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TOPIC PAPER

Long-term outcomes of anastomotic urethroplasty for radiation-induced strictures

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Abstract

Purpose To present our experience with excision and primary anastomosis (EPA) of radiation-induced urethral strictures (RUS) in men, including risk factors for stricture recurrence and long-term recurrence rates.

Methods A retrospective review was performed of patients who underwent EPA of RUS between 2007 and 2018 at a single tertiary referral center. Demographic information, stricture location and length, complications, and stricture recurrence were analyzed. Univariate and multivariate Cox regression analyses were performed to identify variables impacting recurrence.

Results EPA was performed in 116 patients with RUS. The majority of patients (86.2%, 100/116) underwent at least one prior urologic intervention. Mean stricture length was 2.3 cm. Stricture recurrence occurred in 19.0% (22/116) at a mean of 8.6 months. For patients with at least 1 year of postoperative follow-up (mean 30.7 months), stricture recurrence significantly increased to 36.6% (15/41; $p=0.03$). On univariate and multivariate analyses, postoperative complications were associated with stricture recurrence ($p<0.001$).

Conclusion EPA remains a viable option for men with RUS. Nearly two-thirds of RUS patients remain recurrence-free with long-term follow-up following EPA.

Keywords Urethral stricture · Radiation · Urethroplasty · Excision and primary anastomosis

Introduction

Pelvic radiation is a well-documented risk factor for urethral stricture formation. Risk of stricture varies by radiation type and dosage, with reported incidence between 1.5–2% with external beam radiotherapy (EBRT), 1.8–4% with brachytherapy, and 4.9–11% with combined EBRT and brachytherapy [1-3].

Radiation leads to vascular damage, ischemia, and fibrosis of the urethra [1, 4]. These tissue changes can promote initial urethral stricture formation and contribute to higher recurrence and complication rates following endoscopic or open intervention [4, 5]. Over 90% of radiation-induced urethral strictures (RUS) involve the bulbomembranous urethra near the sphincteric complex [6]. Treatment of RUS therefore carries a higher risk of postoperative stress urinary incontinence—one recent study reported a 33% rate of de novo stress urinary incontinence rate following urethroplasty [7]. Postoperative stress urinary incontinence in these patients can be problematic, as radiation also portends poor outcomes of subsequent artificial urinary sphincter placement [8, 9].

Other complications including urinary tract infections, wound breakdown, fistula formation, and stricture recurrence are more prevalent following urethroplasty of radiation-induced strictures compared to non-irradiated cases [5, 10]. Given the increased morbidity and complexity of these cases, we reviewed our experience with over a decade of anastomotic urethroplasty of RUS at a high-volume tertiary center.

Materials and methods

Following approval by an institutional review board, we performed a retrospective study of men undergoing urethroplasty for RUS by a single surgeon at a tertiary academic

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center between 2007 and 2018. Only patients with urethroplasty for strictures attributed to prior pelvic radiation were included. Patient characteristics including age, smoking history, radiation type, prior urologic interventions, and clinical data were reviewed.

Stricture location was documented based on retrograde and/or antegrade urethrography prior to definitive repair. All patients underwent EPA urethroplasty without graft or flap as previously described [11]. Positive preoperative cultures were treated with 5–7 days of culture-specific antibiotics, and we used broad-spectrum IV antibiotics prior to incision. Strictures were limited to the bulbomembranous urethra, with isolated anterior urethral strictures, bladder neck stenoses, and/or panurethral strictures excluded. Length of stricture was determined at the time of definitive repair. Postoperatively, patients were typically discharged with a urethral catheter for 3 weeks, with a low-dose prophylactic antibiotic prescribed during this period. A voiding cystourethrogram (VCUG) was obtained at the time of catheter removal to assess for anastomotic leak.

All postoperative complications were documented, with urinary incontinence and erectile dysfunction excluded, because they were commonly chronic comorbid conditions with inconsistent reporting in this population. Recurrence was defined by recurrent stricture ≤ 16F in caliber on cystoscopy, stricture on VCUG, and/or operative intervention for urethral stricture disease. To limit bias in our recurrence rate due to loss of follow-up, we separately assessed patients with long-term postoperative urologic follow-up of a minimum of 1 year.

