60.5%, and 60.5% at one, five, and 10 years, respectively. No differences in ED ($p = 0.53$) or 90-day complications ($p = 0.77$) were observed across etiologies. Satisfaction was significantly lower in the radiation group (83.9% vs. 92.2%, $p = 0.04$).

Conclusions: In general, urethroplasty with BMG is effective but may yield inferior outcomes in the radiated subgroup of patients. Whenever technically feasible, an anastomotic approach with stricture excision may be preferred in the radiated setting.

INTRODUCTION

Urethral stricture is an impactful and prevalent condition, with bulbar strictures representing the most commonly affected segment of urethra.¹ While endoscopic management remains most frequently employed, long-term success is poor and may lead to increased stricture complexity with repeated interventions.^{2,3} This has led to widespread recognition of urethroplasty as the most definitive treatment and recommended option for recurrent urethral stricture of all etiologies.⁴ Over the past two decades, substitution urethroplasty using buccal mucosal grafts (BMG) has emerged as the gold-standard for bulbar urethral strictures requiring tissue transfer, owing to favorable BMG tissue characteristics, ease of harvest, and consistently high reported success.⁵ Buccal mucosa provides robust vascularity due to a pan-laminar plexus which in turn provides rapid inosculation and increased resistance to infection, making it particularly well suited for urethral reconstruction.⁶ The widespread adoption of BMG urethroplasty has been supported by multiple large series demonstrating durable stricture-free outcomes exceeding 85% in heterogeneous bulbar stricture populations.⁷⁻⁸ The success of urethroplasty with BMG has resulted in expanding its use to all lengths and etiologies of bulbar urethral stricture even in instances where anastomotic urethroplasty has been historically performed.^{9,10} Wound healing principles suggest that the biological milieu in which a graft is placed may significantly influence long-term success and thus stricture etiology may be a significant contributor to surgical success in urethroplasty with BMG.¹¹ The pathophysiology of radiation-associated injury is characterized by progressive endarteritis, fibrosis, and impaired tissue vascularity in the radiated field, all of which may compromise graft take and durability.^{12,13} However, most outcome data are derived from mixed cohorts in which stricture etiology is either incompletely reported, not specifically analyzed, non-comparative, or heterogeneous techniques, limiting the ability to counsel patients regarding etiology-specific risk of recurrence.¹⁴⁻¹⁷

Given the increasing use of BMG urethroplasty across a wide spectrum of stricture etiologies, a clearer understanding of etiology-specific outcomes is needed. Therefore, the objective of the present study was to evaluate long-term outcomes following bulbar urethroplasty with BMG, with a specific focus on stricture etiology as a determinant of recurrence, complications, sexual function, and patient satisfaction in a large, single-center cohort with extended follow-up. We hypothesize that while bulbar BMG urethroplasty would demonstrate high overall durability, patients with radiation-associated strictures will experience significantly higher risk of stricture recurrence compared to other etiologies and potentially a corresponding increase in peri-operative complications.

METHODS

Study design and patient population

A retrospective cohort of 1,870 males undergoing anterior urethroplasty between September 2003-May 2023 were reviewed at a single tertiary center. A total of 914 patients who underwent single-stage bulbar urethroplasty using BMG were included for analysis. Patients with at least one postoperative cystoscopic evaluation and a minimum follow-up of 12 months were included. Patients with strictures extending outside of the bulbar urethra into the membranous or penile were excluded due to the potential for increased complexity and cohort heterogeneity confounding the effect of stricture etiology. Preoperative evaluation included urethroscopy and retrograde urethrogram to determine stricture location, length, and complexity. Relevant clinical data including comorbidities (e.g., diabetes, smoking status, obesity class 2 or higher (BMI ≥ 35)), prior endoscopic management, and catheter status were obtained from regional and provincial electronic records and supplemented by standardized telephone interviews. Obesity was defined as BMI ≥ 35 based on regional criteria. Bulbar urethroplasty onlay technique was determined based on stricture location and intra-operative findings with an overall preference for dorsal onlay. Patients were followed at 3 weeks postoperatively for a voiding trial, with cystoscopic evaluation at 3–4 months, and annually thereafter. All procedures were performed by a single reconstructive urologist.

