

Review

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Urethroplasty in a post irradiation urethral stricture - a review

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Abstract

Radiotherapy-induced urethral strictures (RIUS) decrease quality of life and present a great challenge for surgical reconstruction, especially due to proximal location, compromised vascular supply, and poor wound healing. It is unclear whether urethroplasty is an option in cases with stricture resulting from exposure to pelvic radiation. We review the pathophysiology, diagnostic workup, and disease-specific aspects of RIUS. Furthermore, we discuss several management alternatives such as excision and primary anastomosis, as well as techniques for open reconstruction with flaps. The most extensive techniques in the treatment of strictures include, for example, those using gracilis muscle flaps, as they can involve periurethral tissue to provide sufficient vascularity for excellent post-surgery urethral healing. In brief, RIUS represent a significant challenge. In carefully chosen patients, urethroplasty should be considered as a feasible and durable treatment. However, medical practitioners should always take into consideration that the results of urethroplasty in RIUS are not comparable to urethroplasties without a radiation background.

Keywords: Urethra, stricture, radiotherapy, urethroplasty, buccal mucosa graft, gracilis muscle flap, stricture

INTRODUCTION

Radiotherapy (RT) is a popular and successful method for treating pelvic malignancies. Half of the patients



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with cancer are treated with RT^[1]. However, this treatment is not without side effects and urethral strictures are among the possible complications. Urethral strictures are reported for nearly 32% of patients^[2]. The damage to this tissue involves multiple factors, both directly and indirectly linked to RT^[3]. This pathology is uncommon and, in many cases, not reported as important, despite being associated with high morbidity^[4]. In addition, the reconstructive urologist must be trained to understand and manage post-irradiation urethral pathologies due to their complexity and the need for numerous operative techniques.

EPIDEMIOLOGY, INCIDENCE, AND ETIOLOGY

Post-RT pelvic complications are often moderate to severe, usually occurring following treatment for malignant pelvic tumors^[5,6]. Recent reports list a 2% incidence rate and a risk of urethral narrowing for approximately 25 years following RT. The most common type of RT leading to urethral stricture (US) is prostate cancer brachytherapy (BT)^[7]. Recent studies report a bulbomembranous stricture rate following BT of 8% versus 4% for external beam radiation therapy (EBRT)^[8]. Health-related studies have reported on the relevance of functional morbidity resulting from cancer treatments. A long-term functional decline over a period of 15 years has been found in primary treatments, such as radical prostatectomy or RT^[9]. Although bulbomembranous stenosis accounts for 100% of post-radiation strictures, a narrowing can theoretically form at any location of the urethra. The type of radiation and the radiation dosage used also have an impact on the overall incidence of urethral stricture^[10]. Merrick *et al.* described that the behavior between radiation and doses (expressed as the dose delivered 20 mm from the prostatic apex) and the time of hormonal manipulation were predictive of urethral damage after RT^[11].

RT damages living cells both directly by inducing cellular apoptosis and DNA mutation and indirectly through the action of hydroxide free radicals^[12]. Ballek *et al.* studied the correlation between radiation and urethral strictures, inadequate perfusion, and poor wound healing due to vascular compromise^[13]. Due to the effects of radiation on the epithelium, fibroblasts are not able to provide sufficient collagen to meet the demands of healing. Tightening of fibroblasts and scar formation due to collagen maturation are also endangered^[14]. Over time, the metaplasia induces fibrotic changes in the corpus spongiosum, resulting in a narrower urethral lumen^[15].

For the genitourinary reconstructive surgeon, it is of utmost importance to assess the quality of tissue. It will allow for a highly successful surgery.