Table 1 Demographics and prior urologic procedures

	All ($n = 116$)	Long-term follow-up ($n = 41$)
Age (years)	72.3 (52–88)	74.2 (52–88)
ASA score	2.5 (1–3)	2.6 (1–3)
BMI	28.2 (19.1–51.7)	28.1 (21.3–43.0)
Obesity	32 (27.6%)	13 (31.7%)
Diabetes	29 (25.0%)	9 (22.0%)
Tobacco use		
Never smoker	56 (48.3%)	18 (43.9%)
Former smoker	48 (41.4%)	19 (46.3%)
Current smoker	12 (10.3%)	4 (9.8%)
Type of radiation		
EBRT	74 (63.8%)	26 (63.4%)
Brachytherapy	28 (24.1%)	12 (29.3%)
Combined	14 (12.1%)	3 (7.3%)
Stricture length (cm)	2.3 (0.5–5.0)	2.4 (1.5–4.0)
Prior interventions		
Any prior intervention	100 (86.2%)	38 (92.7%)
Self-catheterization	31 (26.7%)	14 (34.1%)
Dilation	61 (52.6%)	27 (65.9%)
DVIU	44 (37.9%)	14 (34.1%)
TURP/PVP	6 (5.2%)	1 (2.4%)
Prostatectomy	5 (4.3%)	2 (4.9%)
Cryotherapy	1 (0.9%)	1 (2.4%)
Urolume	1 (0.9%)	1 (2.4%)
Urethroplasty	6 (5.2%)	0
AUS	1 (0.9%)	0
Follow-up (months)	13.5 (0.03–75.0)	30.7 (12.2–75.0)

ASA American Society of Anesthesiologists physical status classification system, *BMI* body mass index, *EBRT* external beam radiation therapy, *IMRT* intensity modulated radiation therapy, *DVIU* direct vision internal urethrotomy, *TURP* transurethral resection of prostate, *PVP* photoselective vaporization of prostate, *AUS* artificial urinary sphincter

Statistical analysis

Recurrence-free survival was calculated using the Kaplan–Meier method and compared with the log-rank test. Hazard ratio and 95% confidence interval for univariate and multivariate analyses were performed using Cox regression. Fisher's exact test was used to compare recurrence rates. All tests were two-sided with $p \leq 0.05$ considered significant. Interval variables were reported in mean values and ranges unless otherwise specified. IBM SPSS Statistics version 25.0 was used for data analysis.

Results

Patient demographics

A total of 116 patients with a history of pelvic radiation underwent EPA urethroplasty for RUS between January 2007 and December 2018 at our institution. Patient characteristics are summarized in Table 1. The mean age was 72.3 years. All patients had a prior history of pelvic radiation, with the majority (63.8%, 74/116) undergoing external beam radiation. Mean stricture length was 2.3 cm.

Prior interventions

Prior urethral interventions were quite common, with a history of at least one previous urologic procedure in 86.2% (100/116) of patients. The most frequent interventions included dilation (52.6% [61/116]) and direct vision internal urethrotomy (DVIU) (37.9% [44/116]) (Table 1). In this cohort, 58.6% (68/116) of patients underwent preoperative suprapubic tube placement.

Complications

Postoperative complications were analyzed. Excluding stricture recurrence, urinary incontinence, and erectile dysfunction, a total of 20 postoperative complications occurred in 14.7% (17/116) of patients (Table 2). There were no postoperative de novo urethral fistula.

Stricture recurrence

Overall success rate was 81.0% (94/116), with a mean postoperative follow-up of 13.5 months (Fig. 1). Among the patients with recurrent strictures (22/116), mean time to recurrence was 8.6 months. Management included 17 endoscopic treatments (typically balloon dilation), 7 open surgical repairs (including 3 cystoprostatectomies with urinary diversion), and 2 patients managed with chronic suprapubic tube.