Study outcomes and data analysis

The primary outcome was stricture-free survival, with recurrence defined as failure to easily and atraumatically pass a 16 French flexible cystoscope at follow-up. Secondary outcomes included 90-day complications (Clavien ≥ 2), de novo erectile dysfunction and patient satisfaction (collected via non-validated global assessment). Erectile dysfunction was defined as a new or worsening change in erectile quality based on patient report at the 4 month cystoscopy. Urinary tract infection (UTI) was defined as a positive urine culture in the presence of infectious symptoms.

Descriptive statistics were used to summarize baseline characteristics. Continuous variables were compared using Student's t-test and categorical variables were assessed using

Chi-square or Fisher's exact test, as appropriate. Univariable and multivariable Cox proportional hazard regression analysis was used to evaluate potential predictors of long-term stricture recurrence. Variables deemed clinically relevant and plausible in the univariate analysis were tested in a stepwise fashion to ensure stability; significant variables were then incorporated into the multivariable analysis. Kaplan-Meier survival analysis with log-rank testing was performed to compare variables associated with stricture recurrence. A p-value of <0.05 was considered statistically significant. Statistical analysis was conducted using SPSS24® (IBM Corp., Armonk, NY).

RESULTS

A total of 914 patients who underwent single-stage bulbar urethroplasty with buccal mucosal graft (BMG) were included in the analysis. 13 were excluded due to insufficient follow-up. Study population demographics are outlined in Table 1. The median age of the cohort was 48 years (IQR 36-60) and stricture length was 4.0 cm (IQR 3.5-5). The most common stricture etiology was idiopathic (64.7%), followed by trauma (13.1%), iatrogenic (11.2%), and radiation for prostate cancer (3.4%). Of the patients with radiation associated stricture, 58.1% (18) had external beam radiotherapy and 41.9% (13) had prior brachytherapy. The median time from radiation was 62.0 months (IQR 46-94). The majority of patients (91.0%) failed prior endoscopic treatment, with a median of two prior procedures (IQR 1-3). The majority of patients were reconstructed with a dorsal onlay approach (98.1%). The median duration of follow-up was 103 months (IQR 57-163) and over the follow-up period 62 patients experienced stricture recurrence with 1, 5 and 10 year estimated stricture-free survival of 94.9%, 92.2%, and 91.0% (Table 1). 8.6% of patients experienced a 90-day complication (Clavien ≥ 2), most commonly wound (3.9%) or UTI (3.3%). De novo erectile dysfunction was reported in 6.0% of patients with an overall satisfaction of 92.2%.

Stricture-free survival

Table 2 depicts univariable and multivariable Cox regression analysis examining clinical variables associated with stricture recurrence. On both univariable and multivariable Cox regression, etiology in particular radiation (Hazard Ratio (HR) 6.3, 95% Confidence Interval (95%CI) 3.0–13.0; $p<0.0001$) was independently associated with recurrence as well as stricture length (HR 1.2, 95%CI 1.1–1.3; $p=0.0001$), diabetes (HR 2.0, 95%CI 1.1–3.7; $p=0.02$), and prior urethroplasty (HR 2.4, 95%CI 1.3–4.5; $p=0.007$).

Kaplan-Meier survival analysis demonstrated (Figure 1) significant differences in stricture-free survival when stratified by etiology (log-rank $p<0.001$). The number at risk columns align with 0, 2, 5, 10 and 15 year timepoints. Estimated stricture-free survival for patients with radiation stricture was 71.8%, 60.5%, and 60.5% at 1, 5, and 10 years respectively. In contrast, the estimated stricture-free survival among patients with idiopathic strictures was 97.1%, 93.9%, and 93.2% at the same time points.

Secondary outcomes

Second outcomes across stricture etiologies are demonstrated in Table 3. There were no statistically significant differences across etiologic subgroups with respect to the incidence of 90-day postoperative complications ($p=0.77$), baseline erectile dysfunction ($p=0.30$), or de novo erectile dysfunction ($p=0.53$). Patient-reported satisfaction was lower in those with radiation-associated strictures when compared to all other etiologies (83.9% versus 92.2%; $p=0.04$).