DIAGNOSTICS

The diagnostic workup is important and can be designed on a case per case basis. Patients with urethral stricture mostly complain of obstructive voiding symptoms. They more often present with storage lower urinary tract symptoms. The most evident symptom is weakening of the urinary flow^[16]. It can be valuable to evaluate preoperative bladder function by performing a urodynamic study. Uroflowmetry will be adequate in a variety of cases^[15]. Uroflowmetry gives us valuable information on bladder function as well as capacity, being a predictor of damage caused by chronic obstruction of urethral stricture. Radiographic examination of the length and location of the stricture is essential. When the retrograde urethrogram is deficient, a voiding urethrocytogram (VCUG) can be performed to evaluate the bladder neck^[17]. The VCUG provides information on the length, location, severity, and number of US. In addition, it provides information on fistulas, urethral duplication, false pathway, and the status of the bladder neck. Cystoscopy is a fast and relatively easy way to identify a urethral stricture. This procedure provides evidence about the location and remaining caliber of the damaged urethra. Anterograde cystoscopy with a flexible device can be performed when the patient has had a cystostomy to visualize the proximal urethra and the bladder neck, as well as the presence and extent of radiation necrosis of the prostate, which is important to recognize as

the necrotic tissue should be resected before a urethroplasty is attempted. In addition, cystoscopy is unable to provide information regarding the surrounding spongiofibrosis. In some cases, urethroscopy alone is considered deficient for a thorough diagnostic workup and more imaging exams are warranted. Endoscopic management, such as dilation followed by direct visual internal urethrotomy of radiation-induced strictures as the first-line treatment, has been proposed. However, these men have a high risk for recurrence, which reportedly amounts to nearly 50% for patients who have undergone BT^[18].

According to the European Association of Urology guidelines for urethral stricture diagnostics, the workup should consist of medical history, physical examination, and laboratory, ultrasonography, and functional studies^[19]. Currently, there is no single strict algorithm for US diagnosis; it depends on each patient's age and compliance, as well as the etiology.

TREATMENT

Radiotherapy-induced urethral strictures are a challenge, especially because of compromised vascular supply, proximal location, and poor wound healing. Overall, the post-radiation anatomy and characteristics of the patients must be considered when planning treatment^[20]. In this review, we focus on excision and primary anastomosis (EPA), buccal mucosa graft (BMG) urethroplasty, and flaps. A comparison of success rates for the different techniques is provided in [Table 1](#)^[21].

Excision and primary anastomosis

In urethral reconstruction with innovative fasciocutaneous flaps and a wide range of tissues for grafting, stricture EPA remains the gold standard in reconstruction for properly selected patients. Patient selection is limited by the length and location of the stricture, but the generally excellent long-term results with EPA warrant its consideration in post-radiation urethral reconstruction.

The success of EPA relies on careful patient selection. From a strict anatomic perspective, only short strictures (< 2 cm) located between the suspensory ligament and the membranous urethral area are amenable to excision.

A suprapubic foley catheter to allow for tissue recovery is important for urethral rest, allowing the urethra to rest for several weeks prior to urethroplasty. Urethral rest has numerous advantages as it allows for a precise determination of the stricture area before urethroplasty. In addition, it allows for a decrease in the periurethral inflammation, which might otherwise delay the wound healing process. Asymptomatic and symptomatic bacteriuria are important to manage to avoid postoperative infection, including in the 24 h before the procedure. The perineum must be adequately exposed for urethroplasty. A vertical midline approach is made in the perineum; after dissection of the subcutaneous tissue and fascia of Colles, the bulbospongiosus muscle is encountered and transected to expose the urethra. The proximal bulbar urethral is exposed by a circumferential mobilization of the urethra from the penoscrotal junction using sharp dissection. Intraoperative urethroscopy allows the stricture location to be determined. A urethral incision is made at the level of the stricture and examined. Damaged urethral mucosa and spongiofibrosis are further excised until healthy mucosa and corpus spongiosum are reached. It is important to remove this abnormal urethral mucosa to avoid stricture recurrence. Subsequently, both ends of the urethra are widely spatulated for approximately 1 cm and a foley catheter is placed (18 Fr catheter). Absorbable sutures are used to approximate mucosa to mucosa. The anastomosis should be under control, avoiding excessive tension. If it does occur, it demands additional mobilization of the urethra. The bulbospongiosus muscle and fascia of Colles are closed with 3-0 Vicryl. The foley catheter is left in place for three weeks and prophylaxis is continued for 24 h. The follow-up after surgery includes the determination of residual bladder volumes and,