Long-term follow-up

Among the cohort with a minimum of 1 year of postoperative follow-up ($n=41$), the mean follow-up was 30.7 months (Table 1). The rate of recurrence was significantly higher

Table 2 Complications and stricture recurrence

	All ($n=116$)	Long-term follow-up ($n=41$)
Complications		
Patients with complication(s)	17 (14.7%)	9 (22.0%)
UTI	3 (2.6%)	0
Urinary retention	10 (8.6%)	7 (17.1%)
Surgical site infection/wound dehiscence	5 (4.3%)	3 (7.3%)
Catheter issues prompting ER visit	2 (1.7%)	2 (4.9%)
Time to complications (days)	44.1 (1–111)	40.0 (1–111)
Recurrent strictures	22 (19.0%)	15 (36.6%)
Time to stricture recurrence (months)	8.6 (0.7–57.7)	10.8 (0.7–57.7)
Surgical management of recurrent strictures		
Endoscopic treatment	17 (14.7%)	12 (29.3%)
Open surgical	7 (6.0%)	6 (14.6%)
SP tube	2 (1.7%)	2 (4.9%)
Post-urethroplasty AUS placement	12 (10.3%)	8 (19.5%)
AUS explant/revision	3	3
Time to explant/revision (months)	7.6 (6.1–9.5)	7.6 (6.1–9.5)

Long-term follow-up includes only patients with a minimum of 1 year of postoperative urology follow-up

UTI urinary tract infection, *SP* suprapubic, *AUS* artificial urinary sphincter

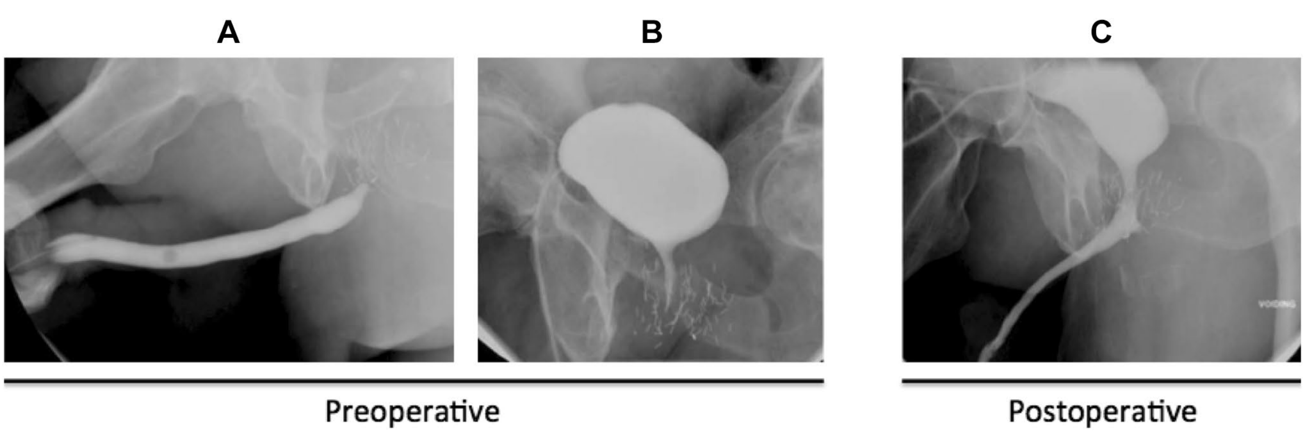

Fig. 1 Preoperative retrograde urethrogram (RUG) (**a**) and voiding cystourethrogram (VCUG) (**b**) on patient with obliterative RUS secondary to brachytherapy. Postoperative VCUG (**c**) after successful EPA urethroplasty

at 36.6% (15/41), for an overall success rate of 63.4% ($p = 0.03$). Artificial urinary sphincters (AUS) were placed in 19.5% (8/41) following urethroplasty, with a mean follow-up of 25.4 months following AUS placement. Of these cases, 37.5% (3/8) required subsequent AUS explantation for erosion ($n = 2$) or infection ($n = 1$) (Table 2). Mean time to removal was 7.6 months.