DISCUSSION

Buccal mucosal graft (BMG) substitution urethroplasty is widely regarded as the de facto gold standard for bulbar urethral strictures requiring tissue transfer owing to the favorable histologic properties of buccal mucosa and high success reported in heterogeneous cohorts.^{5-8,15-17} This success of bulbar urethroplasty using BMG has resulted in the expansion of indications to all stricture etiologies and lengths including short strictures that had previously been treated primarily with anastomotic urethroplasty.^{9,10} However, certain stricture etiologies may be associated with increased risk of recurrence due to etiology-associated factors such as obliterated tissue planes, impaired vascularity, or fibroblast dysfunction.^{11,16} Principles of wound healing suggest that the success of graft-based reconstruction depends not only on graft quality, but also on the biological suitability of the recipient bed.¹¹ Radiation-associated urethral strictures, in particular, represent a unique reconstructive challenge due to chronic vascular compromise, fibrosis, and impaired tissue regeneration.^{12,13} Limited prior study has suggested inferior or at least variable outcomes following urethroplasty with buccal mucosa in radiated patients.^{10,17-21} However, these reports often have either heterogeneous stricture locations, mixed surgical techniques, or small numbers of substitution urethroplasty cases, making it difficult to isolate the performance of BMG specifically.¹⁴⁻²¹ In particular, strictures related to radiation involve not only the bulbar urethra but may extend into the membranous.^{12,21-24} Thus, determining the true performance of BMG can be confounded by a more technically challenging exposure if the posterior urethra is involved. Given these concerns, it is critical to evaluate etiology-specific outcomes in a homogeneous cohort to guide surgical decision-making and patient counselling. The present study was designed to evaluate long-term, etiology-specific outcomes following bulbar urethroplasty with BMG in a large, single-center cohort with extended follow-up, with the hypothesis that radiation would be associated with inferior stricture-free survival and patient-reported outcomes.

Overall outcomes of bulbar urethroplasty with buccal mucosal graft

In the overall cohort of 914 patients, bulbar urethroplasty with BMG demonstrated excellent long-term durability, with estimated stricture-free survival of 94.9%, 92.2%, and 91.0% at 1, 5, and 10 years respectively. These results are consistent with prior large series reporting long-term success exceeding 85% for substitution bulbar urethroplasty.^{7,8,16} The incidence of de novo erectile dysfunction (6.0%) and 90-day complications (8.6%) further support the safety profile of

contemporary bulbar reconstruction.²⁵ Importantly, the durability observed in this study using a predominantly dorsal onlay approach with a median follow-up exceeding eight years, reaffirms BMG urethroplasty as a highly effective reconstructive strategy for most bulbar stricture etiologies.

Differences in stricture-free survival

Despite excellent overall outcomes, etiology emerged as a powerful determinant of stricture recurrence. On multivariable analysis, radiation-associated strictures demonstrated a more than six-fold increased risk of recurrence (HR 6.27, 95%CI 3.03–12.99; $p < 0.001$) independent of stricture length, diabetes, and prior urethroplasty. Stricture-free survival in radiated patients declined to 71.8% at 1 year and 60.5% at 5 years, markedly inferior to idiopathic strictures, which maintained patency rates exceeding 93% at 5 years. Our findings support the hypothesis that radiation-associated bulbar urethral strictures have a significantly higher recurrence risk following substitution urethroplasty with BMG. Ahyai et al. also reported a ~40% failure rate at 48 months in radiated patients undergoing ventral onlay urethroplasty with buccal mucosa.¹⁸ Similarly, Vetterlein et al. found a >30% recurrence rate at a median follow-up of 44 months.²⁰ Other more favourable studies found a recurrence risk of 18% albeit with a short median follow-up of 21 months.²¹ Given that both dorsal and ventral onlay BMG techniques are generally regarded as having comparable outcomes, these findings may best understood through the lens of wound-healing biology.^{26,27} Successful graft take requires rapid plasmatic imbibition followed by inosculation and neovascularization from a healthy recipient bed.¹¹ The deleterious effects of radiation include endarteritis obliterans, reduced capillary density, fibroblast dysfunction, impaired collagen remodeling, resulting in a potentially chronically ischemic and fibrotic peri-urethral environment.^{12,13} Even grafts as resilient as buccal mucosa cannot always overcome a severely compromised peri-urethral milieu, potentially leading to incomplete graft integration and eventual restenosis.⁶ Thus, even the most technically sound reconstructions may be at increased risk of failure in a radiated field when compared to other etiologies. A similar mechanism may also explain why increasing stricture length, diabetes, infectious strictures and prior urethroplasty are also found to be independently associated with recurrence after bulbar urethroplasty.^{7,15,16} The present study isolates BMG performance specifically in the bulbar urethra and confirms that radiation represents a uniquely hostile environment for graft-based reconstruction. In selected cases, adjunctive strategies such as interposition muscle flaps or elaborated anastomotic techniques may be required to overcome the biological limitations imposed by radiation injury.^{23,24,28}