Table 1. Comparison of success rates for different techniques

Source	Number of patients	Location	Mean length (cm)	Intervention	F/U (yr)	Success rate (%)	Time to recurrence (mo)
Ahyai <i>et al.</i> ^[23] (2015)	35	B & BM	2.9	BMGU	2.2	71.1	17
Rourke <i>et al.</i> ^[22] (2016)	72	BM	2.1	EPA (65%)	4	91	29.8
			6.1	Graft/Flap (35%)		75	
Hofer <i>et al.</i> ^[20] (2014)	38	B & BM	2.4	EPA (92%)	3.5	69.7	10.1
			4.25	Graft/Flap (8%)	5.5	85	7

B: Bulbar; BM: bulbomembranous; EPA: excision and primary anastomosis; BMGU: buccal mucosa graft urethroplasty; F/U: follow up.

in some cases, a cystoscopy control for stricture recurrence based on the evolution of the patient^[21].

In the study by Hofer *et al.* (2014) of the 72 men with radiation-induced urethral strictures, 66 (91.7%) underwent urethroplasty with EPA and the remaining 6 (8.3%) underwent substitution urethroplasty using a graft or flap^[20]. The reconstruction was eventually successful in 46 (69.7%) men. Time to reappearance was observed to be 10.2 months and was associated with stricture length greater than 2 cm ($P = 0.013$). RT type did not have a significant impact on risk. In general, EPA is a successful technique for bulbomembranous urethra in patients with RT strictures^[21,22].

Rourke *et al.* (2016) retrospectively reviewed outcomes in 35 patients with bulbomembranous stenosis for RT undergoing urethroplasty^[22]. Of these, 20 had undergone EBRT and 15 BT, presenting with RT-associated stenosis with an average stricture length of 3.5 cm. Almost half of the patients enrolled before the urethroplasty with an indwelling suprapubic catheter as the baseline. The anastomotic repair was performed in 23 patients (65.7%); 12 patients required intraoperative tissue transfers, with either buccal mucosa graft (20.0%) or penile island flap (14.3%). Urethral patency was achieved in 30 patients (85.7%) and confirmed with cystoscopy; no significant difference was observed between the operative techniques. However, 31.4% of patients experienced a complication, but all of these complications, reported within 90 days, were Clavien Grades I-II^[22].

Short-term complications, which include wound and urinary tract infections, occur infrequently and are usually managed easily. Problems with chordee and erectile dysfunction are uncommon.

Substitution urethroplasty

When EPA is not possible for urethral stricture, substitution urethroplasty has become the key treatment, especially with BMG. As for the benefits of BMG, it shows decreased propensity for contraction, its lamina propria is thin with excellent vascularization, it has not been exposed to irradiation, and it has excellent elasticity, which allows it to be easily adapted according to the recipient bed shape^[23]. Long strictures have been found difficult to treat, especially in the irradiated urethras. It is important to fix the graft to a well-vascularized field when performing urethroplasty with dorsal or ventral onlay approaches. Furthermore, a previously irradiated urethra is often poorly vascularized, thereby impeding wound healing^[23,24]. There is currently insufficient evidence regarding ventral onlay BMG and dorsal urethroplasty for the treatment of urethral strictures.

The corpus spongiosum is necessary for the survival of the ventral onlay BMG graft. The most important benefits of the ventral approach are that the urethra, especially proximal, is easier to reach, exposure of the narrow segment is better facilitating evaluation and graft placement, and mobilization of the bulbar urethra

can be omitted^[25]. In a personal communication from 2015, Barbagli and Kulkarni suggested ventral onlay as an ideal technique for bulbomembranous and proximal bulbar urethra strictures. Ahyai *et al.* described a retrospective study of their patients who had undergone ventral onlay urethroplasty^[23]. After a median follow-up of 26.5 months, their success rate was 71.1% (range, 1.0-50.0) with a median time to stricture recurrence of 17.0 months (range, 3.0-44.0)^[23].