Univariate and multivariate analyses

To analyze factors associated with risk of recurrence, we performed Cox regression analysis (Table 3). On univariate and multivariate analyses, postoperative complications, excluding recurrence, urinary incontinence, and erectile dysfunction, significantly increased the risk of stricture recurrence ($p < 0.001$). Postoperative complications remained a significant risk factor for recurrence on univariate ($p = 0.002$) and multivariate ($p = 0.003$) analyses when excluding patients with isolated urinary retention ($n = 8$). For patients with at least 1 year of follow-up, postoperative complications remained the only variable significantly associated with recurrence on either univariate or multivariate analysis (both $p < 0.01$). Kaplan–Meier curves for patients with and without postoperative complications are shown in Fig. 2 (log-rank $p < 0.01$).

Discussion

Radiation-induced urethral strictures pose a complex challenge for the clinician. These strictures often present in elderly men with several comorbid factors. Many patients undergo at least one prior endoscopic intervention before referral to a reconstructive urologist. Such procedures have been shown to complicate urethroplasty, creating longer strictures and higher rates of recurrence [12]. Radiation-induced tissue changes increase the risk of complications following intervention, and the location in

Table 3 Univariate and multivariate analyses of risk factors for stricture recurrence

	Univariate		Multivariate	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Obesity	1.89 (0.81–4.43)	0.14	1.96 (0.75–5.17)	0.17
Diabetes	2.25 (0.90–5.96)	0.08	2.31 (0.82–6.57)	0.12
Current tobacco use	0.94 (0.22–4.04)	0.93	2.52 (0.49–13.08)	0.27
Combination radiotherapy	2.00 (0.66–6.07)	0.22	1.66 (0.44–6.24)	0.45
Prior GU intervention	1.03 (0.30–3.52)	0.96	1.33 (0.35–5.14)	0.68
Stricture greater than 2 cm	1.71 (0.71–4.14)	0.23	1.68 (0.63–4.48)	0.30
Preoperative SP tube	1.16 (0.49–2.73)	0.74	1.19 (0.44–3.20)	0.73
Postoperative complication	4.79 (2.02–11.40)	< 0.001	6.81 (2.52–18.36)	< 0.001

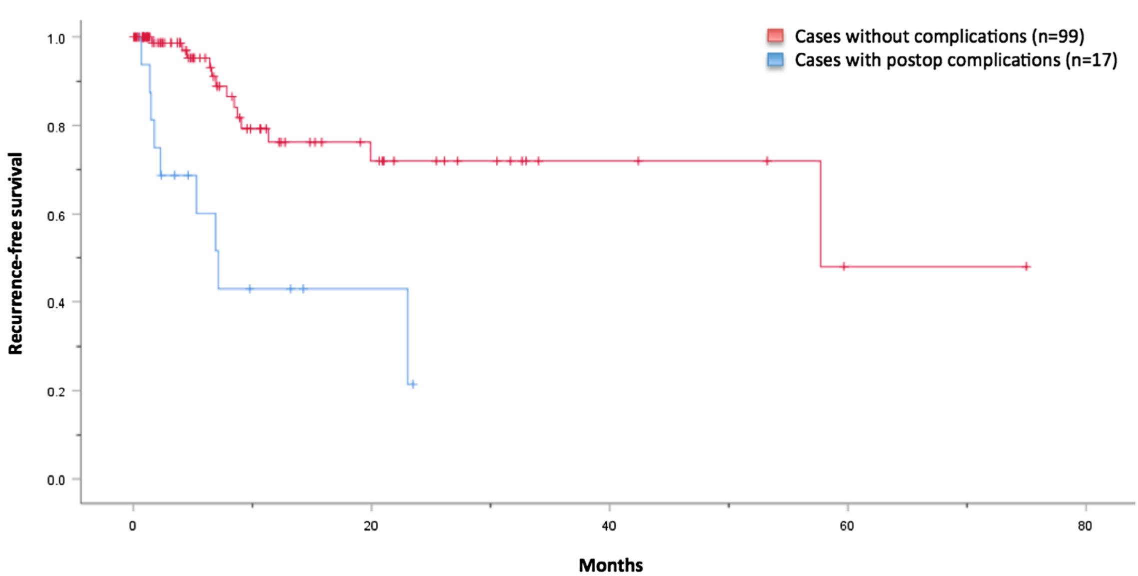

Fig. 2 Recurrence-free survival based on postoperative complications

the bulbomembranous urethra leads to a significant risk of postoperative urinary incontinence.