Differences in complications, erectile dysfunction, and patient satisfaction

Even in well-selected patients, urethroplasty can have significant risks especially in a radiated field.^{17,25} Interestingly, despite inferior stricture-free survival, etiology including radiation was not associated with higher rates of 90-day complications or de novo erectile dysfunction in our cohort. This suggests that short-term perioperative morbidity and sexual function are largely preserved even in radiated patients when urethroplasty is carefully executed. While there were no significant differences in 90-day complications or de novo erectile dysfunction across etiologies, patient satisfaction was lower in the radiated population and possibly iatrogenic strictures. This echoes previous findings from Vetterlein et al. where 29% of patients were not satisfied after urethroplasty for radiation induced strictures. Several factors likely contribute to this. First, stricture recurrence can undoubtedly impact satisfaction, even in a delayed manner. Secondly, a subset of patients may experience persisting lower urinary tract symptoms despite a technically successful reconstruction, a phenomenon described as “LUTS failure.”²⁹ This was previously reported by Vetterlein et al. in the setting of radiation induced urethral stricture.²⁰ Radiation-induced bladder dysfunction, detrusor underactivity, poor compliance, and sphincteric injury may all contribute to ongoing symptoms independent of urethral caliber.^{10,19,20,23} Some of these features may also occur in patients with iatrogenic strictures. Lastly, patients with radiation-associated strictures may undergo reconstruction with limited awareness of the long-term urethral sequelae of pelvic radiotherapy and the biologic constraints on reconstructive success.³⁰ These findings underscore the importance of comprehensive preoperative counseling in radiated patients with explicit discussion of recurrence risk, the possibility of persistent urinary symptoms, and the potential need for alternate treatment strategies. Aligning expectations may be as critical as surgical technique in optimizing patient-reported outcomes in this high-risk population.

Strength, limitations, and study importance

The primary strengths of this study include its large sample size, extended follow-up, consistent surgical technique, and robust etiology-specific analysis within a single-center cohort. By isolating bulbar BMG urethroplasty and applying uniform definitions of recurrence, this study provides high-quality evidence to guide patient counseling and surgical decision-making. Limitations include the retrospective design, reliance on non-validated measures of erectile function and patient satisfaction, and the absolute number of radiated patients. The retrospective design and non-validated assessment tools may introduce a selection bias. While the incidence of incontinence in patients with isolated bulbar urethral strictures without extension into the membranous or posterior urethra (i.e. vesicourethral anastomotic stenosis) is low, this outcome is not specifically reported but would be relevant to a patient population with posterior urethral involvement. The number of radiated patients relative to the entire study cohort may further introduce variability into the study findings. As a single-center study, the results may be reflective of specific surgical expertise and may not be universally applicable. Additionally, radiation dose was not reliably available, precluding more granular analysis of radiation severity.

Despite these limitations, the magnitude and consistency of the observed effect strongly support the biological plausibility of the findings. The clinical importance of this study lies in its ability to refine expectations for both surgeons and patients. While BMG urethroplasty remains highly effective for most bulbar strictures, radiation-associated disease represents a distinct reconstructive entity in which substitution grafting performs less favorably. These data support consideration of alternative strategies such as excision-based reconstruction or vascularized tissue transfer in appropriately selected radiated patients.^{23,24,28} Future multi-institutional studies comparing different BMG onlay and anastomotic techniques in radiated patients with long-term and patient-reported outcomes are warranted.

CONCLUSIONS

In general, substitution bulbar urethroplasty with BMG is a highly effective treatment but may be less effective in patients with radiation-associated strictures. The higher recurrence and reduced satisfaction in this subgroup suggests that alternative reconstructive strategies such as anastomotic urethroplasty may be more appropriate in radiated tissue beds whenever technically feasible.

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FIGURES AND TABLES

Figure 1. Kaplan-Meier survival curve demonstrating stricture-free survival stratified by stricture etiology.