After the bulbar urethra is exposed and the stricture identified, the urethra is approached dorsally or ventrally with a vertical incision^[21]. The stricture should be incised and surpassed proximally and distally to the defect. The bulbar urethra is mobilized if a dorsal onlay will be performed, exposing the urethra and moving it away from the corpora cavernosa. The BMG is sutured into the urethrotomy field and quilted into the corpora cavernosa as the graft bed. After three weeks, the Foley catheter is removed^[20].

The success rate of urethroplasty with BMG is between 79% and 96%, with a recent systematic review demonstrating an overall 15.6% failure rate for substitution urethroplasty^[24]. However, a viable graft bed for urethral reconstruction is vital. In these special cases with radiation-related strictures, previous reconstructions are unique in that local flaps or graft places on these tissues are likely to be compromised by fibrotic and ischemic surfaces. Accordingly, Meeks *et al.* reported stricture recurrence in one out of eight patients who had undergone a substitution graft^[26]. Compared to EPA, the sparing of the cavernous nerves located dorsally to the posterior urethra during dissection in BMG might advantageously result in the preservation of erectile function after surgery or at least have less of a negative impact^[26].

Flaps and pedicle grafts

The quest for a long-term, safe, stricture-free, hairless urethral lumen in patients with complex anterior and posterior strictures and compromised genital skin remains one of the continuing challenges of reconstructive urologic surgery^[24]. In severe cases in which prior RT or additional successive failed reconstructive techniques have resulted in extreme scar tissue with inadequate vascularization, flaps or pedicle grafts can be considered as an alternative^[21].

Palmer *et al.* (2015) described the use of a ventral mucosal graft and gracilis muscle flap^[27]. They studied the harvesting and mobilization of the gracilis muscle above the perineum and suturing to the flap making a ventral buccal graft onlay^[27]. This research studied 20 cases with severe urethral narrowing, with a mean stricture length of 8.2 cm. Strictures were located in the posterior urethra with or without bulbar urethral involvement in 50% of cases (10), bulbomembranous urethra in 35% (7), bulbar urethra in 10% (2), and proximal pendulous urethra in 5% (1). The etiologies included RT in 45% (9 of 20), idiopathic in 20% (4), trauma in 15% (3), prostatectomy in 10% (2 of 20), and hypospadias failure and transurethral surgery in 10% (2). Urethroplasty was described as successful in a follow-up of 40 months in 16 patients (80%), with reoccurrence taking place within 10 months after surgery. However, this research has limited significance as it is a retrospective study with a small sample size^[27].

Rourke *et al.* published a series of 35 cases describing penile skin flaps in five patients with long post-radiation urethral strictures^[22], finding no significant differences compared to other techniques. However, the limited number of patients restricts the comparison between techniques in this study. Some authors do not recommend this technique as the primary treatment for post-radiation urethral strictures^[28].

Currently, the evidence shows that flaps and pedicle flaps do not have a significant benefit in the application of urethral stenosis in irradiated patients; however, in combination with other techniques, they can be useful.

CONCLUSION

Radiotherapy causes urethral stricture, and its management presents a challenge for medical practitioners as well as patients. Urethroplasty remains the pillar of surgical treatment for these patients to improve their quality of life by avoiding chronic urethral or suprapubic catheterization. Most urethral strictures are located in the bulbomembranous urethra and are manageable with excision and primary anastomosis. We conclude that reconstructive genitourinary surgeons must reserve the graft tissue or flaps in extensive defects due to the characteristics of irradiated tissues to avoid a failure in the management in these cases.

DECLARATIONS

Authors' contributions

Drafting of the manuscript, important intellectual content, and technical support: Guerra C

Drafting of the manuscript and critical revision of the manuscript: Aleksic P

Drafting of the manuscript and critical revision of the manuscript for important intellectual content: Guerra C

Drafting of the manuscript and technical support: Davila S

Drafting of the manuscript and supervision of the manuscript: Pušica S

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All authors declared that there are no conflicts of interest.

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