Stricture recurrence

Success rates for urethroplasty with a prior history of radiation range from 70–90% in several case series with short follow-up [4]. In our experience, the overall success rate was 81%. Prior studies have suggested that stricture recurrence rates continue to increase with longer monitoring [13, 14]. In the subset of patients with at least 1 year of follow-up, our success rate decreased significantly to 63.4%. This, along with recurrence as late as 4.8 years (57.7 months) postoperatively, corroborates the need for long-term clinical follow-up to accurately monitor for stricture recurrence.

Post-urethroplasty interventions

Stricture recurrences in our cohort tended to be soft, focal, and managed endoscopically, as this has been shown to be a reasonable option for isolated recurrent strictures following urethroplasty [15]. Our preference has been to manage recurrent RUS with balloon dilation (24 Fr UroMax®). In our series, nearly 20% of patients with long-term follow-up pursued AUS placement, which required re-operation in 37.5% (3/8).

Other management options

Endoscopic therapy is a reasonable consideration in appropriately selected patients with radiation strictures, but carries a recurrence rate of at least 40–60% even in series with short follow-up [6, 16]. Some authors suggest much lower success rates in this patient population [17]. Patients considering endoscopic treatment should be counseled on the expected lower durability, possible need for repeated procedures, risk of post-procedural SUI, and possible future complexity of open intervention [13]. Intermittent self-dilation can negatively impact quality of life [18], and may not be a viable long-term option if stricture caliber decreases.

In our experience, suprapubic tubes offer benefit for many patients prior to urethroplasty. Suprapubic tubes allow for antegrade and retrograde imaging to assist in counseling, surgical planning, and to prevent pre-procedural urinary obstruction. Some patients may elect to be managed with suprapubic tube indefinitely, in particular those with stress urinary incontinence at presentation. More than half of these men may experience improvement or resolution of SUI symptoms with SP tube alone [19]. In comparison, previous groups have demonstrated that de novo SUI may be as high as 30–40% after urethroplasty, and those with prior incontinence often have exacerbation of symptoms [7, 11, 20]. However, chronic suprapubic tubes have known disadvantages, including urinary tract infections, bladder stones, and lower urinary tract symptoms, among others [19].

Limitations

Our study is limited by the nature of a single surgeon and retrospective series. Neither grafts nor flaps were included in our cohort due to concern of poor vascularity of the radiated tissue bed. However, other groups have reported successful outcomes with buccal mucosa graft urethroplasty [14] and use of gracilis muscle flaps for improved tissue bed vascularity [21].

Some patients in our series had limited follow-up, which may impact the overall complication and recurrence rate. To account for this, we separately analyzed individuals with extended urologic follow-up at our center. However, in our practice, geographically remote patients with successful postoperative outcomes were often followed locally by the referring urologist. As such, patients with complications and/or recurrence could theoretically have longer follow-up relative to those with successful outcomes in remote locations.

Urinary incontinence and erectile dysfunction were frequently present preoperatively and inconsistently reported, so these were not analyzed, limiting our overall complication rate. When assessing risk factors for stricture recurrence, we included postoperative complications such as urinary retention and UTI. These complications, in particular urinary retention and possibly UTI, may simply be the first sign of stricture reformation in some cases. However, with an average presentation 8 months earlier than documented recurrence and a significant impact excluding urinary retention, this remains a clinically significant finding. Patients with postoperative complications may warrant closer follow-up and/or testing to evaluate for recurrence. Finally, further studies will be necessary to determine outcomes following salvage treatment for stricture recurrence.

Conclusion

In this RUS population, both postoperative complications and longer follow-up significantly increase recurrence rates following urethroplasty. However, EPA urethroplasty remains a viable long-term solution for the majority of patients with urethral strictures secondary to pelvic radiation.

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