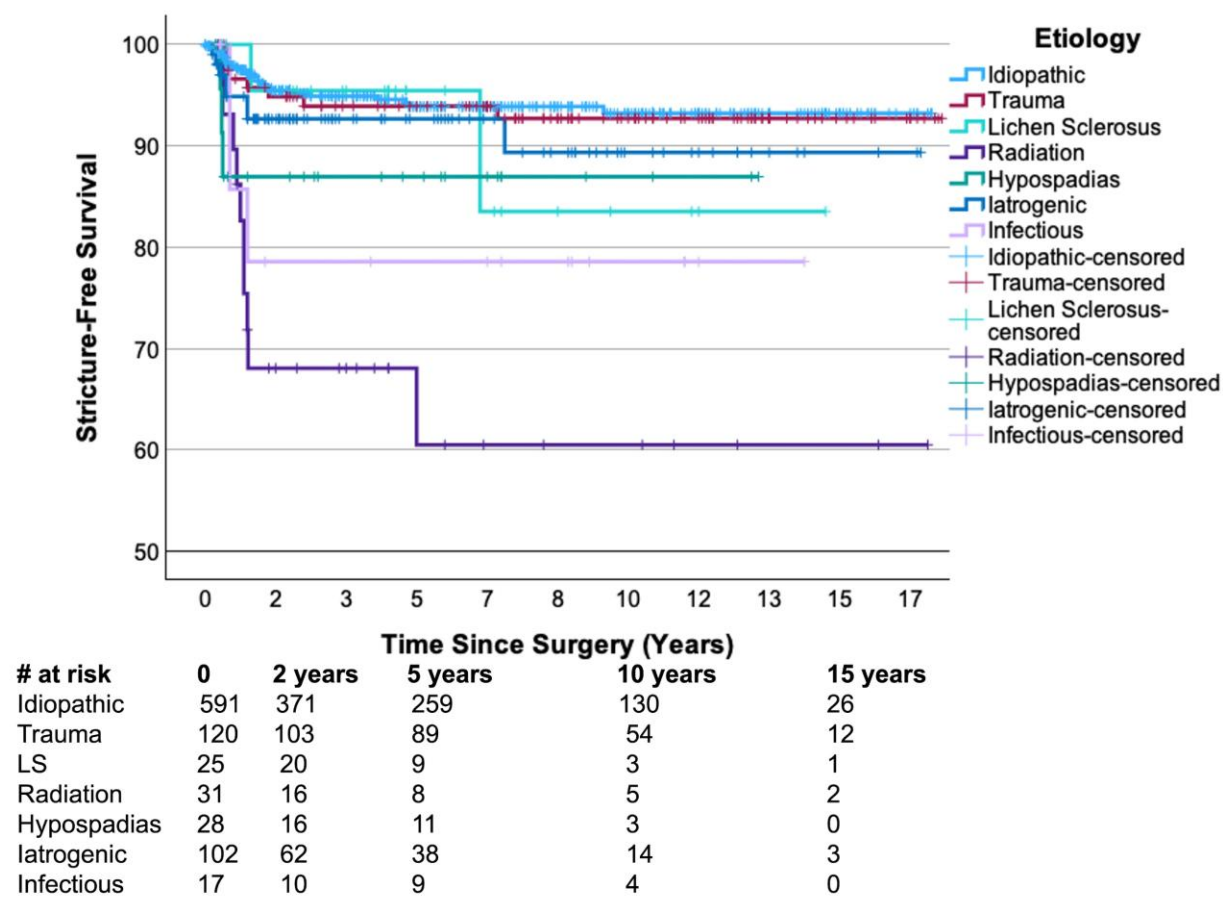


Table 1. Demographics and outcomes of the entire buccal mucosal graft bulbar urethroplasty cohort	
Variable	% (N)
Number of patients	914
Patient age (years)	Median 48 (IQR 36–60)
Stricture length (cm)	Median 4.0 (IQR 3.5–5.0)
Stricture etiology	
Idiopathic	64.7% (591)
Trauma	13.1% (120)
Lichen sclerosus	2.7% (25)
Radiation	3.4% (31)
Hypospadias	3.1% (28)
Iatrogenic	11.2% (102)
Infectious	1.9% (17)
Failed prior endoscopic treatment	91.0% (832)
Number of prior endoscopic treatments	Median 2 (IQR 1–3)
Previous urethroplasty	10.3% (94)
Diabetes	13.1% (120)
Smoker	15.5% (142)
Comorbidity present	28.0% (255)
Obesity (BMI ≥ 35)	16.4% (150)
Surgical technique	
Dorsal onlay	98.1% (897)
Ventral onlay	1.9% (17)
Length of follow-up (months)	Median 103 (IQR 57–163)
Estimated mean recurrence-free survival (years)	16.0 (95% CI 15.7–16.4)
Number of stricture recurrences	62
Estimated stricture-free survival	
1 year	94.9%
2 years	93.3%
5 years	92.2%
10 years	91.0%
90-day complication (Clavien ≥ 2)	8.6% (79)
UTI	3.9% (36)
Wound	3.3% (30)
Catheter	0.5% (5)
Cardiac	0.1% (1)

Pulmonary	0.5% (5)
Other	0.5% (5)
De novo erectile dysfunction	6.0% (55)
Patient satisfaction	92.2% (843)

BMI: body mass index; CI: confidence interval; IQR: interquartile range; UTI: urinary tract infection.

Table 2. Univariable and multivariable Cox regression analysis of clinical variable-associated stricture recurrence

Variable	Number of recurrences	Univariable		Multivariable	
		Hazard ratio (95% CI)	p	Hazard ratio (95% CI)	p
Age (years)	N/A	1.01 (0.99–1.03)	0.21		
Stricture length (cm)	N/A	1.16 (1.06–1.26)	<0.001	1.17 (1.06–1.29)	0.001
Diabetes		2.18 (1.22–3.90)	0.009	2.04 (1.12–3.70)	0.02
Yes	12.5% (15/120)				
No	5.9% (47/794)				
Smoking		0.86 (0.41–1.81)	0.70		
Yes	5.6% (8/142)				
No	7.0% (54/772)				
Obesity (BMI>35)		1.70 (0.94–3.09)	0.08		
Yes	9.3% (14/150)				
No	6.3% (48/764)				
Preoperative bacteriuria		1.09 (0.62–1.91)	0.76		
Yes	7.8% (17/218)				
No	6.5% (45/696)				
Location			0.07		
Mid-proximal bulbar	6.4% (54/839)	Reference			
Distal bulbar	10.7% (8/75)	1.98 (0.94–4.17)			
Etiology			<0.001		<0.001
Idiopathic	4.7% (28/591)	Reference		Reference	
Trauma	6.7% (8/120)	1.11 (0.50–2.44)		1.02 (0.46–2.25)	
Lichen sclerosus	8.0% (2/25)	1.55 (0.37–6.50)		0.78 (0.17–3.61)	
Radiation	32.3% (10/31)	7.38 (3.58–15.21)		6.27 (3.03–12.99)	<0.001
Hypospadias	10.7% (3/28)	2.68 (0.82–8.82)		1.43 (0.40–5.13)	

Iatrogenic	7.8% (8/102)	1.62 (0.74–3.56)		1.32 (0.60–2.91)	
Infectious	17.6% (3/17)	3.80 (1.15–12.49)		3.35 (1.01–11.2)	p=0.05
Number of endoscopic treatments	N/A	1.01 (0.96–1.06)	p=0.77		
Prior urethroplasty		2.57 (1.42–4.66)	p=0.002	2.41 (1.28–4.54)	p=0.007
Yes					
No	14.9% (14/94) 5.9% (48/820)				

Bolded values indicate statistical significance. BMI: body mass index; CI: confidence interval.

Table 3. Secondary outcomes of 90-day complications, erectile function, and patient satisfaction stratified by stricture etiology

Outcome	Idiopathic	Trauma	Lichen sclerosis	Radiation	Hypospadias	Iatrogenic	Infectious	p
90-day complication	7.8% (46/591)	10.8% (13/120)	8.0% (2/25)	9.7% (3/31)	7.1% (2/28)	9.8% (10/102)	17.6% (3/17)	p=0.77
Baseline ED	6.8% (40/591)	8.3% (10/120)	4.0% (1/25)	16.1% (5/31)	3.6% (1/28)	9.8% (10/102)	0.0% (0/17)	p=0.30
De novo ED	6.9% (41/591)	6.7% (8/120)	4.0% (1/25)	3.2% (1/31)	0.0% (0/28)	2.9% (3/102)	5.9% (1/17)	p=0.53
Patient satisfaction	91.5% (541/591)	96.7% (116/120)	100.0% (25/25)	83.9% (26/31)	92.9% (26/28)	87.3% (89/102)	100.0% (17/17)	p=0.04

Bolded values indicate statistical significance. ED: erectile dysfunction.